CRYSTALLINE RECOMBINANT INTERFERON WITH ALTERED SPATIAL CONFIGURATION, THREE-DIMENSIONAL STRUCTURE AND USES THEREOF

FIELD OF THE INVENTION

[0001] This invention relates in general to crystalline recombinant interferon with altered spatial configuration, its crystallization method and three-dimensional structure thereof, uses of said crystal and its three-dimensional structure, and mimetics of said recombinant interferon.

BACKGROUND OF THE INVENTION

[0002] Interferon (IFN) is a kind of soluble protein produced by a variety of cells which has many important biological functions, including anti-viral, anti-tumor, and immunoregulatory functions. Interferons can be divided into type I, type II, and type III interferons according to the differences in the types of producing cells, receptors and biological activities etc. Type I IFNs, which are mostly induced by viruses and synthetic double-stranded RNA, are also known as anti-viral interferons. There are three forms of type I interferons: IFNα, INFβ, IFNω. Type II IFN, also known as immune interferon or IFNγ, is produced by the T cells, and is an important immunoregulatory factor *in vivo*. Type III interferon is made up of IFN-λ molecules.

[0003] In recent years, many companies in the world have engaged in the research of interferon, as exemplified by a number of pertinent patents and disclosure documents. For example, U.S. Patent Nos. 4,695,623 and 4,897,471 disclosed new types of human interferon polypeptides which have amino acid sequences containing the common or predominant amino acids found in naturally occurring α-interferon polypeptides. That new type of interferon was named IFN-con (consensus interferon α). The disclosed amino acid sequences were named IFN-con1, IFN-con2 and IFN-con3. Genes encoding IFN-cons and gene expression in *Escherichia coli* were also disclosed. Compared with leukocyte interferon or other type I interferons, studies have shown that recombinant IFN-con has higher anti-viral, anti-proliferative and natural killer cell activities *in vitro*.

[0004] U.S. Patent No. 5,372,808 disclosed the use of human IFN-con in the treatment of diseases. Compared with previous clinically approved α-interferon such as Intron®A (IFN-α2b, SGP) produced by Schering-Plough, recombinant human IFN-con has been shown to have lower side-effects. By the end of 1997, the FDA had approved the use of human IFN-con, which was produced by Amgen and sold under the brand name Infergen® (interferon alfacon-1), for clinical treatment of hepatitis C.

[0005] Both U.S. Patent No. 7,364,724 and Chinese Patent Publication No. CN1740197A (incorporated in their entirety as references to this application) disclosed a recombinant interferon (hereafter referred to as "rSIFN-co") that has enhanced efficacy, fewer side-effects and can be used in high doses. The said recombinant interferon has the same amino acid sequence as Infergen®, but has different spatial structure and biological efficacy. In addition, the above-mentioned Chinese Patent Publication No. CN1740197A also disclosed the crystal form of said recombinant interferon and its crystallization method thereof; however, the crystals were of poor quality, had loose internal structures and an X-ray diffraction resolution as low as 5 Å such that they were not suitable for obtaining useful structural information from further analysis of the protein spatial structure. It is of great interest to obtain good quality crystals of the said recombinant interferon with altered structure and functions at high X-ray diffraction resolution so as to determine the three-dimensional structure of said recombinant interferon, establish its model, and take advantage of said structure and model to perform drug design and to improve the efficacy of known interferons.

SUMMARY OF THE INVENTION

[0006] This invention relates to the crystal of the recombinant interferon disclosed by U.S. Patent No. 7364724 and Chinese Patent Publication No. CN1740197A, and this recombinant interferon comprises the amino acid sequence of SEQ ID NO: 1. Further, this invention provides the crystallization method of this recombinant interferon and the composition comprising said crystal. In addition, this invention provides the three-dimensional structure of this recombinant interferon, which is different from the three-dimensional structure of IFN-α2b published in the art and the three-dimensional structure of Infergen® from Amgen (U.S.) based on computational modelling. Also provided are uses of said three-dimensional structure for identifying

the candidate compound interacting with said interferon, designing mimetics of said interferon and performing rational drug design based on computer. Still further, this invention provides mimetics of said recombinant interferon, composition comprising said mimetics and uses of said crystal, mimetics or composition for preparation of medicament for treatment of viral diseases and/or tumors.

BRIEF DESCRIPTION OF THE DRAWINGS

[0007] Figure 1 shows a monocrystal of the recombinant interferon (rSIFN-co) of the present invention usedin crystal structure analysis.

[0008] Figure 2 shows an X-ray diffractogram of the rSIFN-co crystal (2.6Å resolution).

[0009] Figure 3 shows a partial 1.0σ electron-density map of 2Fo-Fc format within the crystal structure of rSIFN-co.

[0010] Figure 4 shows a distribution map of the average temperature factors along the amino acid residues for all the atoms of rSIFN-co. (a) A chain; (b) B chain.

[0011] Figure 5 shows the (Φ, Ψ) value distribution on the Ramachandran plot of all the amino acid residues in the model of the rSIFN-co protein molecular structure. Based on an analysis of 118 structures with resolution of at least 2.0Å and R-factor no greater than 20%, a good quality model would be expected to have over 90% in the most favoured regions; the statistical data as follows:

Plot statistics		
Residues in most favoured regions [A, B, L]	240	90.6%
Residues in additional allowed regions [a, b, l, p]	24	9.1%
Residues in generously allowed regions [~a, ~b, ~l, ~p]	1	0.4%
Residues in disallowed regions	0	0.0%
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Number of non-glycine and non-proline residues	265	100.0%
Number of end-residues (excl. Gly and Pro)	127	
Number of glycine residues	18	
Number of praline reidues	6	

Total number of residues	416	

[0012] Figure 6 shows a unit cell packing diagram of rSIFN-co.

[0013] Figure 7 shows the assembled structure of the rSIFN-co dimers.

[0014] Figure 8 shows the organization of rSIFN-co crystallographic dimers (Fig. 8a, Fig. 8b) and the root-mean square deviation (RMSD) of α carbon atoms (the boxes represent missing residues) (Fig. 8c).

[0015] Figure 9 shows the monomolecular structure of rSIFN-co (main chain demonstrated only); (A) Side view; (B) Top view; (C) Topology diagram; (D) Topological organization of the secondary structures.

[0016] Figure 10 shows the sequence alignment between the secondary structures of rSIFN-co and its amino acid sequence; the gray boxes represent amino acid residues that were not set up in the structure; the blue boxes represent amino acid residues which were set up as Ala or Gly. The solid lines represent two pairs of disulfide linkages and the green subscripts represent one disulfide linkage that has been constructed in the structure.

[0017] Figure 11 shows the sequence alignment of rSIFN-co protein and homologous IFN polypeptides.

[0018] Figure 12 shows a comparative diagram of the three-dimensional structure of rSIFN-co and IFN-α2b.

[0019] Figure 13 shows the superimposed image of rSIFN-co (in red) and IFN-α2b (in yellow).

[0020] Figure 14 shows the comparative differences between the three-dimensional structure of rSIFN-co and the computational model of Infergen® from Amgen (U.S.).

[0021] Figure 15 shows (a) the combined model of protein IFN-α and its receptor; (b) the diagram of the functional domain of protein IFN-α (the important functional domain is illustrated by blue ring).

[0022] Figure 16 shows the mean enzyme concentration in blood-time curve after subcutaneous injection of 9 μg rSIFN-co and 9 μg IInfergen® to 18 subjects.

DETAILED DESCRIPTION OF THE INVENTION

[0023] The following is a detailed description of the invention provided to aid those skilled in the art for practicing the present invention.

Recombinant Interferon (rSIFN-co)

[0024] The purified recombinant interferon, which has been crystallized in this invention, is obtained from the method disclosed by the examples 1 and 2 of the

specification of the U.S. Patent No. 7364724 and/or pages 11-17 of the specification of the Chinese Patent Publication No. CN1740197A. The characterization of this recombinant interferon is disclosed in the U.S. Patent No. 7364724 and/or the Chinese Patent Publication No. CN1740197A. In one embodiment, the amino acid sequence of the present recombinant interferon, as well as the nucleotide sequence encoding the same, are shown below:

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    M  C  D  L  P  Q  T  H  S  L  G  N  R  R  A  L  I  L  L  A
  1 ATGTGCGACC TGCCGCAGAC CCACTCCCTG GGTAACCGTC GTGCTCTGAT CCTGCTGGCT
    TACACGCTGG ACGGCGTCTG GGTGAGGGAC CCATTGGCAG CACGAGACTA GGACGACCGA

    Q  M  R  R  I  S  P  F  S  C  L  K  D  R  H  D  F  G  F  P
 61 CAGATGCGTC GTATCTCCCC GTTCTCCTGC CTGAAAGACC GTCACGACTT CGGTTTCCCG
    GTCTACGCAG CATAGAGGGG CAAGAGGACG GACTTTCTGG CAGTGCTGAA GCCAAAGGGC

    Q  E  E  F  D  G  N  Q  F  Q  K  A  Q  A  I  S  V  L  H  E
121 CAGGAAGAAT TCGACGGTAA CCAGTTCCAG AAAGCTCAGG CTATCTCCGT TCTGCACGAA
    GTCCTTCTTA AGCTGCCATT GGTCAAGGTC TTTCGAGTCC GATAGAGGCA AGACGTGCTT

    M  I  Q  Q  T  F  N  L  F  S  T  K  D  S  S  A  A  W  D  E
181 ATGATCCAGC AGACCTTCAA CCTGTTCTCC ACCAAAGACT CCTCCGCTGC TTGGGACGAA
    TACTAGGTCG TCTGGAAGTT GGACAAGAGG TGGTTTCTGA GGAGGCGACG AACCCTGCTT

    S  L  L  E  K  F  Y  T  E  L  Y  Q  Q  L  N  D  L  E  A  C
241 TCCCTGCTGG AAAAATTCTA CACCGAACTG TACCAGCAGC TGAACGACCT GGAAGCTTGC
    AGGGACGACC TTTTTAAGAT GTGGCTTGAC ATGGTCGTCG ACTTGCTGGA CCTTCGAACG

    V  I  Q  E  V  G  V  E  E  T  P  L  M  N  V  D  S  I  L  A
301 GTTATCCAGG AAGTTGGTGT TGAAGAAACC CCGCTGATGA ACGTTGACTC CATCCTGGCT
    CAATAGGTCC TTCAACCACA ACTTCTTTGG GGCGACTACT TGCAACTGAG GTAGGACCGA

    V  K  K  Y  F  Q  R  I  T  L  Y  L  T  E  K  K  Y  S  P  C
361 GTTAAAAAAT ACTTCCAGCG TATCACCCTG TACCTGACCG AAAAAAAATA CTCCCCGTGC
    CAATTTTTTA TGAAGGTCGC ATAGTGGGAC ATGGACTGGC TTTTTTTTAT GAGGGGCACG

    A  W  E  V  V  R  A  E  I  M  R  S  F  S  L  S  T  N  L  Q
421 GCTTGGGAAG TTGTTCGTGC TGAAATCATG CGTTCCTTCT CCCTGTCCAC CAACCTGCAG
    CGAACCCTTC AACAAGCACG ACTTTAGTAC GCAAGGAAGA GGGACAGGTG GTTGGACGTC

    E  R  L  R  R  K  E  (SEQ ID NO:1)
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481 GAACGTCTGC GTCGTAAAGA ATAA (SEQ ID NO:2)

CTTGCAGACG CAGCATTTCT TATT (SEQ ID NO:3)

[0025] Moreover, the circular dichroism spectrum (CD) of the present recombinant interferon in ranges of 190-250nm and 250-320nm is significantly different from the corresponding CD of INFERGEN® when determined under the same conditions (see page 3, lines 22-25, example 3 and Figs. 6A-D of the Chinese Patent Publication No. CN1740197A,).

[0026] In addition, the three-dimensional structure of the present recombinant interferon is also different from the three-dimensional structure of IFN-α2b published in the art (see Fig. 12) and the three-dimensional structure of INFERGEN® based on computational modeling (see KORN, AP et al., Journal of Interferon Research 1994, 14: 1-9). There are obvious differences between the AB loops of the two, and their BC loops also cannot overlap completely (see Fig. 14).

[0027] Furthermore, after intramuscular injection of the present recombinant interferon into subjects whose BMI ranged from 18 to 23, the time of blood sample collection was plotted against the concentration of 2-5A oligonucleotidase (also referred to as 2', 5'-OAS) in the serum of the subjects. The chart generally shows a two-peak pattern, and the resulting area under the curve of this chart is significantly greater than that of INFERGEN® after injection under the same conditions. The half-life period of this recombinant interferon is longer than that of INFERGEN® after injection into the body.

[0028] The experimental results have also confirmed that the present recombinant interferon is more effective than any interferon used clinically at present (including INFERGEN®). For example, for HBV, the recombinant interferon from this invention is capable of not only inhibiting DNA replication of HBV, but also inhibiting secretion of both hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg). The efficiency of inhibiting DNA replication of hepatitis B core antigen (HBcAg) by this interferon is about twice that of INFERGEN®. The *in vitro* pharmacodynamics of the present recombinant interferon shows that it is capable of not only inhibiting the DNA replication of HBV, but also inhibiting secretion of both hepatitis B surface antigen and hepatitis B e antigen. The

cytotoxicity of the present recombinant interferon is only 1/8 that of the current clinically used interferons, but its antiviral activity is as much as 5-20 times greater; meanwhile, the biological responses of the present recombinant interferon is more effective, more broad-spectrum and longer lasting in the human body.

[0029] Furthermore, with respect to prevention of viral diseases or treatment of tumor, the present recombinant interferon shows higher antiviral activity and less side effects compared with any other interferons (including INFERGEN®). For example, this recombinant interferon possesses not only an antiviral activity 20 times as great as that of the interferons currently in clinical use, but also a more effective anti-tumor (such as breast cancer and cervical cancer) function compared with recombinant human interferon α (including INFERGEN®). It also shows greatly reduced toxic side effects and can be safely used in large dosages (each dose > 10 million IU), making it possibleto treat viral diseases or tumors which require large dosages of interferon.

[0030] Thus, the present recombinant interferon has a different spatial configuration, enhanced biologic activities and different pharmacokinetics characteristics as compared with INFERGEN®.

[0031] As used herein, the terms 'spatial configuration', 'spatial structure', 'three-dimensional structure' and 'three-dimensional configuration' can be used interchangeably.

[0032] Therefore, in one embodiment, the present recombinant interferon comprises the amino acid sequence of SEQ ID NO: 1 and is encoded by the nucleotide sequence comprising SEQ ID NO: 2. Further, the present recombinant interferon has the amino acid sequence of SEQ ID NO: 1, and is encoded by the nucleotide sequence of SEQ ID NO: 2. In comparison with interferons such as INFERGEN®, which has the amino acid sequence of SEQ ID NO: 1 or the same amino acid sequence as the present recombinant interferon, but is not encoded by the nucleotide sequence of SEQ ID NO: 2, , the present recombinant interferon has a different spatial configuration and/or enhanced biologic activities and/or different pharmacokinetics characteristics. For example, the present recombinant interferon has a different spatial configuration and

enhanced biologic activities, different spatial configuration and different pharmacokinetics characteristics, or enhanced biologic activities and different pharmacokinetics characteristics. Further, said different spatial configuration includes: the circular dichroism spectrum (CD) of the present recombinant interferon at 190-250nm and/or 250-320 nm is significantly different from the corresponding CD of INFERGEN® when determined under the same conditions. The enhanced biological activities include: enhanced antiviral activity, enhanced anti-tumor activity, less side effects and/or could be used in large dosages (e.g. each dose > 10 million IU). For example, said enhanced biological activities can be enhanced antiviral activity and enhanced anti-tumor activity and the like. Furthermore, said tumors can be breast cancer and cervical cancer. The different pharmacokinetics characteristics include: after intramuscular injection of the recombinant interferon in subjects whose BMI ranged from 18 to 23, the time of blood sample collection was plotted against the concentration of 2-5A oligonucleotidase in the serum of the subjects, and the resulting area under the curve of this chart is significantly greater and/or the half-life of this recombinant interferon in the body is longer than those of INFERGEN® after injection under the same conditions

[0033] In another embodiment, the present recombinant interferon can be produced by the method comprising the following steps: introducing a nucleotide sequence comprising SEQ ID NO: 2 that encodes the recombinant interferon into an isolated host cell; culturing the host cell under appropriate condition for expression of the recombinant interferon; and harvesting the recombinant interferon, wherein the recombinant interferon has an amino acid sequence of SEQ ID NO: 1, and the recombinant interferon inhibits secretion of hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg) of Hepatitis B Virus. Further, said host cell is *Escherichia coli*, such as *Escherichia coli* LGM 194. Further, the nucleotide sequence comprising SEQ ID NO: 2 is under the control of the promoter P_{BAD}. Further, the harvesting step comprises extraction of the interferon from the fermentation broth, collection of the inclusion bodies, denaturation and renaturation of the harvested interferon. Still further, the harvesting step also comprises separation and purification of the recombinant interferon (see the claims of U.S. Patent No. 7364724).

Crystalline Recombinant Interferon and Crystallization Method Thereof

Crystalline recombinant interferon

[0034] This invention provides a crystalline recombinant interferon.

[0035] In one embodiment, this invention provides a crystalline recombinant interferon comprising the amino acid sequence of SEQ ID NO: 1. Further, this crystal belongs to the trigonal system. In one embodiment, the space group of this crystal is $P3_121$. In some embodiments, the unit cell parameters of this crystal are a = b = 77.92 Å, c = 125.935 Å, α = β = 90°, γ = 120° , with a variability of at most 5% in all cell parameters. In some embodiments, said crystal contains two molecules in one asymmetric unit. In some embodiments, said crystal comprises covalently or non-covalently bound metal ions. Further, said mental ions can be magnesium ion, zinc ion and the like, these metal ions can mediate the formation of the interferon dimers in the crystal. In some embodiments, said recombinant interferon is encoded by the nucleotide sequence comprising SEQ ID NO: 2.

[0036] In a still further embodiment, this invention provides a crystalline recombinant interferon comprising the amino acid sequence of SEQ ID NO: 1, preferably the recombinant interferon having the amino acid sequence of SEQ ID NO: 1, in which the space group of this crystal is $P3_121$, with two molecules in one asymmetric unit, and the unit cell parameters are a = b = 77.92 Å, c = 125.935 Å, $\alpha = \beta = 90°$, $\gamma = 120°$, with a variability of at most 5% in all cell parameters. Further, such recombinant interferon is encoded by the nucleotide sequence comprising SEQ ID NO: 2, preferably encoded by the nucleotide sequence of SEQ ID NO: 2.

Crystallization Method

[0037] This invention provides a method for preparing or culturing the present crystalline recombinant interferon.

[0038] In one embodiment, this invention provides a method for preparing or culturing the present crystalline recombinant interferon, comprising the steps of: concentrating the recombinant interferon to about 3 - 3.5 mg/ml, and leaving it in the crystallization solution containing Li_2SO_4, CAPS (3-(cyclohexylamino)-1-propanesulfonic acid) and $MgCl_2$ for an appropriate period of time to obtain the crystal. Further, said method for culturing crystal is performed at room temperature such as 293K. In some embodiments, this crystal can be cultured by the hanging drop method or the sitting drop method, preferably the hanging drop method (also referred to as hanging drop vapor diffusion method). In some embodiments,

said crystallization solution contains about 1.0 - about 1.5M Li_2SO_4, about 0.05 - about 0.15M CAPS (3-(cyclohexylamino)-1-propanesulfonic acid) and about 0.01 - about 0.03 M $MgCl_2$. In some embodiments, the pH value of the crystallization solution is in the range of about 10.5 - about 12.0, preferably about 11.1. In some embodiments, said crystallization solution contains 1.2M Li_2SO_4, 0.1M CAPS (3-(cyclohexylamino)-1-propanesulfonic acid), pH 11.1, 0.02 M $MgCl_2$. In some embodiments, the method for culturing the crystal includes leaving the crystallization solution containing said recombinant interferon to stand for about 1 day to about 2 weeks, preferably about 2 days to about 10 days, more preferably about 3 days to about 1 week, such as 3 days to 1 week.

X-ray crystallographic analysis

[0039] Each of the constituent amino acids of interferon disclosed herein is defined by a set of structural coordinates (also known as "atomic coordinates"). The term "structural coordinates" refers to Cartesian coordinates derived from mathematical equations related to the patterns obtained by the diffraction of a monochromatic beam of x-rays by the atoms (scattering centers) of the present interferon in crystalline form. The diffraction data are used to calculate an electron density map of the repeating unit of the crystal. The electron density maps are then used to establish the positions of the individual atoms of the interferon protein or protein/ligand complex.

[0040] Slight variations in structural coordinates can be generated by mathematically manipulating the interferon or interferon/ligand structural coordinates. For example, the structural coordinates disclosed herein could be manipulated by crystallographic permutation, fractionalization, addition or subtraction of the entire set, inversion, or any combination of the above. Alternatively, modifications in the crystal structure due to mutations, additions, substitutions, and/or deletions of amino acids, or other changes in any of the components that make up the crystal, could also yield variations in structural coordinates. Such slight variations in the individual coordinates will have little effect on the overall configuration. If such variations are within an acceptable standard error as compared to the original coordinates, the resulting three-dimensional shape is considered to be structurally equivalent.

[0041] It should be noted that slight variations in individual structural coordinates of the interferon of the present invention are not expected to significantly alter the nature of the entities such as ligands that could associate with the interferon or portion thereof (e.g. the AB

or the BC loop). As used herein, the “AB loop” of the present recombinant interferon means the amino acid residues 25-33 of the present recombinant interferon having the amino acid sequence of SEQ ID NO: 1; namely, the AB loop has the amino acid sequence SPFSCLKDR as shown in SEQ ID NO: 4; and the “BC loop” of the present recombinant interferon means the amino acid residues 44-52 of the present recombinant interferon having the amino acid sequence of SEQ ID NO: 1; namely, the BC loop has the amino acid sequence DGNQFQKAQ as shown in SEQ ID NO: 5. In this context, the phrase "associated with" refers to a condition of proximity between a ligand, or portions thereof, and an interferon molecule or portions thereof. The association may be non-covalent, wherein the juxtaposition is energetically favored by hydrogen bonding, van der Waals forces, or electrostatic interactions, or it may be covalent. Thus, for example, a ligand that binds to the binding pocket or region of an interferon would also be expected to bind to or interact with a structurally equivalent binding pocket or region.

[0042] In this invention, any molecule or molecular complex, or any portion thereof, that has a root mean square deviation of conserved residue backbone atoms (e.g. N, Cα, C, O, preferably Cα) of less than about 0.65 Å, when superimposed on the relevant backbone atoms described herein, is considered "structurally equivalent". That is to say, the crystal structures of those portions of the two molecules are substantially identical, within acceptable error. Particularly preferred structurally equivalent molecules or molecular complexes are those that are defined by the entire set of structural coordinates disclosed herein ± a root mean square deviation from the conserved backbone atoms of those amino acids of less than about 0.65 Å. More preferably, the root mean square deviation is at most about 0.5 Å, and even more preferably, at most about 0.35 Å. Other embodiments of this invention include a molecular complex defined by the structural coordinates for the AB or the BC loop disclosed herein ± a root mean square deviation of less than about 0.65 Å, preferably at most about 0.5 Å, and more preferably at most about 0.35 Å.

[0043] The term “root mean square deviation” means the square root of the arithmetic mean of the squares of the deviations. It is a way to express the deviation or variation from a trend or object. In one embodiment, the "root mean square deviation" defines the variation in the backbone of a protein from the backbone of interferon or a portion thereof as defined by the structural coordinates described herein.

[0044] X-ray structural coordinates define a unique configuration of points in space. Those skilled in the art would understand that a set of structural coordinates for a protein or a protein/ligand complex, or a portion thereof, defines a relative set of points that, in turn, defines a configuration in three dimensions. A similar or identical configuration can be defined by an entirely different set of coordinates, provided that the distances and angles between coordinates remain essentially the same. In addition, a scalable configuration of points can be defined by increasing or decreasing the distances between coordinates by a scalar factor while keeping the angles essentially the same.

[0045] Various computational analyses can be used to determine whether a molecule or a portion thereof is "structurally equivalent", defined in terms of its three-dimensional structure, to the interferon disclosed herein, or part of it. For example, comparisons between different structures, different conformations of the same structure, or different parts of the same structure can be made by various computational analyses. In one embodiment, such analysis can be divided into four steps: (1) load the structures to be compared; (2) define the atom equivalences in these structures; (3) perform a fitting operation; and (4) analyze the results.

Three-dimensional structure of Recombinant Interferon (rSIFN-co)

[0046] This invention provides the three-dimensional structure of the present recombinant interferon.

[0047] This three-dimensional structure is different from the three-dimensional structure of IFN-α2b published in the art (see Fig. 12) and the structure of the computational model of INFERGEN® of U.S. Amgen (see Fig. 14), especially in the AB and BC loops.

[0048] In one embodiment, the three-dimensional structure of said recombinant interferon contains the atomic coordinates of recombinant interferon as shown in table 7, said atomic coordinates optionally have a variability of root mean square deviation from the conserved backbone atoms, preferably Cα (also referred to as 'α carbon atom'), of less than about 0.65 Å, preferablyor about 0.5 Å, and more preferably about 0.35 Å.

[0049] In one embodiment, in the above-mentioned three-dimensional structure of the

recombinant interferon, each monomer of said recombinant interferon is composed of 6 segments of α-helix, a segment of 3_{10} helix, and the connecting peptides between them. The corresponding amino acid residue locations of said 6 segments of the α-helices are 13-20, 50-68, 70-76, 79-100, 114-133, and 138-160; the corresponding amino acid residue location of said segment of 3_{10} helix is 40-43. The folding of the monomer structure belongs to the helical cytokine type, having the following characteristics: after superimposition of the Cα-backbone of said recombinant interferon and the Cα-backbone of IFN-α2b protein using least squares method, the location root-mean-square deviation of Cα in the 25-33 residues (AB loop) of said recombinant interferon and Cα in the corresponding residues of IFN-α2b protein is 3.63Å±5%.

[0050] Preferably, the location root-mean-square deviation of Cα at residue 25 of said recombinant interferon and IFN-α2b protein is 3.291Å±5%, the location root-mean-square deviation of Cα at residue 26 is 4.779Å±5%; the location root-mean-square deviation of Cα at residue 27 is 5.090Å±5%; the location root-mean-square deviation of Cα in the 28 residue is 3.588Å±5%; the location root-mean-square deviation of Cα at residue 29 is 2.567Å±5%, the location root-mean-square deviation of Cα at residue 30 is 2.437Å±5%; the location root-mean-square deviation of Cα at residue 31 is 3.526Å±5%; the location root-mean-square deviation of Cα at residue 32 is 4.820Å±5%; and the location root-mean-square deviation of Cα at residue 33 is 2.756Å±5%.

[0051] More preferably, the location root-mean-square deviation of Cα at residues 44-52 (BC loop) of said recombinant interferon and Cα in the corresponding residues of IFN-α2b protein is 2.90Å±5%. Wherein, the location root-mean-square deviation of Cα at residue 44 of both said recombinant interferon and IFN-α2b protein is 1.614Å±5%; the location root-mean-square deviation of Cα at residue 45 is 1.383Å±5%; the location root-mean-square deviation of Cα at residue 46is 2.735Å±5%; the location root-mean-square deviation of Cα at residue 47 is 2.709Å±5%; the location root-mean-square deviation of Cα at residue 48 is 5.018Å±5% ; the location root-mean-square deviation of Cα at residue 49 is 4.140Å±5% ; the location root-mean-square deviation of Cα at residue 50 is 3.809Å±5% ; the location root-mean-square deviation of Cα at residue 51is 2.970Å±5%; and the location root-mean-square deviation of Cα at residue 52 is 0.881Å±5%. The "location root-mean-square deviation" listed above are all root-mean-square deviations of the coordinate positions.

[0052] In another aspect, this invention provides a selected portion of the three-dimensional structure of the present recombinant interferon, which contains atomic coordinates of one or more amino acid residues from amino acid residues 25-33 and/or 45-52 in table 7. In some embodiments, the "one or more amino acid residues" described herein include 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 amino acid residues. In some embodiments, the "selected portion of said three-dimensional structure" contains the atomic coordinates of the amino acid residues 25-33 and/or 44-52 in table 7. In some embodiments, the "selected portion of the three-dimensional structure" contains the atomic coordinates of at least 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100 amino acid residues in table 7. In some embodiments, said atomic coordinates have a variability of root mean square deviation from the conserved backbone atoms (preferably Cα) of less than about 0.65 Å, preferably about 0.5 Å, and more preferably about 0.35 Å.

[0053] In another aspect, this invention provides the protein spatial structure model comprising the three-dimensional structure of the present recombinant interferon. In one embodiment, said protein spatial structure model could be an electron density map, a wire-frame model, a chicken-wire model, a space-filling model, a stick-model, a ribbon model and a molecular surface model and the like.

[0054] In still another aspect, the present invention provides a scalable three-dimensional configuration of points, wherein at least a portion of said points are derived from the structural coordinates disclosed herein, or from peptides comprising the AB loop or the BC loop of the present recombinant interferon. In one embodiment, the scalable three-dimensional configuration of points is displayed as a holographic image, a stereo diagram, a model, or a computer-displayed image.

The Application of Three-Dimensional Structure

Screening/designing candidate substance that could interact with recombinant interferon

[0055] In one aspect, this invention provides a method for screening/designing candidate

compounds that could interact with the present recombinant interferon. Further, said method utilizes the three-dimensional structure of the present recombinant interferon. Still further, said method is based on a computer. In one embodiment, this invention provides a computer-based method for identifying candidate compounds that could interact with recombinant interferon, said method comprises the steps of: (a) providing a three-dimensional structure comprising the atomic coordinates of the recombinant interferon as shown in table 7, said atomic coordinates optionally have a variability of root mean square deviation from the conserved backbone atoms (preferably Cα) of less than about 0.65 Å, preferably about 0.5 Å, and more preferably about 0.35 Å; and (b) selecting a candidate compound that comprises structural features capable of interacting with said three-dimensional structure or selected portion thereof, thereby identifying a candidate compound that could interact with said recombinant interferon. In some embodiments, said structural features are selected from the group consisting of antigenic sites, hydrophilic properties, surface accessibility, and structural motifs. In some embodiments, the selection and identification of candidate compounds in step (b) comprises: (i) generating three-dimensional structures for a plurality of candidate compounds; and (ii) fitting each of the three-dimensional structures of step (i) against the three-dimensional structure of step (a) or selected portion thereof to find the most energetically favorable interaction, thereby identifying a candidate compound that could interact with the recombinant interferon. In some embodiments, said method further comprises the steps of: (c) obtaining or synthesizing the candidate compound; and (d) contacting the candidate compound with said recombinant interferon to determine the ability of the candidate compound to interact with said recombinant interferon. Further, the step of determining the ability of the candidate compound to interact with said recombinant interferon may further comprise measuring the activity of said recombinant interferon when contacted with the candidate compound. Interferon activities to be measured include, for example, antivirus activity, anti-tumor activity, anti-proliferation activity, natural killer cell activation, and immunomodulatory activity. In some embodiments, said candidate compound is a ligand bound to said recombinant interferon or selected portion thereof. For example, said ligand is selected from the group consisting of receptor, modifier, agonist and antagonist, said receptor could be IFNAR1, IFNAR2 or their complex, and said selected portion comprises one or more amino acid residues from the amino acid residues 25-33 (AB loop) and/or 45-52 (BC loop) of said recombinant interferon. Further, said selected portion comprises the amino acid residues 25-33 and/or 44-52 of said recombinant interferon.

[0056] In another aspect, the present invention provides a method for determining potential ligands that bind to the present recombinant interferon. In one embodiment, the method includes exposing a crystal disclosed herein to one or more samples comprising potential ligands, and determining whether a ligand-interferon molecular complex is formed.

[0057] In another aspect, the present invention provides a method for acquiring structural information to design potential ligands that can form molecular complexes with interferon. In one embodiment, the method includes exposing a crystal disclosed herein to one or more samples comprising potential ligands, and determining whether a ligand-interferon molecular complex is formed.

[0058] In another aspect, the present invention provides a computer-assisted method for determining, designing, or making potential modifiers of interferon activity. In one embodiment, the method includes screening a library of chemical or biological entities.

[0059] Those skilled in the art can utilize crystallography to screen and identify chemical or biological entities that may become ligands of an interferon (*see e.g.* in U.S. Patent No. 6,297,021). For example, a preferred method may include obtaining a crystal of unliganded interferon; exposing the unliganded interferon to one or more test samples that contain potential ligands of the interferon; and determining whether a ligand-interferon molecular complex is formed. The interferon may be exposed to potential ligands by various methods including, but not limited to, soaking an interferon crystal in a solution of one or more potential ligands or co-crystallizing interferon in the presence of one or more potential ligands.

[0060] Structural information from said ligand-interferon complexes may preferably be used to design new ligands that bind tighter and more specifically, have desired special biological activities, have better safety profiles or combinations thereof than known ligands.. For example, the calculated electron density map directly reveals the binding event, identifies the bound chemical or biological entities, and provides a detailed three-dimensional structure of the ligand-interferon complex. Once a hit is found, a series of analogs or derivatives of the hit may be screened for tighter binding or desired biological activity by traditional screening methods. Optionally, the ligand-interferon complex may be iteratively exposed to additional

potential ligands so that two or more hits may preferably be linked together to identify or design a more potent ligand.

Obtaining structurally homologous molecules/ Designing interferon mimetics

[0061] The structural coordinates disclosed herein can be used to aid in obtaining structural information about another crystallized molecule or molecular complex. The method of this invention allows determination of at least a portion of the three-dimensional structure of molecules or molecular complexes which contain one or more structural features that are similar to the structural features of the interferon disclosed herein. These molecules are referred to herein as "structurally homologous". Similar structural features can include, for example, regions of amino acid identity, conserved active site or binding site motifs and similarly arranged secondary structural elements (e.g., α helices and β sheets). In another embodiment, structural homology is determined by aligning the residues of two amino acid sequences to optimize the number of identical amino acids along the lengths of their sequences; gaps in either or both sequences are permitted in making the alignment in order to optimize the number of identical amino acids; however, the amino acids in each sequence must remain in their proper order. Preferably, a structurally homologous molecule is a protein that has an amino acid sequence sharing at least 65% identity with SEQ ID NO:1. More preferably, a protein that is structurally homologous to the interferon of the present invention includes a contiguous stretch of at least 50 amino acids that shares at least 80% amino acid sequence identity with the analogous portion of SEQ ID NO:1. Methods for generating structural information about the structurally homologous molecule or molecular complex are well-known in the art.

[0062] The structural coordinates disclosed herein are also useful for solving the crystallographic structures of related interferons, interferon mutants or interferon homologs complexed with a variety of ligands. This approach enables the determination of the optimal sites for interaction between a ligand and an interferon, e.g. between candidate interferon modifiers and interferon. Potential sites for modification within the various binding sites of the molecules can also be identified. This information provides an additional tool for determining the most efficient binding interactions, for example, increased hydrophobic interactions between an interferon and a ligand.

[0063] In one embodiment, the present invention also provides a computer-based method for designing a mimetic of the recombinant interferon, comprising the steps of: (a) generating three-dimensional structures for a plurality of mimetics; and (b) fitting each of the three-dimensional structures of step (a) against the three-dimensional structure comprising the atomic coordinates of the recombinant interferon as shown in table 7 or selected portion thereof to find the best fitted mimetic of said recombinant interferon, said atomic coordinates optionally have a variability of root mean square deviation from the conserved backbone atoms (preferably Cα) of less than about 0.65 Å, preferably about 0.5 Å, and more preferably about 0.35 Å.

Rational drug design

[0064] Computational techniques can be used to screen, identify, select and/or design chemical entities or ligands capable of associating with interferons or structurally homologous molecules. Knowledge of the structural coordinates of the interferon disclosed herein permits the design and/or identification of synthetic compounds and/or other molecules which have a shape complementary to the conformation of the interferon disclosed herein. In particular, computational techniques can be used to identify or design chemical entities or ligands, such as receptors, modifiers, agonists and antagonists, that associate with the interferon or a portion thereof (e.g. the AB or the BC loop). Potential modifiers may bind to or interfere with all or a portion of an active site of interferon, and can be competitive, non-competitive, or uncompetitive inhibitors; or interfere with dimerization by binding at the interface between the two monomers. Once identified or screened for biological activity, these inhibitors/agonists/antagonists may be used therapeutically or prophylactically to block or enhance interferon activity. Structure-activity data for analogues of ligands that bind to or interfere with interferon can also be obtained computationally.

[0065] The term "chemical entity", as used herein, refers to chemical compounds, complexes of two or more chemical compounds, and fragments of such compounds or complexes. Chemical entities that are determined to associate with the interferon of the present invention are potential drug candidates. A graphical three-dimensional representation of the structure of the present interferon or a structurally homologous molecule, as identified herein, or portions thereof may thus be advantageously used for drug discovery. The structural coordinates of the chemical entity are used to generate a three-dimensional image

that can be computationally fitted to the three-dimensional image of an interferon or a structurally homologous molecule by one of many computation methods and techniques available in the art.

[0066] One embodiment of the method of drug design involves evaluating the potential association of a known chemical entity or ligand with the interferon or a structurally homologous molecule. The method of drug design thus includes computationally evaluating the potential of a selected chemical entity or ligand to associate with any of the molecules or molecular complexes set forth herein. In another embodiment, the method of drug design involves computer-assisted design of chemical entities or ligands that associate with the present interferon, its homologs, or portions thereof. Chemical entities or ligands can be designed in a stepwise fashion, one fragment at a time, or may be designed as a whole or "*de novo*".

[0067] Thus, in one embodiment, the present invention provides a computer-based method of rational drug design, comprising the steps of: (a) providing the three-dimensional structure comprising atomic coordinates of the recombinant interferon as shown in table 7, said atomic coordinates optionally have a variability of root mean square deviation from the conserved backbone atoms (preferably Cα) of less than about 0.65 Å, preferably about 0.5 Å, and more preferably about 0.35 Å; (b) providing a plurality of molecular fragments, and generating three-dimensional structures thereof; (c) fitting each of the three-dimensional structures of step (b) against the three-dimensional structure of step (a) or selected portion thereof; and (d) assembling the selected molecular fragments into a molecule to form a candidate drug. In one embodiment, said method may further comprise the steps of: (e) obtaining or synthesizing the candidate drug; and (f) contacting the candidate drug with said recombinant interferon to determine the ability of the candidate drug to interact with said recombinant interferon.

[0068] In some embodiments of this invention, the selected portion of said three-dimensional structure comprises the atomic coordinates of one or more amino acid residues from amino acid residues 25-33 (amino acid sequence as shown in SEQ ID NO: 4) and/or 45-52 (amino acid sequence as shown in SEQ ID NO: 5) in table 7. Further, the selected portion of said three-dimensional structure comprises the atomic coordinates of the amino acid residues 25-33 (amino acid sequence as shown in SEQ ID NO: 4) and/or 45-52

(amino acid sequence as shown in SEQ ID NO: 5) in table 7, said atomic coordinates optionally have a variability of root mean square deviation from the conserved backbone atoms (preferably Cα) of less than about 0.65 Å, preferably about 0.5 Å, and more preferably about 0.35 Å.

Homology modeling

[0069] In one aspect, using homology modeling, a computer model of an interferon homolog can be built or refined without crystallizing the homolog. First, a preliminary model of an interferon homolog is created by sequence alignment, secondary structure prediction, screening of structural libraries, or any combination of these techniques. Computational software may be used to carry out the sequence alignments and secondary structure predictions. Structural incoherencies, e.g., structural fragments around insertions and deletions, can be modeled by screening a structural library for peptides of the desired length and suitable conformation. If the interferon homolog has been crystallized, the final homology model can be used to solve the crystal structure of the homolog by techniques known in the art. Next, the preliminary model is subjected to energy minimization to yield an energy minimized model. The energy minimized model may contain regions where stereochemical restraints are violated; in such cases, these regions are remodeled to obtain a final homology model using one of many techniques known in the art.

[0070] In another aspect, the present invention provides a method for obtaining structural information about a molecule or a molecular complex of unknown structure. In one embodiment, the method includes crystallizing the molecule or molecular complex; generating an x-ray diffraction pattern from the crystallized molecule or molecular complex; and applying the x-ray diffraction pattern to at least a portion of the structural coordinates of the interferon disclosed herein to generate a three-dimensional electron density map of at least a portion of said molecule or molecular complex of unknown structure.

[0071] In another aspect, the present invention provides a method for modeling an interferon homolog. In one embodiment, the method includes aligning the amino acid sequence of a putative interferon homolog with the amino acid sequence of the present interferon and incorporating the sequence of the putative homolog into a model of interferon formed from the structural coordinates disclosed herein to yield a preliminary model of

interferon homolog; subjecting the preliminary model to energy minimization to yield an energy minimized model; and remodeling regions of the energy minimized model where stereochemical restraints are violated to yield a final model of the interferon homolog.

Interferon mimetics

[0072] The present invention provides interferon mimetics.

[0073] In one aspect, the present invention provides a peptide comprising a sequence as disclosed herein, or a derivative, active portion, analogue, variant or mimetic, and uses thereof. Thus, in one embodiment, the present invention provides a mimetic of the interferon which comprises the amino acid sequence as shown in SEQ ID NO: 4 and/or SEQ ID NO: 5. In one embodiment, after superimposition of the Cα-backbone of the three-dimensional structure of said recombinant interferon and the Cα-backbone of the three-dimensional structure of IFN-α2b protein using least squares method, the location root-mean-square deviation of Cα at residues 25-33 of said recombinant interferon and Cα in the corresponding residues of IFN-α2b protein is 3.63Å±5%. In some embodiments, in comparison with the corresponding residues of IFN-α2b, the deviations of α carbons of residues 25-33 of said recombinant interferon are 3.291Å±5%, 4.779Å±5%, 5.090Å±5%, 3.588Å±5%, 2.567Å±5%, 2.437Å±5%, 3.526Å±5%, 4.820Å±5% and 2.756Å±5% respectively. In some embodiments, after superimposition of the Cα-backbone of the three-dimensional structure of said recombinant interferon and the Cα-backbone of the three-dimensional structure of IFN-α2b protein using least squares method, the location root-mean-square deviation of Cα at residues 44-52 of said recombinant interferon and Cα in the corresponding residues of IFN-α2b protein is 2.90Å±5%. In some embodiments, in comparison with the corresponding residues of IFN-α2b, the deviations of α carbons of residues 44-52 of said recombinant interferon are 1.614Å±5%, 1.383Å±5%, 2.735Å±5%, 2.709Å±5%, 5.018Å±5%, 4.140Å±5%, 3.809Å±5%, 2.970Å±5%, and 0.881Å±5% respectively. In some embodiments, the mimetic is a functional mimetic or a structural mimetic. In some embodiments, the mimetic is a mimetic of the present recombinant interferon (rSIFN-co). Further, the mimetics do not comprise INFERGEN®. In some embodiments, the three-dimensional structure of said interferon mimetic is similar to that of the present recombinant interferon (rSIFN-co). In particular, both three-dimensional structures can be the same or essentially the same at the AB and BC loops. Further, the three-dimensional structure of said interferon mimetic comprises the atomic

coordinates of amino acid residues 25-33 (AB loop) and/or 44-52 (BC loop) in table 7, said atomic coordinates optionally have a variability of root mean square deviation from the conserved backbone atoms, preferably Cα, of less than about 0.65 Å, preferably about 0.5 Å, and more preferably about 0.35 Å.

[0074] The present invention comprises variant peptides in which individual amino acids can be replaced by other closely related amino acids as is understood in the art. For example, individual amino acid may be replaced as follows: any hydrophobic aliphatic amino acid may be replaced by any other hydrophobic aliphatic amino acids; any hydrophobic aromatic amino acid may be replaced by any other hydrophobic aromatic amino acids; any neutral amino acid with a polar side chain may be replaced by any other neutral amino acids with a polar side chain; an acidic amino acid may be replaced by any other acidic amino acids; and a basic amino acid may be replaced by any other basic amino acids. As used herein, "mimetic", "functional/structural mimetic" relate to peptide variants or organic compounds having the same functional/structural activity as the polypeptide disclosed herein. Examples of such mimetic or analogues include chemical compounds or peptides which are modeled to resemble the three-dimensional structure of the interferon disclosed herein (the three-dimensional structure comprise the atomic coordinates of recombinant interferon as shown in table 7), particularly compounds and peptides having the above arrangement of amino acid residues. Thus, as used herein, "mimetic of the present recombinant interferon" refers to a peptide variant or organic compound which has the same function/structure-activity as the present recombinant interferon (rSIFN-co), especially those having the same AB loop and/or BC loop spatial structure as the present recombinant interferon, but is not the present recombinant interferon When the "mimetic" is a peptide variant, the length of its amino acid sequence is generally similar to that of the present recombinant interferon. For example, said amino acid sequence of the mimetic can comprise about 120-200 amino acid residues, preferably about 140-180 amino acid residues, more preferably about 150-175 amino acid residues, still more preferably about 160-170 amino acid residues; for example, about 164, 165, 166 or 167 amino acid residues. Alternatively, such a "mimetic" can be a peptide variant having a shorter amino acid sequence than the present recombinant interferon but comprising the AB loop and/or BC loop. For example, it can comprise about 10-100 amino acid residues, preferably about 15-80 amino acid residues.

[0075] Suitable mimetics or analogues can be generated by modeling techniques generally known in the art. This includes the design of "mimetics" which involves the study of the functional interactions and the design of compounds which contain functional groups arranged in such a manner that they could reproduce those interactions.

[0076] The design of mimetics of compounds with known pharmaceutical activity is a known approach based on lead compounds for drug development.. This might be desirable where the active compound is difficult or expensive to synthesize or where it is unsuitable for common methods of administration; e.g. polypeptides are not well suited as active agents for oral compositions as they tend to be quickly degraded by proteases in the alimentary canal. Mimetic design, synthesis and testing may be used to avoid randomly screening a large number of molecules for a target property.

[0077] There are several steps commonly taken in the design of a mimetic from a compound/peptide having a given target property. Firstly, determine the particular parts of the compound/peptide that are critical and/or important in determining the target property. In the case of a peptide, this can be done by systematically varying the amino acid residues in the peptide, e.g. by replacing each residue in turn. These parts or residues constituting the active region of the compound are known as its "pharmacophore".

[0078] Once the pharmacophore has been identified, its structure can be modeled according to its physical properties, e.g. stereochemistry, bonding, size and/or charge, using data from a range of sources, e.g. spectroscopic techniques, X-ray diffraction and NMR data. Computational analysis, similarity mapping (which models the charge and/or volume of a pharmacophore, rather than the bonding between atoms) and other techniques can be used in this modeling process. In a variant of this approach, the three-dimensional structures of the ligand and its binding partner are modeled. This can be especially useful where the ligand and/or binding partner change conformation on binding, allowing further consideration of the model while designing the mimetic.

[0079] Afterwards, select a template molecule onto which chemical groups that mimic the pharmacophore can be grafted. The template molecule and the chemical groups to be grafted can be conveniently selected so that the mimetic, besides maintaining the biological activities of the lead compound, would be easy to synthesize, likely be pharmacologically acceptable,

and not degrade *in vivo*. The mimetics found by this approach can then be screened to see whether they have the target property, or to what extent they exhibit it. Further optimization or modification can then be carried out to arrive at one or more final mimetics for *in vivo* or clinical testing.

[0080] In another aspect, the present invention provides an unliganded molecule including at least a portion of the interferon disclosed herein, e.g. the unliganded molecule may comprise SEQ ID NO:4 or SEQ ID NO:5 (the sequence of the AB loop and the BC loop respectively of the interferon described herein). Further, the unliganded molecule has sequence as shown in SEQ ID NO:4 or SEQ ID NO:5.

Composition and Therapeutic Application

[0081] The present invention provides a composition comprising a crystalline form of the present recombinant interferon or a mimetic of the present recombinant interferon. In one embodiment, the composition is a pharmaceutical composition. In one embodiment, said pharmaceutical composition further comprises a pharmaceutically acceptable carrier.

[0082] Whether it is a polypeptide, antibody, peptide, nucleic acid molecule, small molecule, mimetic or other pharmaceutically useful compounds according to the present invention that is to be administered to an individual, the preferred dosage is a "prophylactically effective amount" or a "therapeutically effective amount" (although prophylaxis may be considered a therapy), this dosage being sufficient to provide its beneficial effects to the individual. The actual amount, frequency and time-course of administration will depend on the nature and severity of the disease being treated. Prescription of treatment, e.g. decisions on dosage etc., is within the responsibility of medical doctors and other medical workers. Depending on the circumstances, pharmaceutical compositions may be administered alone or in combinations.

[0083] Pharmaceutical compositions according to the present invention, and those for use with the present invention, may include, in addition to the active ingredient, a pharmaceutically acceptable excipient, carrier, buffer, stabilizer or other materials well known to those skilled in the art. Such materials should be non-toxic and should not interfere with the efficacy of the active ingredient. The exact nature of the carrier or other materials will depend on the route of administration, which may be oral or by injection, e.g. cutaneous,

subcutaneous or intravenous. Examples of techniques and protocols mentioned above can be found in Remington's Pharmaceutical Sciences, 16th edition, Osol, A. (ed.), 1980.

[0084] In some embodiments, said pharmaceutical composition can be formulated into the following dosage forms, including: tablets, capsules, oral liquids, patches, injections, sprays, suppositories, and solution preparations. The recommended dosage form is injection, such as subcutaneous or intravenous injection, and the carrier in the pharmaceutical composition may be any acceptable drug carrier, including binders, disintegrating agents, lubricants, fillers, solubilizers, buffers, preservatives, thickeners, chelating agents and other adjuvants.

[0085] On the basis of the different purposes of this invention, "pharmaceutically acceptable carriers" may be any of the standard pharmaceutical carriers. For example, known appropriate carriers include, but are not limited to, phosphate buffered saline and various wetting agents. Other carriers may include additives used for tablets, granules, and capsules. Typical carriers often contain: starch, emulsion, sugar, cellulose, certain types of clay, gelatin, stearic acid and its salts such as magnesium stearate or calcium stearate, talc, plant oils, gums, glycol or other known excipients. Such carriers may also include flavorings and color additives or other ingredients. The composition of these carriers can be formulated using known methods.

[0086] Furthermore, since the mimetics of the present recombinant interferon have the AB loop and/or BC loop structures (such as the above specific AB loop and/or BC loop space structures) of the present recombinant interferon, they are expected to be capable of treating viral diseases and/or tumor similar to the present recombinant interferon.

[0087] Therefore, in another aspect, the present invention provides a use of the crystal of the present recombinant interferon, an interferon mimetic or a composition comprising said crystal or mimetic for the preparation of medicament for treating viral diseases and/or tumors.

[0088] In another aspect, the present invention provides a method for the treatment of viral diseases and/or tumors, said method comprises administering to a subject an effective amount of the crystal of the present recombinant interferon, an interferon mimetic or a composition comprising said crystal or mimetic.

[0089] In another aspect, the present invention also provides a pharmaceutical composition for the treatment of viral diseases and/or tumors, comprising an effective amount of the crystal of the present recombinant interferon, an interferon mimetic or a composition comprising said crystal or mimetic.

[0090] In some embodiments, said viral diseases may include: hepatitis A, hepatitis B, hepatitis C, other types of hepatitis, viral infections caused by Epstein-Barr virus, human immunodeficiency virus (HIV), Ebola virus, severe acute respiratory syndrome (SARS) virus, influenza virus, cytomegalovirus, herpes simplex virus, or other type of herpes virus, papovavirus, pox virus, picornavirus, adenovirus, rhinovirus, human T-cell leukemia viruses type I, or human T-cell leukemia viruses type II, or human T-cell leukemia virus type III.

[0091] In some embodiments, said tumor is cancer or solid tumors, and said tumors may include: skin cancer, basal cell carcinoma and malignant melanoma, renal cell carcinoma, liver cancer, thyroid cancer, nasopharyngeal cancer, solid tumors, prostate cancer, stomach/abdominal cancer, esophageal cancer, rectal cancer, pancreatic cancer, breast cancer, ovarian cancer, superficial bladder cancer, hemangioma, epidermoid cancer, cervical cancer, non-small cell lung cancer, small cell lung cancer, glial stromal tumors, leukemia, acute leukemia, chronic leukemia, chronic myelogenous leukemia, hairy cell leukemia, lymphadenoma, multiple myeloma, polycythemia, Kaposi's sarcoma.

[0092] This invention will be described in details using the following examples which are included merely for the purpose of illustrating certain aspects and embodiments of the present invention, and are not intended to limit the scope of this invention. Modifications may be made to the invention described herein without deviating from the scope of the invention.

[0093] All publications, patents and patent applications cited herein are incorporated by reference in their entireties, both individually and collectively, into this application.

EXAMPLES

EXAMPLE 1

Production of Recombinant Interferon rSIFN-co

[0094] This example describes the preparation of recombinant interferon rSIFN-co (stock solution). (Refer to Examples 1 and 2 of U.S. Patent No. 7,364,724, and pages 11-17 of the specification of Chinese Patent publication No. CN1740197A.)

1. Gene cloning

[0095] Based on the published encoding DNA sequence and deduced amino acid sequence of INFERGEN® (Klein ML, et al., Structural characterization of recombinant consensus interferon-alpha. Journal of Chromatography, 1988; 454: 205- 215), the DNA encoding sequence was redesigned using *E. Coli* codon usage (The Wisconsin Package, by Genetics Computer Group, Inc. Copyright 1992, Medison, Wisconsin, USA) under conditions that preserve the amino acid sequence, and then the full-length cDNA of rSIFN-co was synthesized.

rSIFN-co cDNA sequence synthesis

Synthesis of the rSIFN-co cDNA 5'-terminus and 3'-terminus partial molecules

[0096] PCR was used to directly synthesize the 5'-terminus 280bp (fragment I) and 3'-terminus 268bp (fragment II) partial molecules of the rSIFN-co cDNA. There was a 41-bp overlap of the complementary nucleotide sequences between the 3' end of fragment I and the 5' end offragment II.

(1) Chemical synthesis of oligodeoxynucleotide fragment

Oligomer A:

5'ATGTGCGACCTGCCGCAGACCCACTCCCTGGGTAACCGTCGTGCTCTGATCCTGCTGGCTCA
GATGCGTCGTATCTCCCCGTTCTCCTGCCTGAAAGACCGTCACGAC3'

Oligomer B:

5'CTGAAAGACCGTCACGACTTCGGTTTCCCGCAGGAAGAATTCGACGGTAACCAGTTCCAGA
AAGCTCAGGCTATCTCCGTTCTGCACGAAATGATCCAGCAGACCTTC3'

Oligomer C:

5'GCTGCTGGTACAGTTCGGTGTAGAATTTTTCCAGCAGGGATTCGTCCCAAGCAGCGGAGGAG
TCTTTGGTGGAGAACAGGTTGAAGGTCTGCTGGATCATTTC3'

Oligomer D:

5'ATCCCTGCTGGAAAAATTCTACACCGAACTGTACCAGCAGCTGAACGACCTGGAAGCTTGCG
TTATCCAGGAAGTTGGTGTTGAAGAAACCCCGCTGATGAAC3'

Oligomer E:

5'GAAGAAACCCCGCTGATGAACGTTGACTCCATCCTGGCTGTTAAAAAATACTTCCAGCGTATC

ACCCTGTACCTGACCGAAAAAAAATACTCCCCGTGCGCTTGGG3'

Oligomer F:

5'TTATTCTTTACGACGCAGACGTTCCTGCAGGTTGGTGGACAGGGAGAAGGAACGCATGATTT CAGCACGAACAACTTCCCAAGCGCACGGGGAGTATTTTTTTTCGGTCAGG3'

(2) PCR

[0097] PCR I for synthesizing rSIFN-co 5'-terminus partial molecule: using oligodeoxynucleotide fragment B as a template, oligodeoxynucleotide fragments A and C as primers, the rSIFN-co 5'-terminus partial molecule with a length of 280bp was synthesized by PCR.

The PCR I reaction mixture is as follows: (units: μl) (Total volume: 50μl)

sterilized distilled water without nuclease	39
10×Pfu buffer (Stratagene, La Jolla, CA, USA)	5
dNTP mixture (2.5 mmol/L for each dNTP)	2
Oligomer A primer (25 μmol/L)	1
Oligomer C primer (25 μmol/L)	1
Oligomer B template (1 μmol/L)	1
Pfu DNA polymerase (Stratagene, La Jolla, CA, USA) (25 U/μl)	1

PCR I reaction cycle: 95°C 2 min→(95°C 45s→65°C 1 min→72°C 1 min) × 25 cycles→72°C 10 min→4°C

[0098] PCR II for synthesizing rSIFN-co 3'-terminus partial molecule: using oligodeoxynucleotide fragment E as a template, oligodeoxynucleotide fragments D and F as primers, the rSIFN-co 3'-terminus partial molecule with a length of 268bp was synthesized by PCR.

The PCR II reaction mixture is as follows: (units: μl) (Total volume: 50 μl)

sterilized distilled water without nuclease	39
10×Pfu buffer (Stratagene, La Jolla, CA, USA)	5
dNTP mixture (2.5 mmol/L for each dNTP)	2
Oligomer D primer (25 μmol/L)	1
Oligomer E primer (25 μmol/L)	1
Oligomer F template (1 μmol/L)	1
Pfu DNA polymerase (Stratagene, La Jolla, CA, USA) (25 U/μl)	1

PCR II reaction condition and cycle: same as PCR I

Assembling of full-length rSIFN-co cDNA

[0099] Fragments I and II were assembled together to give the complete full-length cDNA sequence of rSIFN-co using the overlapping and extending PCR method. Restriction enzyme sites Nde I and Pst I were introduced to the 5'-terminus and 3'-terminus of the sequence respectively, so that the rSIFN-co cDNA sequence can be cloned into the plasmid.

(1) Chemically synthesized primers

Oligomer G: 5'ATCGGCCATATGTGCGACCTGCCGCAGACCC3'

Oligomer H: 5'ACTGCCAGGCTGCAGTTATTCTTTACGACGCAGACGTTCC3'

(2) Overlapping and extending PCR

PCR reaction mixture (units: μl)	(Total volume: 50μl)
sterilized distilled water without nuclease	38
10×Pfu buffer (Stratagene, La Jolla, CA, USA)	5
dNTP mixture (2.5 mmol/L for each dNTP)	2
primer G (25 μmol/L)	1
primer H (25 μmol/L)	1
*fragment I PCR product (1 μmol/L)	1
* fragment II PCR product (1 μmol/L)	1
Pfu DNA polymerase (Stratagene, La Jolla, CA,USA) (25 U/μl)	1

*Separating and purifying the PCR product with STRATAPREP PCR purification kit produced by Stratagene (La Jolla, CA), then dissolving the PCR product into sterilized distilled water.

PCR reaction condition and cycle: same as PCR I.

rSIFN-co gene cloning and sequence analysis

[0100] The pLac T7 plasmid was used as vector for cloning rSIFN-co cDNA. The pLac T7 plasmid was reconstructed from the pBLUESCRIPT II KS(+) plasmid produced by Stratagene (La Jolla, CA, USA).

[0101] PCR product containing rSIFN-co full-length cDNA was purified with STRATAPREP PCR purification kit produced by Stratagene (La Jolla, CA), followed by

digestion with Nde I and Pst I. At the same time, the pLac T7 plasmid was double digested with Nde I and Pst I. These double-digested DNA fragments were separated using 1% agarose gel electrophoresis followed by recovery and purification of a 507-bp rSIFN-co DNA fragment and a 2.9-kb plasmid DNA fragment with Wizard DNA purification kit produced by Promega (Fitchburg, WI, USA). These fragments were ligated by T4 DNA ligase to form a recombinant plasmid. DH5α competent cells (Gibco) were transformed with the recombinant plasmid. After culturing overnight at 37°C, the positive recombinant colony, named as pHY-1, was identified.

[0102] DNA sequencing was performed with SEQUITHERM^{TM} Cycle Sequencing Kit following instruction provided by the manufacturer (Epicentre Technologies Ltd, Madison, WI, USA) using the universal primer T7 and T3. The DNA sequencing result showed that the sequence was consistent with the theoretical design.

[0103] The sixteen N-terminus amino acids and four C-terminus amino acids of the purified recombinant rSIFN-co were sequenced. The results were shown below:

N-terminus:

Cys-Asp-Leu-Pro-Gln-Thr-His-Ser-Leu-Gly-Asn-Arg-Arg-Ala-Leu-

MET at N-terminus was resected in mature protein.

C-terminus:

Arg-Arg-Lys-Glu-COOH

Full-length nucleotide sequence of rSIFN-co is shown as SEQ ID NO:2 and the amino sequence is shown as SEQ ID NO:1.

Construction, transformation, enzyme digestion and identification, and hereditary stability of expression vector

Construction and transformation of expression vector

[0104] *E. Coli* expression vector pBAD18 was digested with Nde I and linearized, then fully digested with Xba I. Electrophoresis with 1% agarose gel and purification with QIAEX II kit (QIAGEN) were performed to give a 4.8-kb fragment from pBAD18 having been digested with Nde I and Xba I.

[0105] At the same time, the pHY-1 plasmid was double digested with Ndel and Xba I and, after separation with 1% agarose gel electrophoresis, a 715-bp fragment was purified. This

fragment was ligated with the above 4.8-kb fragment from pBAD18 using T4 DNA ligase to produce the recombinant plasmid. The recombinant plasmid was used to transform DH5α-competent cells. The transformed cells were spread on LB-Amp agar plate, and then cultured overnight at 37°C.

Screening for positive clones

[0106] *E. Coli.* colonies from the above LB-plate were randomly chosen, and clones containing recombinant plasmid with full length rSIFN-co cDNA were screened using endonuclease digestion and PCR analysis. One of the PCR positive recombinant plasmid was named pHY-5, and the strain containing pHY-5 plasmid was named PVIII. PVIII was amplified and stored at -80°C with glycerol freezing medium for future use.

High expression of rSIFN-co gene in *E. Coli* LMG194

[0107] In the pHY-5 plasmid, rSIFN-co gene was under the control of the strong promoter P_{BAD} which is regulated by the AraC protein. AraC is a protein encoded by the AraC gene located in the same plasmid. In the absence of arabinose, the dimer of AraC binds to O_2 and I_2 forming a 210-bp loop. This conformation leads to a complete inhibition of transcription. In the presence of arabinose, the dimer of AraC is released from O_2 and binds to I_1 and I_2 eliminating the inhibition on transcription. Arabinose binding deactivates, represses and even activates the transcription of P_{BAD} promoter, which stimulates P_{BAD} to mediate high expression of rSIFN-co. rSIFN-co expression level is more than 50% of the total bacterial protein.

2. Separation and purification

(1) Preparation of producing strains

[0108] The *E.coli* strain LMG194 with expression vector pHY-5 was inoculated in LB culture medium, then shaken at 200rpm overnight (about 18h) at 37 °C. To the medium was added 50% of 30% glycerine. After mixing, the medium was stored at -20°C in 1 ml aliquots for use as the producing strain;

(2) Preparation of grade –I seed strain

[0109] The producing strain was inoculated in LB culture medium (1 L containing Tryptone 10g, Yeast extracts 5g and NaCl 10g) at a ratio of 1%, then shaken at 200 rpm overnight (about 18h) at 37°C, for use as grade-I seed strain;

(3) Fermentation and collection of the strain

[0110] Grade-I seed strain was added to RM media (1 L containing Casein 20 g, $MgCl_2$ 1 mmol/L (0.203 g), Na_2HPO_4 4g, KH_2PO_4 3 g, NaCl 0.5 g and NH_4Cl 1g) at a ratio of 10% and cultured at 37°C, pH 7.0. Fermentation was carried out until OD_{600} reached about 2.0, then arabinose (20% solution) was added until a final concentration of 0.02% as an inductor; after 4 hours, the strain was collected and centrifuged to give a pellet;

(4) Preparation of inclusion bodies

[0111] The strain pellet was re-suspended with an appropriate amount of buffer A (100 mmol/L Tris-HCl, pH 7.5, 10 mmol/L EDTA, 100 mmol/L NaCl), and kept at -20°C overnight. The strain was thawed and broken by a homogenizer, then centrifuged. The pellet was washed with buffer B (50 mmol/L Tris-HCl, pH 7.5, 1 mol/L Urea,10 mmol/L EDTA, 0.5% Triton X-100), buffer C (50 mmol/L Tris-HCl, pH 7.5, 2 mol/L Urea, 10 mmol/L EDTA, 0.5% Triton X-100) and then precipitated; this was repeated once, and the pellet was then washed once with distilled water to give inclusion bodies.

(5) Renaturation treatment

[0112] The inclusion body was dissolved in 6 mol/L Guanidine-HCl (or urea) to obtain a slightly cloudy denaturation solution, which was then centrifuged at a speed of 10000 rpm. The supernatant was collected and used to determine the protein concentration. The denaturation solution was added in three portions into a renaturation buffer (0.5 mol/L Arg, 150 mmol/L Tris-HCl, pH 7.5, 0.2 mmol/L EDTA) and then stirred continuously at 4°C overnight (about 18 h). The solution was dialyzed sequentially with ten times its volume of 10 mol/L phosphate buffer (PB) , 5 mol/L PB buffer and distilled water; After dialysis, the pH was adjusted with 2 mol/L HAc-NaAc (pH 5.0). The solution was left to stand and then filtered.

(6) HS cation column chromatography

[0113] A column was prepared with 20 mmol/L HOAc-NaOAc (pH 5.0), loaded with the renaturation product obtained from step (5) at a speed of 30 ml/min, washed with 20 column volumes (CV) of 20 mmol/L HOAc-NaOAc (pH 5.0) to remove other proteins; washed with 5 CV of 20 mmol/L HOAc-NaOAc (pH 5.0) containing 0.15 mol/L NaCl to remove other proteins; then washed with 3 CV of 20 mmol/L HOAc-NaOAc (pH 5.0)

containing 0.18 mol/L NaCl to remove other proteins. Finally, 20 mmol/L HOAc-NaOAc (pH 5.0) containing 0.25 mol/L NaCl was used to elute the target protein, thereby obtaining an HS-eluted protein solution.

(7) Copper ion affinity chromatography (chelating SEPHAROSE^{TM} FAST FLOW)

[0114] The HS-eluted protein solution was added into PB buffer of 0.2 mol/L (pH 6.6). 4 mol/L NaCl was added to adjust the NaCl concentration to 1 mol/L and pH to 6.0, and the solution was ready for loading. A column was prepared with 50 mmol/L Na_2HPO_4 (pH 5.5) containing 1 mol/L NaCl, and loaded at a rate of 1 ml/min. The column was washed with 50 mmol/L Na_2HPO_4 (pH 5.0) to remove other proteins, then washed with 50 mmol/L Na_2HPO_4 (pH 4.0) to remove other proteins. Finally, 50 mmol/L Na_2HPO_4 (pH 3.6) was used to elute the target protein to obtain the chelating column-eluted target protein solution.

(8). HS column chromatography

[0115] The protein solution eluted from the chelating column was diluted 30 folds and its pH adjusted to 5.0, then loaded onto an HS column which was eluted with PB buffer, pH 7.0, containing 0.5 mol/L NaCl to give the recombinant interferon (Protein Stock Solution).

EXAMPLE 2

Preparation of Recombinant Interferon

Lyophilized injection formula (lyophilized powder)

rSIFN-co stock solution of the present invention	34.5 μg/ml
phosphate buffer, pH 7.0	10 mmol/L
glycine	0.4 mol/L

Preparation method:

[0116] Materials were weighed according to the formula, dissolved in sterile and pyrogen-free water for injection, sterilized by filtration through a membrane with 0.22 μm pores, and then stored at 6-10 °C. Samples passed the sterility test and pyrogen test, before aliquoted into vials. Every vial contained a single dose of 0.3-0.5. All the aliquoted samples were lyophilized in a lyophilization machine.

Aqueous injection formula

rSIFN-co stock solution of the present invention	34.5 μg/ml
phosphate buffer, pH 7.0	25 mmol/L
NaCl	0.4 mol/L

Preparation method:

[0117] Materials were weighed according to the formula, dissolved in sterile and pyrogen-free water for injection, sterilized by filtration through a membrane with 0.22 μm pores, and then stored at 6-10 °C. Samples passed the sterility and pyrogen test before aliquoted into vials. Every vial contained a single dose of 0.3-0.5 . Final products were stored in the dark at 2-10 °C.

EXAMPLE 3

In vitro study of rSIFN-co and INFERGEN® against human breast cancer cells

[0118] This example describes the *in vitro* study of rSIFN-co and INFERGEN® against human breast cancer cells.

[0119] The present recombinant interferon (rSIFN-co) and INFERGEN® produced by Amgen (U.S.) were used as test drugs to study their effects on cell proliferation, apoptosis and expression of oncogenes in MCF-7 and resistant strain MCF-7/ADR.

A. Methods

1. Cell culture

[0120] Human breast cancer cell line MCF-7 and adriamycin resistant strain MCF-7 (MCF-7/ADR) were cultured in 25 cm^2 or 75 cm^2 flasks respectively. After the cells covered the bottom of the flasks, they were trypsinized with 0.25% trypsin. Cells in the logarithmic growth phase were harvested for experiments.

2. Detecting the effects of different concentrations of rSIFN-co on cell proliferation with the MTT colorimetric assay

[0121] Experimental grouping: each cell strain was divided into 3 groups (with 11 small groups in total): rSIFN-co group (0.02, 0.078, 0.313, 1.25, 5.0 μg/ml), INFERGEN® group (0.02, 0.078, 0.313, 1.25, 5.0μg/ml) and blank control group (RPMI1640 medium containing

10% fetal bovine serum (Sigma, America), also known as RPMI1640 complete medium). rSIFN-co and INFERGEN® were diluted into the desired concentrations (final ethanol concentration <1%) with the RPMI1640 complete medium, and stored at 4°C.

[0122] MCF-7 cells and MCF27/ADR cells in the logarithmic growth phase were diluted with RPMI1640 medium containing 10% fetal bovine serum to 1.25×10^5/ml cell suspension. Trypan blue method was used to ensure >95% cell viability. The cells were seeded in 96-well culture plates, 100 μL per well. 24h, 48h, 72h after drugs were added according to the groupings mentioned above, conventional MTT assay was used to detect cell proliferation (absorbance detected with microplate reader at the wavelength of 490nm). Each group had two wells as parallel samples. The experiment was repeated three times. The effects of different drug concentrations at different time on cell growth inhibition were calculated according to the following formula:

Cell Growth Inhibition Rate (%)= (Value of A in control group - Value of A in experimental group) / Value of A in control group × 100%

3. Apoptosis detection with flow cytometry (FCM)

[0123] Experimental grouping: each cell strain was divided into 3 groups: rSIFN-co group (5 μg/mL), INFERGEN® group (5 μg/mL), and blank control group (containing 10% calf serum RPMI1640 culture medium).

[0124] FCM detection: the cells were collected 48h after drugs were added, then the cells were suspended as single cells and dyed with propidium iodide (PI). The apoptosis rate was assayed with the Elite Esp-based flow cytometer (Coulter, USA), and the results were analyzed with the software supplied with the equipment. These experiments were repeated 3 times.

4. Immunohistochemical detection of cellular oncogene expression

Experimental grouping:

[0125] Each cell strain was divided into 3 groups. rSIFN-co (5 μg/mL), INFERGEN® (5 μg/mL), and RPMI1640 containing 10% fetal bovine serum were added to the medium of MCF-7 cell cultures. And rSIFN-co (5 μg/mL), INFERGEN® (5 μg/mL) and RPMI1640 containing 10% fetal bovine serum were also added to the medium of MCF-7/ADR cell cultures.

Immunohistochemical detection of P53, Bcl-2, CerbB-2 expression:

[0126] The coverslips were treated with acid, washed and sterilized under high pressure, and then placed in 6-well culture plates. The MCF-7 and MCF-7/ADR cells in logarithmic growth phase were digested into single cell suspensions with 0.25% trypsin. The cells were inoculated into 6-well plates, each well 1×10^5, and cultured at 37°C in a CO_2 incubator for 24h. After the cells adhered to the walls, drugs were added to each group. After 48 h, the coverslips were removed. Conventional immunohistochemical SABC staining was performed, all concentrations at 1:100.

Criteria for evaluation of results:

[0127] Staining results were determined according to the methods of Volm (Volm M, et al., European Journal of Cancer, 1997, 33 (3), 691-693), wherein yellow or brown particles appearing in cell nucleus (P53), cytoplasm (Bcl-2) or membrane (CerbB-2) were taken as positive results. Five fields of view (FOV) on each slide under high magnification (400 ×) were randomly selected, counting 200 cells per field. Two factors determined if there was expression in each group of cells. Scoring was done according to the intensity of staining for each cell, 0 point for no coloring, 1 point for light yellow, 2 points for brown, 3 points for tan. The average would be the average staining intensity for a group of cells. Percentage of positive cells: no 0 point for no staining; 1 point for <25% stained cells; 2 points for 25%-50%; 3 points for > 50%. Sum of the two scores: 0 means negative expression; 2-4 means positive; 4- 6 means strongly positive. These experiments were double blind (stainers and observers both do not know the grouping of the slides).

B. Statistical methods

Statistical analysis of experimental data:

[0128] All the experimental data were tested with the t test, variance analysis and rank correlation analysis using the SPSS 11.5 statistical package. *P* value <0.05 means that the difference was statistically significant.

C. Results

1. Effects on the proliferation of MCF-7 and MCF-7/ADR cells

(1) MCF-7 Cells

[0129] rSIFN-co could inhibit the proliferation of MCF-7 cells. Each cell group treated with 0.02, 0.078, 0.313, 1.25, 5.0 μg/mL of rSIFN-co and INFERGEN® showed a significant decrease in its absorbance (OA) compared with the blank control groups. The inhibitory effects of rSIFN-co and INFERGEN® showed no significant differences at the early stages (24h, 48h) ($P>0.05$). After over 72 h of treatment, the % inhibition of rSIFN-co was higher than that of INFERGEN® at the same concentrations except at the lowest concentration of 0.02 μg/mL, the differences were statistically significant ($P<0.05$) (shown in Table 1-1).

Table 1-1 *In vitro* growth inhibition of the MCF-7 cells (%, n = 6)

Dose (μg/mL)		24h	48h	72h
INFERGEN®	0.02	8.59±2.26	8.28±2.27	10.43±3.59
	0.078	13.84±1.96	7.80±2.01	9.47±2.48
	0.312	15.53±1.51	9.30±3.28	13.39±4.37
	1.25	17.58±0.62	12.76±1.63	14.41±0.83
	5.0	19.98±5.22	26.69±3.47	24.93±2.53
rSIFN-co	0.02	7.78±4.32	11.60±0.77	12.53±0.70
	0.078	15.71±3.68	13.03±3.27	16.77±2.22*
	0.312	17.49±1.34	14.80±2.40	22.73±6.06*
	1.25	20.07±1.01	24.65±2.18	27.62±1.81*
	5.0	24.79±4.01	30.77±3.09	44.75±2.32*

*$P<0.05$, vs. INFERGEN®

(2) MCF-7/ADR Cells

[0130] rSIFN-co could inhibit the proliferation of MCF-7/ADR cells. Each cell group treated with 0.02, 0.078, 0.313, 1.25, 5.0 μg/mL of rSIFN-co and INFERGEN® showed a significant decrease in its absorbance (OA) compared with the control groups. The inhibitory effect of rSIFN-co was higher than that of INFERGEN® at the same concentrations except at the lowest concentration of 0.02 μg/mL as shown by analysis of variance, the differences were statistically significant ($P<0.05$) (shown in Table 1-2).

Table 1-2 *In vitro* growth inhibition of MCF-7/ADR (%, n = 6)

Dose (μg/mL)		24h	48h	72h
INFERGEN®	0.02	16.36±0.96	24.97±0.33	28.87±6.20
	0.078	23.01±2.11	28.04±0.85	30.90±3.34

	0.312	26.69±2.49	29.64±2.78	43.02±2.11
	1.25	31.64±1.17	49.87±1.74	46.68±2.42
	5.0	37.61±0.96	57.24±0.80	62.52±4.01
rSIFN-co	0.02	16.24±2.30	34.20±1.80	34.80±1.38
	0.078	29.70±1.40*	33.92±1.35*	48.71±1.04*
	0.312	33.46±1.04*	41.52±5.27*	47.71±0.40*
	1.25	38.80±2.16*	52.50±0.73*	52.70±1.01*
	5.0	48.36±6.52*	67.65±4.40*	69.44±0.95*

*$P<0.05$, vs. INFERGEN®

2. Effect on apoptosis of MCF-7 and MCF-7/ADR cells

[0131] Compared with the control group, 5μg/mL of rSIFN-co and INFERGEN® induced apoptosis of MCF-7 and MCF-7/ADR cells after treatment for 48h, the differences were statistically significant (P <0.01). rSIFN-co showed stronger apoptosis-inducing activities on MCF-7 and MCF-7/ADR than INFERGEN® at the same concentrations, the differences were statistically significant (P <0.01) (shown in Table 1-3).

Table 1-3 The % apoptosis of MCF-7 after 48h treatment (%, n = 6)

	Blank control	INFERGEN®	rSIFN-co
MCF-7	7.27±1.19	19.67±0.95*	23.10±0.80*▲
MCF-7/ADR	8.40±0.70	34.80±3.20*	65.63±4.60*▲

* $P<0.01$, vs. control; ▲$P<0.01$, vs. INFERGEN®

3. Effect on expression of P53, CerbB-2 and Bcl-2 in each cell group

[0132] rSIFN-co down-regulated the expression of P53 in MCF-7 cells compared with the control group, the difference was statistically significant (P <0.05). Although INFERGEN® decreased the expression of P53, the decrease was not significantly different (P >0.05) compared with the control group. Both rSIFN-co and INFERGEN® down-regulated the expression of P53 in MCF-7/ADR compared with the control group, the difference was statistically significant (P<0.05), but rSIFN-co and INFERGEN® at the same concentration showed no significant difference between them (P > 0.05).

[0133] rSIFN-co down-regulated the expression of CerbB-2 in both MCF-7 and

MCF-7/ADR as compared with the control group, the difference was statistically significant (P <0.01). CerbB-2 expression was decreased after INFERGEN® treatment; however, the decrease was not significantly different (P > 0.05) compared with the control group.

[0134] rSIFN-co and INFERGEN® both up-regulated the expression of Bcl-2 in MCF-7 compared with the control group, the difference was statistically significant (P <0.01), but rSIFN-co showed stronger activities than INFERGEN® at the same concentration, the difference was statistically significant (P = 0.001). rSIFN-co and INFERGEN® both up-regulated the expression of Bcl-2 in MCF-7/ADR compared with the control group, the difference was statistically significant (P <0.01). Results are shown in Table 1-4.

Table 1-4 Effect on the expression of P53, CerbB-2 and Bcl-2 in MCF-7 48h after treatment (n = 5).

Groups		Blank control	INFERGEN®	rSIFN-co
P53	MCF-7	4.17±0.0120	3.78±0.0851	2.62±0.0208★
	MCF-7/ADR	4.09±0.0361	2.68±0.0100★	2.60±0.0089★
CerbB-2	MCF-7	4.08±0.0322	3.15±0.3469	2.61±0.0120*
	MCF-7/ADR	4.06±0.0030	3.82±0.0404	3.70±0.0291*
Bcl-2	MCF-7	2.59±0.0153	3.93±0.0306*	4.02±0.0252*
	MCF-7/ADR	3.64±0.0252	3.93±0.0176*	4.02±0.0145*

★$P<0.05$, * $P<0.01$, vs. control.

EXAMPLE 4

In vitro study of rSIFN-co and INFERGEN® against cervical cancer cell

[0135] This example describes the *in vitro* study of rSIFN-co and INFERGEN® in inhibiting the growth and inducing apoptosis of cervical cancer cell.

[0136] The present recombinant interferon (rSIFN-co) and INFERGEN® produced by Amgen (U.S.) were used as test drugs to study their effects on growth inhibition and apoptosis induction of cervical cancer Caski cells (HPV16 +).

A. Methods

1. Caski cells growth inhibition test

1.1 Cell culture and grouping

[0137] Drug samples were diluted with RPMI-1640 culture medium containing 10% fetal bovine serum. Cervical cancer Caski cells were cultured in a 96-well plate. Cells were prepared as single cell suspension using culture medium with a cell concentration of 1×10^5/ml. To each well was added 100 μl of cell suspension. rSIFN-co and INFERGEN® were added to the plate at a concentration gradient of 0.156 μg/ml, 0.625 μg/ml, 2.5 μg/ml and 10μg/ml. RPMI-1640 medium containing 10% fetal bovine serum was used as control group. Each concentration was triplicated. The cells were cultured at 37°C with 5% CO_2 in an incubator for 72h.

1.2 Cell growth inhibition test by MTT method

[0138] MTT reagent (Sigma Company, U.S.) was prepared at 5 mg/ml, and 10 μl MTT reagent was added to each well. The plate was shaken gently to homogenize the reagent, incubated at 37°C with 5% CO_2 for 4h, whereupon blue crystals could be seen at the bottom of the wells. The supernatant was removed, and 100 μl of DMSO were added to each well, then the absorbance at 570 nm was measured with a microplate reader after the blue crystals dissolved at room temperature.

1.3 Calculation of cell growth inhibition

$$\text{Cell growth inhibition} = \left(1 - \frac{\text{OD value of sample well}}{\text{OD value of control well}}\right) \times 100\%$$

2. Apoptosis test on Caski cells

2.1 Cell culture and grouping

[0139] The Caski cells were divided into 7 groups and cultured in RPMI-1640 medium containing 10% inactivated fetal bovine serum in a 96-well plate. Group 1 was cultured for 72h as control group. Groups 2-4 were cultured with different concentrations of rSIFN-co: 0.156 μg/ml, 0.625 μg/ml, 2.5 μg/ml. Groups 5-7 were cultured with different concentrations of INFERGEN®: 0.156 μg/ml, 0.625 μg/ml, 2.5 μg/ml.

2.2 Apoptosis rate of Caski cells determined by flow cytometry (FCM)

[0140] Each group of cells were centrifuged at 1000 r/min for 5min. The supernatant was removed, and the cells were tested for apoptosis with Annexin V/PI double dying method.

Each specimen containing 1×10^6 viable cells was washed once with incubation buffer and centrifuged at 1000 r/min for 5 min. The cells were re-suspended with 100 μl marker solution, incubated at room temperature for 15 min in the dark, and centrifuged at 1000 r/min for 5 min to precipitate the cells. The cells were washed once with an incubation buffer, triturated with a fluorescent solution, then incubated at 4°C for 20 min. in the dark, while shaken frequently, before being tested with FCM.

B. Statistical Analysis

[0141] All quantitative analysis data were expressed as $x\pm s$. Variance analysis was used to analyze the variance between different drugs and different concentrations, and the statistical analysis was performed with the SPSS 14.0 software package.

C. Results

1. Caski cells growth inhibition test

[0142] Both rSIFN-co and INFERGEN® inhibited the growth of Caski cells, and this effect increased with increasing concentrations of interferons. The effect of rSIFN-co was greater than that of INFERGEN® in groups of 0.625, 2.5 and 10 μg /ml. The differences displayed in Table 2-1 showed statistical significance (P <0.01):

Table 2-1 Inhibitory effect on Caski cells ($x\pm s$)

Drug concentration (μg /ml)	Cell growth inhibition rate	
	rSIFN-co	INFERGEN®
0.156	8.6±2.1	7.3±2.2
0.625	17.6±3.3①	7.4±4.0
2.5	42.7±1.5①	9.7±1.6
10	67.3±4.4①	53.0±5.8

①Compared with INFERGEN® at the same concentration, $P<0.01$

2. Inducing apoptosis in Caski cells

[0143] Both rSIFN-co and INFERGEN® induced apoptosis in Caski cells, and the effect was positively correlated with increasing concentrations of interferons. The effect of rSIFN-co at low concentration (0.156 μg/ml) was higher than that of INFERGEN®. The difference displayed in Table 2-2, showed statistical significance ($P<0.01$):

Table 2-2 Apoptotic effect on Caski cells ($x\pm s$)

Drug concentration μg /ml)	Cell growth inhibition rate	
	rSIFN-co	INFERGEN®
0	21.3±3.9	21.3±3.9
0.156	53.5±4.6[1,2]	47.6±3.1[1]
0.625	64.9±3.3[1]	67.1±3.6[1]
2.5	74.4±1.3[1]	72.0±2.6[1]

[1] Compared with controls, $P<0.01$.

[2] Compared with INFERGEN® at the same concentration, $P<0.01$.

EXAMPLE 5

Study of the pharmacokinetics and bioequivalence of rSIFN-co and INFERGEN®

[0144] This example describes the research work on the pharmacokinetics and bioequivalence between rSIFN-co and INFERGEN®. The present recombinant interferon rSIFN-co and INFERGEN® produced by Amgen (U.S.) were taken as test drugs to compare their pharmacokinetics and bioequivalence.

[0145] It is difficult to undertake pharmacokinetics study of interferon in healthy people . As the level of medicinal interferon in blood plasma is very low after injection, enzyme-linked immunosorbent assay (ELISA) or virus cytopathic inhibition assay can hardly measure it directly in the serum of healthy adults. Currently, the detection marker for pharmacokinetics study of interferon is generally 2', 5'-OAS (2-5A oligonucleotidase), which is a product induced by interferon, and also an indicator of its efficacy.

A. Subject and Method

1. Subject

[0146] There were 18 healthy male volunteers with an average age of 22.8±1.4, height of 170±5.0 cm, BMI of 20.5±2.4, and body weight of 59.4±7.2 kg. Subjects were determined to be normal by a comprehensive physical examination, laboratory tests (including hematology, urine, liver and kidney functions) and electrocardiogram. The subjects did not use any drugs

within 4 weeks prior to the test, and did not use any drugs known to damage the organs within 3 months prior to the test. They had no history of allergy to the test drugs; and they volunteered for the test and signed an informed agreement.

2. Method

[0147] The experimental scheme was approved by the Medical Ethics Committee of West China Hospital, Sichuan University, operated in accordance with relevant guidelines of GCP of the PRC.

2.1 Materials

Reagents:

[0148] Lyophilized powder of recombinant interferon for injection (Test preparations, i.e. the recombinant interferon rSIFN-co of the present invention, 9 μg/vial). Comparison preparation: INFERGEN® injection (compare reagent, 9 μg/vial) produced by Amgen (U.S.).

[0149] 2-5A Kit: Eiken' Radioimmunoassay Kit was supplied by Eiken Chemical Co., LTD. The Kit includes: (1) I^{125}-labelled 2',5'-OAS, (2) Anti-2',5'-OAS serum, (3) 2',5'-OAS Standard vial (each contains 0, 10, 30, 90, 270 or 810 pmol/dL 2',5'-OAS), (4) Buffer, (5) Blank serum, (6) Poly(I)-poly(C) agarose gel, (7) ATP, (8) Mercaptoethanol, and (9) Quality control serum.

2.2 Experimental design and Dosing methods

[0150] Using the randomized controlled crossover trial, 18 subjects were randomly divided into A and B groups, nine in each group, separate subcutaneous injections of 9μg rSIFN-co and 9μg INFERGEN® was made alternately in two cycles, one week of wash period.

[0151] Fast from 8 pm the day before the test until 2 h after dose the next morning, subcutaneous injection was taken in brachial deltoid muscle at 7:00 am. All the subjects were required to have standard meals (food without high fat), and forbidden to smoke, drink alcohol, tea, coffee beverages, and refrain from strenuous exercises. All other drugs were banned during the tests.

2.3 Collecting and testing of blood samples

[0152] 4 ml of blood samples were drawn before dosing, while 3.5 ml of blood samples were drawn from the elbow vein opposite the injection site at 2, 6, 12, 18, 22, 24, 26, 30, 34, 38, 42 and 48 hours after the injection; the samples were centrifuged immediately, and the resulting serum preserved at -20 ℃ until they were tested for the 2', 5'-OAS concentration.

3. Statistical methods

[0153] Using the DAS ver1.0 statistical software, test Test preparation and compare preparation were compared by the paired t test using the statistical software DAS ver1.0.

B. Results

[0154] According toBased on the measured serum 2',5'-OAS concentration of the blood samples, the mean enzyme concentration-time curves were plotted in Figure 16.

[0155] As shown in Figure 16, after subcutaneous injection with 9 μg of rSIFN-co or 9 μg of INFERGEN®, the two enzyme concentration-time curves had basically the same trend; but after subcutaneous injection of rSIFN-co, the concentration at the peak of the enzyme concentration-time curve was significantly higher than that of INFERGEN®.

$$F = \left(\frac{AUC_{\text{test preparation}}}{AUC_{\text{compare preparation}}}\right) \times \left(\frac{\text{compare preparation dosage}}{\text{test preparation dosage}}\right) \times 100\%$$

[0156] The relative bioavailability (F) of test preparation (rSIFN-co) compared to the compare preparation (INFERGEN®) was calculated by the following formula:

$$F = \left(\frac{AUC_{\text{test preparation}}}{AUC_{\text{compare preparation}}}\right) \times \left(\frac{\text{compare preparation dosage}}{\text{test preparation dosage}}\right) \times 100\%$$

[0157] The results showed that the relative bioavailability of rSIFN-co (F0 ~ 48) was 125.4%. The Tmax difference between test preparation and compare preparation was not statistically significant (t = 1.458, P = 0.163). The difference between AUC0-48 and Cmax was statistically significant (t = 2.730, P = 0.014; t = 2.347, P = 0.031), and test preparation was higher than the compare preparation.

[0158] In addition, the INFERGEN® group was more severe than the rSIFN-co group in terms of the incidence, extent and duration of the adverse reactions that were compared.

C. Conclusion

[0159] (1) After subcutaneous injection, both rSIFN-co and INFERGEN® induced the production of 2', 5'-OAS. The pharmacokinetics curves of the two drugs were of the same trend, and the main pharmacokinetics parameters showed no statistical difference.

[0160] (2) Both the C_{max} and AUC_{0-48} of 2', 5'-OAS induced by rSIFN–co were higher than that of INFERGEN®, indicating that the efficacy of rSIFN-co might be better than INFERGEN® under the same dosage.

[0161] (3) The INFERGEN® group was more severe than the rSIFN-co group in the incidence, extent and duration of the adverse reactions that were compared.

[0162] (4) It was discovered, after plotting the mean enzyme concentration- time curves based on the the serum 2', 5' oligoadenylate synthase (2',5'-OAS) concentration measured at different times, the 2', 5'-OAS concentration induced by rSIFN-co generally had double peaks and the area under the curve was significantly greater than that obtained by INFERGEN® when each was separately injected under the same conditions. An increment in the area under the curve was not correlated to an increase in the incidence and/or the occurrence degree of the adverse reactions.

EXAMPLE 6

Crystallization of Recombinant Interferon

[0163] The preparation of high-quality rSIFN-co protein monocrystal is a prerequisite for determining its crystal structure. The rSIFN-co used for crystal growth was derived from the said rSIFN-co of the present invention. The preparation method, technical process, crystallization conditions and crystallographic parameters of the rSIFN-co monocrystal were as follow.

[0164] lyophilized powder of the rSIFN-co in the present invention was dissolved in pure water and stored under -20°C at an initial protein concentration of 0.42mg/ml. Prior to crystallization, the rSIFN-co protein samples were concentrated to 3-3.5mg/ml and immediately used for the crystal growth experiments. The hanging drop vapor diffusion

method was used for the crystallization process held at room temperature (293K).

[0165] In the initial crystallization studies, microcrystalline rSIFN-co appeared under different sets of conditions, but it was difficult to obtain high-quality monocrystal that could be used for X-ray diffraction analysis of sufficient resolution. After optimization of a large number of crystallization conditions, it was found that the best quality crystals were obtained using the crystallization solution made up of the following: 1.2 M $LiSO_4$, 0.1 M CAPS (3-(cyclohexylamino)-1-propanesulfonic acid), pH 11.1 and 0.02 M $MgCl_2$. A good monocrystal of rSIFN-co protein was obtained after the crystallization solution prepared with this formula was left standing for 3 days to 1 week. The monocrystal was of the tripartite crystal type, and had a size of0.42×0.08×0.08mm. The rSIFN-co protein crystal used in the X-ray diffraction analysis of the crystal structure is shown in Figure 1.

EXAMPLE 7

Analysis of the Crystal X-Ray Diffraction Data

Collection of crystal diffraction data:

[0166] Data collection was conducted under low temperature condition (100K) using the synchrotron radiation from beamline BL5A at a photon factory in Tsukuba, Japan. The crystal diffraction data was collected using the following steps:

[0167] (1) Under a microscope, a crystal placement tool was carefully used for transferring a crystal from the mother liquor to a loop at the top part of the tool;

(2) Employing the Flash-Cooling technique, the loop containing the crystal was quickly soaked in paraffin oil (Hampton Research, U.S.), which acted as an antifreeze reagent, for several seconds and quickly transferred to the goniometer head of the diffraction apparatus. At this time, the crystal will be instantaneously in a low-temperature nitrogen stream (100K) such that data collection was conducted under the low temperature of 100K;

(3) Data collection was started after setting the required parameters; the light source wavelength was 1.0Å, the detector was a ADSC Quantum 315 CCD (charge-coupled device) and the crystal-to-detector distance was 310 mm. The data was collected using the oscillation method, and for every image the oscillation angle was 1°, the exposure time was 12 seconds, and a total of 110 images were collected (Fig. 2).

Processing and analysis of the diffraction data:

[0168] The complete set of diffraction data collected had to be processed and analyzed using the CCP4 program package before the set of intuitional diffraction images (Figure 2) originally obtained in the diffraction experiment could be used for quality assessment of the diffraction data and structural analysis of the crystal. This process consisted of: 1) indexing: transforming the diffraction data to crystallography index (h, k, l), and calculating unit cell parameters and space group; 2) parameter modification: refining parameters such as the unit cell parameters, crystal-to-detector distance and angle, and degree of mosaicity etc; 3) integration: obtaining the intensity information from the diffraction spots; 4) merging data: merging all the diffraction spots that arose due to symmetry or are duplicated to generate a complete set of data with only independent diffraction spots; 5) transforming the intensity data into structure amplitudes. The details on the collection of rSIFN-co crystal diffraction data and results of the analysis are shown in Table 3.

TABLE 3

RDetails on the collection of rSIFN-co crystal diffraction data and results of the analysis

Data acquisition conditions	
X-ray source	PF, BL-5A
Wavelength (Å)	1.0
Detector	ADSC Quantum 315 CCD
Distance (mm)	310
Temperature (K)	100
Data acquisition statistics	
Space group (number of molecules/asymmetric unit)	$P3_121(2)$
Cell parameters	
a=b (Å)	77.920
c (Å)	125.935
α=β=90°, γ=120°	
Solvent content (%)	56.7
Resolution coverage (Å)	67.58-2.60
Diffraction spots (I/ σ (I)>0)	86556
Unique diffraction spot (I/ σ (I)>0)	14052
Outermost shell	2.74-2.60
Symmetry related diffraction spot quality factor R (%):	
Overall, (Outermost shell)	7.1 (25.8)
Signal to noise ratio	21.2(4.5)
Intigrity(%): overall, (Outermost shell)	99.5(100.0)
Redundancy: overall, (Outermost shell)	6.2(6.5)

EXAMPLE 8

Analysis of the Crystal Structure

Determination of the crystal diffraction phase and construction of the rSIFN-co initial molecular structural model

[0169] The molecular replacement method was adopted to solve for the rSIFN-co crystal structure; the crystal structure (PDB number 1B5L) of sheep INF-τ (54% sequence homology to rSIFN-co) was selected as the homologous structural model. The software program PHASER was used for computing its rotation function and translation function which was then used to presume the location and orientation of the rSIFN-co molecule in a unit cell. Based on the Laue groups and the systematic absence law, its space group was determined to be $P3_121$ and the molecular model was correspondingly modified (viz. preserving residues 13-25, 37-69, 79-101, 114-151 in the 1B5L structure); results calculated from this model were as follow: Z-score was 15.71, IL-gain was 307.79, Clash was 0. The molecules heaped up reasonably in a unit cell, and IL-gain gradually rose during the process of molecular replacement. This indicated that an exact solution was obtained and the initial phase of each diffraction point had been determined. In turn, the mtz generated by PHASER, possessing the initial phases, was used for building the electron density map using FFT. The initial molecular structural model obtained was well-matched to the electron density map, demonstrating that the exact phase solution of all the diffraction points of rSIFN-co had been obtained. Based on the results above, the rSIFN-co initial molecular structural model was built.

Rectification of the rSIFN-co structural model

[0170] With the aim of obtaining an accurate rSIFN-co molecular structural model, the coordinates and temperature factors of all the non-hydrogen atoms in the rSIFN-co initial molecular structural model underwent iterative refinement by using molecular modeling techniques and a computerized optimization program.

[0171] program CNS1.1 was used for structural refinement using phaseless population data; 10% of these data was randomly extracted for use as the testing set, and the same randomly extracted testing set was kept throughout. All the atoms in the structural model participated in the refinement, and each atom possessed 4 refining parameters, including coordinates (x, y, z) and isotropic temperature factor B. Computerized automatic refinement and manual

adjustment or building of the model (using software O) took place alternately during the entire refinement process. Restrictive NCS was used at the beginning of the refinement, and was disused once the structural adjustment was basically accomplished. When R_{work} factor (<0.30) and R_{free} factor practically stopped descending, water and solvent molecules were added to the structure to complete the structure rectification. The major indices for the rectification were a R_{work} value of 0.250 and a R_{free} value of 0.286. The major indices of the final rSIFN-co structure rectification are listed in Table 4. The resulting atomic coordinates of rSIFN-co are shown in Table 7.

TABLE 4

Major parameter indices and qualitative statistical results of rSIFN-co molecular structure

Resolution ratio range(outermost shell) (Å)	20.0-2.6
Cutoff point of signal-to-noise	0.0
Crystallographic incongruent indexes (outermost shell) (%)	25.0(36.3)
Free incongruent indexes[1] (outermost shell) (%)	28.6(40.5)
Component of asymmetric unit	
Number of all the residues	293
Number of A chain residues (unbuilt residues)	146 (20)
Number of B chain residues (unbuilt residues)	147 (19)
Molecular number of water and solvent	123
Root mean square deviation[2]	
Bond length (Å)	0.007
Bond angle (°)	1.379
Dihedral angle (°)	19.234
Unfit angle (°)	0.844
Wilson temperature factor ($Å^2$)	70.7
Average temperature factor ($Å^2$)	
Number of all the atoms (2403)	61.76
Atomic number of protein (2254)	61.11
A chain of protein (1120)	58.39
B chain of protein (1134)	63.79
water and solvent (149)	68.21
Statistics of Ramachandran plot (%)[3]	
Optimal regions	90.6
Additionally allowed regions	9.1
common allowed regions	0.4
Disallowed regions	0.0

[1] Free incongruent indices were calculated using 10% of the total diffraction points unmodified;

[2] Root mean square deviation was calculated using relative standard bond length/ bond angle;

[3] Statistics of Ramachandran plot used software PROCHECK.

EXAMPLE 9

Quality Characterization of the quality of the rSIFN-co Molecular Structural Model

Quality Characterization of the quality of the rSIFN-co molecular structural model

[0172] The model: rSIFN-co was displayed intuitively, clearly and accurately. Figure 3 is a typical electron density map matching to the structure of the amino acid residues in a rSIFN-co molecule; the spatial location and orientation of each amino acid residue could be clearly identified.

[0173] (2) Distribution map of the average temperature factors associated with the amino acid residues. (Fig. 4)

[0174] (3) Stereochemical rationality of the rSIFN-co molecule was characterized in the Ramachandran conformational plot (Figure 5), and showed that 90.6% of its amino acid residues were located in the optimal allowed regions, 9.1% were in the allowed regions, 0.4% were in the common allowed regions. This demonstrated that the rSIFN-co molecular structural model was stereochemically rational.

EXAMPLE 10

Crystal Structure Characteristics of the crystal structure of the rSIFN-co Molecule

Stacking and global assignment of the rSIFN-co molecule in a crystal

[0175] Figure 6 shows the stacking manner of the rSIFN-co molecule in an unit cell. An asymmetric unit in the rSIFN-co crystal structure was made of two protein molecules (called crystallographic dimers) (Fig. 7). The embedding area between the dimers was 1033.3Å^2 with each monomer contributing 516.6Å^2.This only accounted for 6.4% of the total area in the monomer. The A, B, F sides of the A chain in the dimer corresponded to the C, D, E sides of the B chain (see Fig. 9). Using the software VADAR, the folding free energies of the monomer and dimer were calculated as -126.9 and -257.1 respectively, which meant that the folding free energy of the dimer was quite close to the free energy of the two isolated

monomers (-126.9×2). This demonstrated that the interaction between the dimers was relatively weakand there were only two weak hydrogen bonds between them A12(ARG) NH2...NH2 B71(Arg), 3.05Å; A145(Arg) NH1...OH B90 (Tyr), 3.14Å.

[0176] The purification process showed that rSIFN-co existed as monomers in solution; the current biochemical function experiments showed that the functional unit of the likes of IFN-α should be monomeric. Therefore, this dimer might be formed from the stacking of crystals.

Dimer Structure of the dimers

[0177] Two single rSIFN-co molecules in an asymmetric unit form one dimer. Figure 8 shows the crystallographic dimeric organization of rSIFN-co. Chain A consisted of residues 11-103 and 111-163 (residues 1-10, 104-110 and 164-166, were not involved in building of this crystal structure since they were not shown in the electron density map); chain B consisted of residues 11-103 and 110-163 (residues 1-10, 104-109, and 164-166, were not involved in building of this crystal structure since they were not shown in the electron density map). In the crystal structure of each monomer, it was observed that the Cys29 and Cys139 formed an intramolecular disulfide bond; the intramolecular disulfide bond from Cys1 and Cys99 was not shown because Cys1 was not involved in building of this crystal structure. Besides, since the density of the side chains were not shown, residues 30-33, 47-49 of chain A and residues 30- 33, 48-50 of chain B were mainly constructed as Ala or Gly. The structures of the two monomers were roughly the same and were linked by non-crystallographic symmetry (from B to A, polar angles Omega, Phi, Kappa were 170.64, 94.56, 118.35, respectively; tx, ty, tz were -1.061, -0.225, 0.155 respectively.). The two monomers were superimposed and compared; apart from the regional flexibility of a few loops on the molecular surface, most of the residues superimposed completely. The distribution of the RMSD of all the Cα associated with the amino acid residues are shown in Figure 8c; 127 residues (13-30, 34-44, 53-101, 115-163) had a RMSD of 0.64 Å for all Cα . The difference in the local structure might be a result of the comparatively large flexibility of this protein and the differences in the environment where the crystal stacked.

Structure of a single molecule

[0178] Each monomer was made up of six α-helices (A, C, C', D, E, F) and one 310 helix (B), which were connected to each other by the connecting peptides between them; the fold of the monomer structure belonged to the helical cytokines (Fig. 9). The amino-acid

residues which corresponded to the six α-helices (A, C, C', D, E, F) were 13-20, 50-68, 70-76, 79-100, 114-133, and 138-160, respectively. Residues 40-43 corresponded to the 310 helix (B). The distribution and organization of these secondary structures are shown clearly in Figure 9. The corresponding relationship between the secondary structures and the amino acid sequence is shown in Figure 10.

Example 11

The three Dimensional Structure of rSIFN-co and IFN-α2b

[0179] Based on their receptors, IFN can broadly be divided into two types: type I and type II. Type I can further be sub-divided into α, β, ω, etc. IFN-α, in turn, contains approximately fifteen different sub-types; the different IFN-α subtypes have sequence homologies of above 80% yet they exhibit diversity in their functions. rSIFN-co is considered to be an unnatural and artificially designed protein. To date, there are only six 3-D structures of type I IFNs (Table 5) and their sequence homology can be seen in the aligned sequences shown in Figure 11.

[0180] From the comparative analysis shown in Table 5 and Figure 11, the crystal structure of IFN-α2b showed the highest similarity to that of rSIFN-co (Fig. 12). It was found, by comparing their sequences, that rSIFN-co had one more Asp (D) than IFN-α2b at residue 45; and, by comparing their 3D structures, rSIFN-co differed markedly from IFN- α2b with respect to the conformation of the AB loop (residues 25-33) and the BC loop (residues 44 -52). The crystal structure of IFN-α2b had been determined at a resolution of 2.9 Å; however, except for the Cα, the coordinates of all other atoms were absent in the Protein Data Bank (PDB code: 1RH2) such that structural comparison between rSIFN-co and IFN-α2b was carried out only at the Cα level. The overall RMSD of all the Cα of the two molecules was 1.577Å; but in the AB loop and BC loop, the RMSD was 3.63Å and 2.9 Å, which were 2.5 times and 2 times that of the total average, respectively. Besides, rSIFN-co contained two molecules in the asymmetric unit of its crystal structure while IFN-α2b had six protein molecules, composed of 3 dimers, in its asymmetric unit. Obviously, the dimeric organization of rSIFN-co was distinctly different from IFN-α2b (Fig. 13).

Table 5

The determined structures of IFNs

Protein name	Source	Method	**Resolution** (Å)	PDB code	Identify of rSIFN-co
rSIFN-co	Synthesis	X-ray	2.6	This invention	
IFN-α 2b	Human	X-ray	2.9	1RH2 (Only Cα)	89%
IFN-α 2a	Human	NMR		1ITF	88%
IFN-τ	Human	X-ray	2.1	1B5L	54%
IFN-β	Human	X-ray	2.2	1AU1	30%
IFN-β	Mouse	X-ray	2.2	1RMI	23%

[0181] It is known that IFN, as a cytokine, first binds with specific receptors on the cell membrane to activate several signal transduction pathways that will generate biological effects in the body, such as antivirus and antitumor effects. rSIFN-co is a type of IFN-α. Since its receptor on the cell membrane is made up of IFNAR1 and IFNAR2, a 3D model of receptor binding with IFN-α was constructed (Fig. 15a). A series of molecular biology experiments were conducted based on this model and the results suggested that IFN-α–like proteins interacted with IFNAR1 and IFNAR2 in a sandwich structure (Fig. 15a), i.e., sides A, B and F interacted with IFNAR2, and the opposite sides C, D, and E interacted with IFNAR1. Meanwhile, site-directed mutagenesis revealed that the AB loop, which interacted with IFNAR2, was the main constituent of the active site of IFN-α-like proteins (Fig. 15). Structural comparison showed that the structure of this important region was distinctly different between rSIFN-co and IFN-α2b (Fig. 12, Table 6). Structural differences in this important region may trigger different physiological or pharmacological effects as a result of changes in the binding characteristics with receptors.

[0182] Apparently, although the molecular skeleton of rSIFN-co was similar to that of IFN-α2b, they differed markedly in the structure of their active sites. Therefore, judging from the local structure closely related to the pharmacological activities of the molecules, it was found that rSIFN-co was a new type of IFN different from IFN-α2b, and their structural differences had led to distinctly different biological and pharmacological characteristics.

Based on the differences in the specific key region of its three dimension structure, rSIFN-co might produce unique physiological and pharmacological effects.

TABLE 6

Root-Mean-Square Deviation (RMSD) of Cα between AB Loop and BC Loop of rSIFN-co and IFN-α2b (unit: Å)

Residue number of AB Loop	RMSD (Å)	Residue number of BC Loop	RMSD (Å)
25	3.291	44	1.164
26	4.779	45	1.383
27	5.090	46	2.735
28	3.588	47	2.709
29	2.567	48	5.018
30	2.437	49	4.140
31	3.526	50	3.809
32	4.820	51	2.970
33	2.756	52	0.881
Average RMSD of AB Loop	3.63	Average RMSD of BC Loop	2.90
RMSD of all Cα atoms		1.60	

Table 7

Atomic coordinates of rSIFN-co

CRYST1	77.920	77.920	125.935	90.00	90.00	120.00	P 31 2 1				
ATOM	1	CB	ASN	A	11	-36.673	14.399	-31.951	1.00	79.36	A
ATOM	2	CG	ASN	A	11	-37.660	14.647	-33.090	1.00	81.91	A
ATOM	3	OD1	ASN	A	11	-37.274	14.829	-34.245	1.00	85.24	A
ATOM	4	ND2	ASN	A	11	-38.947	14.622	-32.764	1.00	82.54	A
ATOM	5	C	ASN	A	11	-34.980	16.273	-31.802	1.00	76.68	A
ATOM	6	O	ASN	A	11	-34.061	16.507	-31.007	1.00	76.57	A
ATOM	7	N	ASN	A	11	-34.283	13.985	-31.533	1.00	78.32	A
ATOM	8	CA	ASN	A	11	-35.239	14.843	-32.283	1.00	77.86	A
ATOM	9	N	ARG	A	12	-35.760	17.226	-32.307	1.00	74.41	A
ATOM	10	CA	ARG	A	12	-35.635	18.622	-31.899	1.00	69.90	A
ATOM	11	CB	ARG	A	12	-35.404	19.525	-33.115	1.00	72.01	A
ATOM	12	CG	ARG	A	12	-34.052	19.300	-33.792	1.00	77.29	A
ATOM	13	CD	ARG	A	12	-33.757	20.318	-34.894	1.00	79.77	A
ATOM	14	NE	ARG	A	12	-32.967	21.461	-34.430	1.00	83.05	A
ATOM	15	CZ	ARG	A	12	-31.669	21.635	-34.679	1.00	84.53	A
ATOM	16	NH1	ARG	A	12	-30.994	20.740	-35.390	1.00	85.41	A
ATOM	17	NH2	ARG	A	12	-31.049	22.721	-34.235	1.00	84.48	A
ATOM	18	C	ARG	A	12	-36.917	19.021	-31.174	1.00	65.99	A
ATOM	19	O	ARG	A	12	-37.334	20.177	-31.210	1.00	65.41	A
ATOM	20	N	ARG	A	13	-37.530	18.037	-30.521	1.00	61.78	A
ATOM	21	CA	ARG	A	13	-38.757	18.209	-29.750	1.00	58.49	A
ATOM	22	CB	ARG	A	13	-39.049	16.937	-28.963	1.00	61.57	A
ATOM	23	CG	ARG	A	13	-40.120	16.061	-29.535	1.00	66.89	A
ATOM	24	CD	ARG	A	13	-40.996	15.577	-28.414	1.00	69.61	A
ATOM	25	NE	ARG	A	13	-42.336	16.134	-28.518	1.00	72.80	A
ATOM	26	CZ	ARG	A	13	-43.253	16.035	-27.562	1.00	75.39	A
ATOM	27	NH1	ARG	A	13	-42.964	15.403	-26.425	1.00	74.38	A
ATOM	28	NH2	ARG	A	13	-44.462	16.555	-27.748	1.00	76.67	A
ATOM	29	C	ARG	A	13	-38.720	19.378	-28.767	1.00	54.28	A
ATOM	30	O	ARG	A	13	-39.709	20.098	-28.625	1.00	54.11	A
ATOM	31	N	ALA	A	14	-37.597	19.555	-28.075	1.00	48.77	A
ATOM	32	CA	ALA	A	14	-37.481	20.645	-27.116	1.00	45.39	A
ATOM	33	CB	ALA	A	14	-36.082	20.689	-26.526	1.00	44.44	A
ATOM	34	C	ALA	A	14	-37.816	21.984	-27.762	1.00	43.36	A
ATOM	35	O	ALA	A	14	-38.656	22.723	-27.262	1.00	42.76	A
ATOM	36	N	LEU	A	15	-37.169	22.287	-28.879	1.00	40.93	A
ATOM	37	CA	LEU	A	15	-37.402	23.542	-29.568	1.00	39.71	A
ATOM	38	CB	LEU	A	15	-36.364	23.730	-30.669	1.00	39.82	A
ATOM	39	CG	LEU	A	15	-34.952	23.714	-30.072	1.00	40.23	A
ATOM	40	CD1	LEU	A	15	-33.913	23.928	-31.151	1.00	39.64	A
ATOM	41	CD2	LEU	A	15	-34.850	24.800	-29.005	1.00	40.94	A
ATOM	42	C	LEU	A	15	-38.802	23.667	-30.130	1.00	40.00	A
ATOM	43	O	LEU	A	15	-39.372	24.751	-30.100	1.00	39.95	A
ATOM	44	N	ILE	A	16	-39.364	22.572	-30.638	1.00	40.32	A
ATOM	45	CA	ILE	A	16	-40.730	22.601	-31.179	1.00	40.64	A
ATOM	46	CB	ILE	A	16	-41.213	21.189	-31.637	1.00	43.33	A
ATOM	47	CG2	ILE	A	16	-42.605	21.283	-32.231	1.00	41.37	A
ATOM	48	CG1	ILE	A	16	-40.257	20.590	-32.673	1.00	44.72	A

ATOM	49	CD1	ILE	A	16	-40.190	21.342	-33.941	1.00	46.03	A
ATOM	50	C	ILE	A	16	-41.682	23.087	-30.080	1.00	41.12	A
ATOM	51	O	ILE	A	16	-42.425	24.051	-30.271	1.00	41.43	A
ATOM	52	N	LEU	A	17	-41.662	22.411	-28.930	1.00	40.37	A
ATOM	53	CA	LEU	A	17	-42.516	22.794	-27.812	1.00	41.00	A
ATOM	54	CB	LEU	A	17	-42.303	21.837	-26.640	1.00	42.66	A
ATOM	55	CG	LEU	A	17	-42.835	20.411	-26.850	1.00	43.03	A
ATOM	56	CD1	LEU	A	17	-42.045	19.434	-25.983	1.00	39.82	A
ATOM	57	CD2	LEU	A	17	-44.328	20.368	-26.526	1.00	40.26	A
ATOM	58	C	LEU	A	17	-42.257	24.233	-27.359	1.00	40.48	A
ATOM	59	O	LEU	A	17	-43.187	25.022	-27.212	1.00	39.35	A
ATOM	60	N	LEU	A	18	-40.986	24.574	-27.161	1.00	40.86	A
ATOM	61	CA	LEU	A	18	-40.594	25.909	-26.718	1.00	40.17	A
ATOM	62	CB	LEU	A	18	-39.073	25.973	-26.597	1.00	40.05	A
ATOM	63	CG	LEU	A	18	-38.378	26.953	-25.641	1.00	42.40	A
ATOM	64	CD1	LEU	A	18	-37.548	27.948	-26.430	1.00	42.15	A
ATOM	65	CD2	LEU	A	18	-39.393	27.657	-24.767	1.00	43.03	A
ATOM	66	C	LEU	A	18	-41.094	26.966	-27.698	1.00	40.88	A
ATOM	67	O	LEU	A	18	-41.230	28.137	-27.345	1.00	39.41	A
ATOM	68	N	ALA	A	19	-41.373	26.539	-28.929	1.00	41.87	A
ATOM	69	CA	ALA	A	19	-41.861	27.432	-29.975	1.00	44.08	A
ATOM	70	CB	ALA	A	19	-41.536	26.866	-31.358	1.00	42.64	A
ATOM	71	C	ALA	A	19	-43.359	27.594	-29.830	1.00	46.35	A
ATOM	72	O	ALA	A	19	-43.905	28.665	-30.090	1.00	47.47	A
ATOM	73	N	GLN	A	20	-44.017	26.517	-29.417	1.00	48.12	A
ATOM	74	CA	GLN	A	20	-45.462	26.519	-29.224	1.00	50.49	A
ATOM	75	CB	GLN	A	20	-45.986	25.075	-29.111	1.00	51.83	A
ATOM	76	CG	GLN	A	20	-45.540	24.097	-30.195	1.00	53.52	A
ATOM	77	CD	GLN	A	20	-46.151	22.712	-29.999	1.00	55.01	A
ATOM	78	OE1	GLN	A	20	-45.806	21.745	-30.693	1.00	52.54	A
ATOM	79	NE2	GLN	A	20	-47.069	22.614	-29.046	1.00	56.71	A
ATOM	80	C	GLN	A	20	-45.855	27.284	-27.941	1.00	51.19	A
ATOM	81	O	GLN	A	20	-47.024	27.634	-27.745	1.00	51.17	A
ATOM	82	N	MET	A	21	-44.874	27.541	-27.080	1.00	49.97	A
ATOM	83	CA	MET	A	21	-45.110	28.204	-25.802	1.00	48.63	A
ATOM	84	CB	MET	A	21	-44.002	27.808	-24.822	1.00	46.02	A
ATOM	85	CG	MET	A	21	-44.097	26.374	-24.330	1.00	43.96	A
ATOM	86	SD	MET	A	21	-42.595	25.764	-23.516	1.00	47.28	A
ATOM	87	CE	MET	A	21	-42.353	27.001	-22.206	1.00	42.84	A
ATOM	88	C	MET	A	21	-45.272	29.723	-25.809	1.00	49.74	A
ATOM	89	O	MET	A	21	-45.696	30.303	-24.807	1.00	49.63	A
ATOM	90	N	ALA	A	22	-44.950	30.375	-26.922	1.00	51.41	A
ATOM	91	CA	ALA	A	22	-45.075	31.828	-26.978	1.00	53.11	A
ATOM	92	CB	ALA	A	22	-44.641	32.362	-28.341	1.00	52.27	A
ATOM	93	C	ALA	A	22	-46.517	32.196	-26.716	1.00	53.84	A
ATOM	94	O	ALA	A	22	-47.428	31.552	-27.227	1.00	52.97	A
ATOM	95	N	ARG	A	23	-46.719	33.225	-25.904	1.00	56.56	A
ATOM	96	CA	ARG	A	23	-48.064	33.683	-25.581	1.00	59.73	A
ATOM	97	CB	ARG	A	23	-48.367	33.484	-24.094	1.00	60.59	A
ATOM	98	CG	ARG	A	23	-48.309	32.059	-23.604	1.00	62.22	A
ATOM	99	CD	ARG	A	23	-48.845	31.998	-22.183	1.00	66.26	A
ATOM	100	NE	ARG	A	23	-50.250	32.397	-22.143	1.00	70.17	A
ATOM	101	CZ	ARG	A	23	-50.744	33.339	-21.345	1.00	71.62	A

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ATOM    102  NH1 ARG A  23     -49.946  33.985 -20.504  1.00 71.69      A
ATOM    103  NH2 ARG A  23     -52.035  33.652 -21.405  1.00 72.49      A
ATOM    104  C   ARG A  23     -48.242  35.158 -25.921  1.00 61.02      A
ATOM    105  O   ARG A  23     -49.334  35.584 -26.284  1.00 62.43      A
ATOM    106  N   ALA A  24     -47.171  35.937 -25.799  1.00 61.98      A
ATOM    107  CA  ALA A  24     -47.236  37.366 -26.080  1.00 63.61      A
ATOM    108  CB  ALA A  24     -46.139  38.093 -25.319  1.00 62.75      A
ATOM    109  C   ALA A  24     -47.139  37.676 -27.570  1.00 65.56      A
ATOM    110  O   ALA A  24     -46.450  36.983 -28.322  1.00 65.76      A
ATOM    111  N   SER A  25     -47.848  38.724 -27.984  1.00 67.91      A
ATOM    112  CA  SER A  25     -47.865  39.157 -29.373  1.00 69.93      A
ATOM    113  CB  SER A  25     -49.175  39.887 -29.698  1.00 71.12      A
ATOM    114  OG  SER A  25     -50.227  38.952 -29.909  1.00 72.49      A
ATOM    115  C   SER A  25     -46.663  40.064 -29.610  1.00 71.13      A
ATOM    116  O   SER A  25     -46.236  40.806 -28.726  1.00 71.22      A
ATOM    117  N   PRO A  26     -46.109  40.027 -30.825  1.00 71.97      A
ATOM    118  CD  PRO A  26     -46.787  39.560 -32.046  1.00 72.50      A
ATOM    119  CA  PRO A  26     -44.938  40.842 -31.165  1.00 73.26      A
ATOM    120  CB  PRO A  26     -44.887  40.767 -32.702  1.00 73.01      A
ATOM    121  CG  PRO A  26     -45.664  39.526 -33.023  1.00 72.89      A
ATOM    122  C   PRO A  26     -45.008  42.284 -30.673  1.00 74.39      A
ATOM    123  O   PRO A  26     -43.979  42.872 -30.322  1.00 74.28      A
ATOM    124  N   PHE A  27     -46.212  42.856 -30.653  1.00 75.25      A
ATOM    125  CA  PHE A  27     -46.375  44.245 -30.222  1.00 75.22      A
ATOM    126  CB  PHE A  27     -47.502  44.910 -30.995  1.00 75.78      A
ATOM    127  CG  PHE A  27     -47.305  44.909 -32.463  1.00 77.48      A
ATOM    128  CD1 PHE A  27     -47.573  43.765 -33.204  1.00 79.44      A
ATOM    129  CD2 PHE A  27     -46.788  46.029 -33.106  1.00 77.96      A
ATOM    130  CE1 PHE A  27     -47.347  43.738 -34.579  1.00 80.53      A
ATOM    131  CE2 PHE A  27     -46.557  46.022 -34.472  1.00 79.57      A
ATOM    132  CZ  PHE A  27     -46.826  44.870 -35.215  1.00 80.89      A
ATOM    133  C   PHE A  27     -46.635  44.449 -28.737  1.00 74.52      A
ATOM    134  O   PHE A  27     -46.415  45.540 -28.218  1.00 74.03      A
ATOM    135  N   ALA A  28     -47.097  43.411 -28.052  1.00 74.01      A
ATOM    136  CA  ALA A  28     -47.394  43.532 -26.637  1.00 73.15      A
ATOM    137  CB  ALA A  28     -47.812  42.175 -26.080  1.00 73.48      A
ATOM    138  C   ALA A  28     -46.241  44.112 -25.822  1.00 73.09      A
ATOM    139  O   ALA A  28     -46.460  44.586 -24.707  1.00 74.58      A
ATOM    140  N   CYS A  29     -45.030  44.090 -26.383  1.00 72.82      A
ATOM    141  CA  CYS A  29     -43.820  44.598 -25.713  1.00 73.33      A
ATOM    142  C   CYS A  29     -42.968  45.450 -26.659  1.00 74.96      A
ATOM    143  O   CYS A  29     -43.340  45.648 -27.812  1.00 75.82      A
ATOM    144  CB  CYS A  29     -42.967  43.432 -25.217  1.00 71.43      A
ATOM    145  SG  CYS A  29     -43.896  42.126 -24.366  1.00 69.57      A
ATOM    146  N   GLY A  30     -41.814  45.931 -26.192  1.00 76.71      A
ATOM    147  CA  GLY A  30     -40.990  46.756 -27.065  1.00 79.56      A
ATOM    148  C   GLY A  30     -39.496  46.977 -26.848  1.00 81.04      A
ATOM    149  O   GLY A  30     -38.987  47.036 -25.725  1.00 80.04      A
ATOM    150  N   GLY A  31     -38.800  47.111 -27.976  1.00 83.09      A
ATOM    151  CA  GLY A  31     -37.365  47.369 -27.994  1.00 86.03      A
ATOM    152  C   GLY A  31     -36.448  46.384 -27.283  1.00 86.91      A
ATOM    153  O   GLY A  31     -36.097  45.330 -27.822  1.00 87.85      A
ATOM    154  N   GLY A  32     -36.030  46.767 -26.078  1.00 86.34      A
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ATOM    155  CA  GLY A  32     -35.161  45.949 -25.244  1.00 85.69      A
ATOM    156  C   GLY A  32     -34.216  44.887 -25.810  1.00 84.42      A
ATOM    157  O   GLY A  32     -34.386  43.694 -25.541  1.00 84.88      A
ATOM    158  N   GLY A  33     -33.200  45.298 -26.562  1.00 82.49      A
ATOM    159  CA  GLY A  33     -32.247  44.327 -27.076  1.00 81.23      A
ATOM    160  C   GLY A  33     -31.315  43.958 -25.929  1.00 80.18      A
ATOM    161  O   GLY A  33     -30.199  44.473 -25.846  1.00 79.67      A
ATOM    162  N   HIS A  34     -31.768  43.066 -25.048  1.00 79.01      A
ATOM    163  CA  HIS A  34     -30.984  42.654 -23.881  1.00 76.91      A
ATOM    164  CB  HIS A  34     -31.932  42.245 -22.742  1.00 76.85      A
ATOM    165  CG  HIS A  34     -31.313  42.323 -21.381  1.00 76.31      A
ATOM    166  CD2 HIS A  34     -31.596  43.113 -20.319  1.00 76.73      A
ATOM    167  ND1 HIS A  34     -30.249  41.534 -20.995  1.00 76.92      A
ATOM    168  CE1 HIS A  34     -29.905  41.835 -19.756  1.00 76.89      A
ATOM    169  NE2 HIS A  34     -30.707  42.791 -19.322  1.00 77.36      A
ATOM    170  C   HIS A  34     -29.992  41.525 -24.168  1.00 74.89      A
ATOM    171  O   HIS A  34     -30.383  40.450 -24.635  1.00 75.01      A
ATOM    172  N   ASP A  35     -28.716  41.783 -23.869  1.00 71.97      A
ATOM    173  CA  ASP A  35     -27.631  40.823 -24.089  1.00 69.11      A
ATOM    174  CB  ASP A  35     -26.366  41.561 -24.542  1.00 71.02      A
ATOM    175  CG  ASP A  35     -25.270  40.617 -25.018  1.00 73.48      A
ATOM    176  OD1 ASP A  35     -25.490  39.904 -26.022  1.00 76.44      A
ATOM    177  OD2 ASP A  35     -24.183  40.591 -24.398  1.00 74.76      A
ATOM    178  C   ASP A  35     -27.318  40.010 -22.837  1.00 66.06      A
ATOM    179  O   ASP A  35     -26.862  40.554 -21.830  1.00 66.03      A
ATOM    180  N   PHE A  36     -27.558  38.705 -22.900  1.00 61.83      A
ATOM    181  CA  PHE A  36     -27.282  37.853 -21.757  1.00 57.75      A
ATOM    182  CB  PHE A  36     -28.283  36.698 -21.674  1.00 57.18      A
ATOM    183  CG  PHE A  36     -29.696  37.146 -21.442  1.00 56.02      A
ATOM    184  CD1 PHE A  36     -30.556  37.357 -22.505  1.00 55.11      A
ATOM    185  CD2 PHE A  36     -30.148  37.415 -20.159  1.00 56.96      A
ATOM    186  CE1 PHE A  36     -31.847  37.827 -22.296  1.00 56.30      A
ATOM    187  CE2 PHE A  36     -31.441  37.889 -19.939  1.00 56.70      A
ATOM    188  CZ  PHE A  36     -32.289  38.097 -21.010  1.00 56.38      A
ATOM    189  C   PHE A  36     -25.870  37.326 -21.835  1.00 55.62      A
ATOM    190  O   PHE A  36     -25.367  36.747 -20.882  1.00 55.22      A
ATOM    191  N   GLY A  37     -25.233  37.534 -22.982  1.00 53.97      A
ATOM    192  CA  GLY A  37     -23.859  37.103 -23.163  1.00 52.66      A
ATOM    193  C   GLY A  37     -23.589  35.614 -23.171  1.00 52.31      A
ATOM    194  O   GLY A  37     -22.627  35.140 -22.572  1.00 52.88      A
ATOM    195  N   PHE A  38     -24.439  34.868 -23.856  1.00 52.34      A
ATOM    196  CA  PHE A  38     -24.272  33.428 -23.960  1.00 53.26      A
ATOM    197  CB  PHE A  38     -25.329  32.873 -24.925  1.00 50.67      A
ATOM    198  CG  PHE A  38     -25.161  31.424 -25.244  1.00 48.53      A
ATOM    199  CD1 PHE A  38     -25.352  30.457 -24.264  1.00 47.04      A
ATOM    200  CD2 PHE A  38     -24.793  31.023 -26.529  1.00 47.77      A
ATOM    201  CE1 PHE A  38     -25.177  29.110 -24.559  1.00 47.91      A
ATOM    202  CE2 PHE A  38     -24.615  29.676 -26.834  1.00 46.88      A
ATOM    203  CZ  PHE A  38     -24.806  28.719 -25.850  1.00 48.21      A
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ATOM    205  O   PHE A  38     -22.481  33.579 -25.547  1.00 55.48      A
ATOM    206  N   PRO A  39     -22.071  32.327 -23.724  1.00 56.41      A
ATOM    207  CD  PRO A  39     -22.373  31.704 -22.422  1.00 56.33      A
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ATOM    208  CA  PRO A  39     -20.711  31.982 -24.158  1.00 57.36      A
ATOM    209  CB  PRO A  39     -20.084  31.414 -22.889  1.00 55.84      A
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ATOM    211  C   PRO A  39     -20.705  30.974 -25.318  1.00 59.32      A
ATOM    212  O   PRO A  39     -20.292  29.824 -25.153  1.00 59.38      A
ATOM    213  N   GLN A  40     -21.159  31.428 -26.487  1.00 61.42      A
ATOM    214  CA  GLN A  40     -21.235  30.616 -27.710  1.00 63.86      A
ATOM    215  CB  GLN A  40     -21.539  31.520 -28.911  1.00 65.01      A
ATOM    216  CG  GLN A  40     -21.996  30.776 -30.148  1.00 67.78      A
ATOM    217  CD  GLN A  40     -22.372  31.713 -31.297  1.00 70.50      A
ATOM    218  OE1 GLN A  40     -22.885  32.818 -31.079  1.00 70.05      A
ATOM    219  NE2 GLN A  40     -22.135  31.262 -32.528  1.00 69.96      A
ATOM    220  C   GLN A  40     -19.979  29.797 -28.011  1.00 64.05      A
ATOM    221  O   GLN A  40     -20.064  28.709 -28.577  1.00 62.19      A
ATOM    222  N   GLU A  41     -18.821  30.329 -27.630  1.00 66.08      A
ATOM    223  CA  GLU A  41     -17.537  29.667 -27.854  1.00 68.16      A
ATOM    224  CB  GLU A  41     -16.405  30.478 -27.216  1.00 68.78      A
ATOM    225  CG  GLU A  41     -16.575  31.993 -27.302  1.00 71.65      A
ATOM    226  CD  GLU A  41     -17.599  32.538 -26.309  1.00 71.91      A
ATOM    227  OE1 GLU A  41     -17.436  32.289 -25.095  1.00 70.55      A
ATOM    228  OE2 GLU A  41     -18.558  33.220 -26.742  1.00 72.43      A
ATOM    229  C   GLU A  41     -17.514  28.249 -27.276  1.00 69.40      A
ATOM    230  O   GLU A  41     -16.971  27.327 -27.884  1.00 70.02      A
ATOM    231  N   GLU A  42     -18.107  28.081 -26.098  1.00 70.37      A
ATOM    232  CA  GLU A  42     -18.134  26.784 -25.437  1.00 70.92      A
ATOM    233  CB  GLU A  42     -18.816  26.907 -24.073  1.00 70.33      A
ATOM    234  CG  GLU A  42     -18.096  27.839 -23.108  1.00 70.66      A
ATOM    235  CD  GLU A  42     -16.674  27.387 -22.810  1.00 71.66      A
ATOM    236  OE1 GLU A  42     -15.901  28.192 -22.245  1.00 71.99      A
ATOM    237  OE2 GLU A  42     -16.329  26.228 -23.134  1.00 70.35      A
ATOM    238  C   GLU A  42     -18.817  25.703 -26.263  1.00 72.31      A
ATOM    239  O   GLU A  42     -18.658  24.515 -25.982  1.00 71.27      A
ATOM    240  N   PHE A  43     -19.565  26.115 -27.285  1.00 74.43      A
ATOM    241  CA  PHE A  43     -20.279  25.169 -28.142  1.00 77.01      A
ATOM    242  CB  PHE A  43     -21.801  25.343 -27.982  1.00 73.77      A
ATOM    243  CG  PHE A  43     -22.266  25.393 -26.551  1.00 70.14      A
ATOM    244  CD1 PHE A  43     -22.212  26.580 -25.829  1.00 69.12      A
ATOM    245  CD2 PHE A  43     -22.728  24.249 -25.916  1.00 69.47      A
ATOM    246  CE1 PHE A  43     -22.608  26.627 -24.498  1.00 66.90      A
ATOM    247  CE2 PHE A  43     -23.126  24.287 -24.579  1.00 68.62      A
ATOM    248  CZ  PHE A  43     -23.065  25.480 -23.873  1.00 67.55      A
ATOM    249  C   PHE A  43     -19.904  25.329 -29.620  1.00 80.52      A
ATOM    250  O   PHE A  43     -19.615  24.350 -30.312  1.00 80.71      A
ATOM    251  N   GLY A  44     -19.917  26.571 -30.093  1.00 84.43      A
ATOM    252  CA  GLY A  44     -19.594  26.849 -31.483  1.00 87.53      A
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ATOM    254  O   GLY A  44     -17.397  27.829 -31.367  1.00 89.88      A
ATOM    255  N   GLY A  45     -17.642  25.933 -32.564  1.00 91.49      A
ATOM    256  CA  GLY A  45     -16.243  25.889 -32.936  1.00 93.11      A
ATOM    257  C   GLY A  45     -15.734  24.468 -33.038  1.00 94.05      A
ATOM    258  O   GLY A  45     -16.213  23.577 -32.333  1.00 93.98      A
ATOM    259  N   GLY A  46     -14.767  24.255 -33.925  1.00 94.77      A
ATOM    260  CA  GLY A  46     -14.195  22.935 -34.098  1.00 95.42      A
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ATOM    261  C   GLY A  46     -13.231  22.606 -32.972  1.00 95.90      A
ATOM    262  O   GLY A  46     -12.194  21.976 -33.199  1.00 96.10      A
ATOM    263  N   GLY A  47     -13.570  23.040 -31.759  1.00 95.61      A
ATOM    264  CA  GLY A  47     -12.726  22.778 -30.606  1.00 95.48      A
ATOM    265  C   GLY A  47     -12.428  21.298 -30.455  1.00 95.42      A
ATOM    266  O   GLY A  47     -11.319  20.921 -30.073  1.00 95.45      A
ATOM    267  N   GLY A  48     -13.425  20.466 -30.760  1.00 94.95      A
ATOM    268  CA  GLY A  48     -13.272  19.023 -30.674  1.00 93.55      A
ATOM    269  C   GLY A  48     -12.943  18.541 -29.279  1.00 93.16      A
ATOM    270  O   GLY A  48     -12.016  19.041 -28.649  1.00 94.44      A
ATOM    271  N   ALA A  49     -13.705  17.566 -28.796  1.00 91.77      A
ATOM    272  CA  ALA A  49     -13.507  17.000 -27.463  1.00 90.57      A
ATOM    273  CB  ALA A  49     -13.219  18.103 -26.449  1.00 90.50      A
ATOM    274  C   ALA A  49     -14.771  16.245 -27.069  1.00 89.91      A
ATOM    275  O   ALA A  49     -15.801  16.855 -26.774  1.00 90.84      A
ATOM    276  N   GLY A  50     -14.690  14.919 -27.068  1.00 88.13      A
ATOM    277  CA  GLY A  50     -15.844  14.113 -26.727  1.00 86.16      A
ATOM    278  C   GLY A  50     -16.495  14.504 -25.416  1.00 85.07      A
ATOM    279  O   GLY A  50     -17.671  14.870 -25.387  1.00 84.82      A
ATOM    280  N   ALA A  51     -15.721  14.442 -24.335  1.00 83.62      A
ATOM    281  CA  ALA A  51     -16.211  14.753 -22.992  1.00 81.83      A
ATOM    282  CB  ALA A  51     -15.276  14.138 -21.955  1.00 82.10      A
ATOM    283  C   ALA A  51     -16.424  16.235 -22.685  1.00 79.92      A
ATOM    284  O   ALA A  51     -17.409  16.602 -22.049  1.00 79.80      A
ATOM    285  N   ALA A  52     -15.504  17.088 -23.115  1.00 77.79      A
ATOM    286  CA  ALA A  52     -15.655  18.511 -22.852  1.00 76.55      A
ATOM    287  CB  ALA A  52     -14.469  19.286 -23.424  1.00 76.24      A
ATOM    288  C   ALA A  52     -16.965  19.027 -23.450  1.00 75.56      A
ATOM    289  O   ALA A  52     -17.473  20.072 -23.037  1.00 76.89      A
ATOM    290  N   ALA A  53     -17.510  18.288 -24.416  1.00 72.47      A
ATOM    291  CA  ALA A  53     -18.756  18.677 -25.080  1.00 68.45      A
ATOM    292  CB  ALA A  53     -18.737  18.220 -26.532  1.00 69.53      A
ATOM    293  C   ALA A  53     -19.980  18.108 -24.374  1.00 64.99      A
ATOM    294  O   ALA A  53     -21.033  18.738 -24.329  1.00 63.06      A
ATOM    295  N   ILE A  54     -19.838  16.903 -23.841  1.00 62.13      A
ATOM    296  CA  ILE A  54     -20.926  16.269 -23.119  1.00 59.68      A
ATOM    297  CB  ILE A  54     -20.601  14.793 -22.815  1.00 59.54      A
ATOM    298  CG2 ILE A  54     -21.606  14.224 -21.820  1.00 60.50      A
ATOM    299  CG1 ILE A  54     -20.611  13.993 -24.117  1.00 59.64      A
ATOM    300  CD1 ILE A  54     -20.368  12.518 -23.930  1.00 59.00      A
ATOM    301  C   ILE A  54     -21.164  17.028 -21.813  1.00 57.90      A
ATOM    302  O   ILE A  54     -22.290  17.095 -21.327  1.00 57.31      A
ATOM    303  N   SER A  55     -20.097  17.601 -21.259  1.00 55.70      A
ATOM    304  CA  SER A  55     -20.184  18.370 -20.023  1.00 54.92      A
ATOM    305  CB  SER A  55     -18.793  18.751 -19.519  1.00 55.15      A
ATOM    306  OG  SER A  55     -18.065  17.604 -19.145  1.00 57.20      A
ATOM    307  C   SER A  55     -20.984  19.640 -20.247  1.00 53.44      A
ATOM    308  O   SER A  55     -22.026  19.837 -19.627  1.00 55.68      A
ATOM    309  N   VAL A  56     -20.494  20.502 -21.127  1.00 50.22      A
ATOM    310  CA  VAL A  56     -21.178  21.752 -21.415  1.00 50.34      A
ATOM    311  CB  VAL A  56     -20.418  22.574 -22.478  1.00 50.53      A
ATOM    312  CG1 VAL A  56     -19.161  23.152 -21.878  1.00 50.53      A
ATOM    313  CG2 VAL A  56     -20.078  21.697 -23.668  1.00 51.00      A
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ATOM    314  C   VAL A  56     -22.610  21.528 -21.894  1.00 49.62      A
ATOM    315  O   VAL A  56     -23.516  22.293 -21.567  1.00 49.30      A
ATOM    316  N   LEU A  57     -22.812  20.475 -22.673  1.00 49.64      A
ATOM    317  CA  LEU A  57     -24.136  20.154 -23.190  1.00 49.65      A
ATOM    318  CB  LEU A  57     -24.032  18.974 -24.152  1.00 51.00      A
ATOM    319  CG  LEU A  57     -25.034  18.931 -25.301  1.00 52.21      A
ATOM    320  CD1 LEU A  57     -25.250  20.322 -25.881  1.00 52.24      A
ATOM    321  CD2 LEU A  57     -24.488  17.992 -26.361  1.00 54.20      A
ATOM    322  C   LEU A  57     -25.054  19.800 -22.027  1.00 47.55      A
ATOM    323  O   LEU A  57     -26.140  20.356 -21.870  1.00 46.60      A
ATOM    324  N   HIS A  58     -24.592  18.862 -21.216  1.00 46.31      A
ATOM    325  CA  HIS A  58     -25.319  18.415 -20.043  1.00 45.33      A
ATOM    326  CB  HIS A  58     -24.482  17.375 -19.301  1.00 46.40      A
ATOM    327  CG  HIS A  58     -25.242  16.619 -18.263  1.00 46.64      A
ATOM    328  CD2 HIS A  58     -25.757  15.368 -18.275  1.00 46.79      A
ATOM    329  ND1 HIS A  58     -25.582  17.164 -17.044  1.00 46.24      A
ATOM    330  CE1 HIS A  58     -26.275  16.280 -16.352  1.00 48.22      A
ATOM    331  NE2 HIS A  58     -26.397  15.180 -17.076  1.00 46.23      A
ATOM    332  C   HIS A  58     -25.649  19.590 -19.118  1.00 43.94      A
ATOM    333  O   HIS A  58     -26.783  19.724 -18.663  1.00 42.85      A
ATOM    334  N   GLU A  59     -24.664  20.442 -18.847  1.00 41.52      A
ATOM    335  CA  GLU A  59     -24.896  21.585 -17.979  1.00 41.77      A
ATOM    336  CB  GLU A  59     -23.600  22.326 -17.702  1.00 43.24      A
ATOM    337  CG  GLU A  59     -23.694  23.232 -16.489  1.00 47.79      A
ATOM    338  CD  GLU A  59     -24.197  22.493 -15.249  1.00 49.54      A
ATOM    339  OE1 GLU A  59     -23.853  21.304 -15.074  1.00 49.34      A
ATOM    340  OE2 GLU A  59     -24.928  23.107 -14.442  1.00 52.72      A
ATOM    341  C   GLU A  59     -25.882  22.536 -18.619  1.00 41.87      A
ATOM    342  O   GLU A  59     -26.719  23.135 -17.942  1.00 41.28      A
ATOM    343  N   MET A  60     -25.770  22.677 -19.935  1.00 42.94      A
ATOM    344  CA  MET A  60     -26.662  23.542 -20.692  1.00 42.22      A
ATOM    345  CB  MET A  60     -26.290  23.512 -22.165  1.00 43.31      A
ATOM    346  CG  MET A  60     -27.230  24.305 -23.017  1.00 45.06      A
ATOM    347  SD  MET A  60     -27.202  26.008 -22.511  1.00 51.70      A
ATOM    348  CE  MET A  60     -27.674  26.784 -24.033  1.00 51.65      A
ATOM    349  C   MET A  60     -28.096  23.052 -20.545  1.00 42.26      A
ATOM    350  O   MET A  60     -29.039  23.839 -20.450  1.00 40.80      A
ATOM    351  N   ILE A  61     -28.245  21.733 -20.534  1.00 40.98      A
ATOM    352  CA  ILE A  61     -29.548  21.123 -20.418  1.00 40.78      A
ATOM    353  CB  ILE A  61     -29.504  19.681 -20.995  1.00 42.85      A
ATOM    354  CG2 ILE A  61     -30.790  18.936 -20.694  1.00 41.14      A
ATOM    355  CG1 ILE A  61     -29.312  19.763 -22.518  1.00 42.64      A
ATOM    356  CD1 ILE A  61     -29.143  18.421 -23.214  1.00 43.13      A
ATOM    357  C   ILE A  61     -30.060  21.159 -18.984  1.00 39.56      A
ATOM    358  O   ILE A  61     -31.195  21.558 -18.744  1.00 39.81      A
ATOM    359  N   GLN A  62     -29.224  20.781 -18.026  1.00 39.29      A
ATOM    360  CA  GLN A  62     -29.639  20.793 -16.627  1.00 38.51      A
ATOM    361  CB  GLN A  62     -28.488  20.338 -15.726  1.00 39.26      A
ATOM    362  CG  GLN A  62     -28.827  20.246 -14.242  1.00 39.53      A
ATOM    363  CD  GLN A  62     -30.002  19.321 -13.941  1.00 40.52      A
ATOM    364  OE1 GLN A  62     -31.042  19.758 -13.438  1.00 39.54      A
ATOM    365  NE2 GLN A  62     -29.840  18.040 -14.248  1.00 39.51      A
ATOM    366  C   GLN A  62     -30.102  22.189 -16.221  1.00 38.93      A
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ATOM	367	O	GLN	A	62	-31.106	22.348	-15.522	1.00	37.04	A
ATOM	368	N	GLN	A	63	-29.383	23.204	-16.683	1.00	39.52	A
ATOM	369	CA	GLN	A	63	-29.741	24.578	-16.353	1.00	40.38	A
ATOM	370	CB	GLN	A	63	-28.644	25.543	-16.797	1.00	41.37	A
ATOM	371	CG	GLN	A	63	-27.350	25.361	-16.049	1.00	42.32	A
ATOM	372	CD	GLN	A	63	-27.523	25.576	-14.563	1.00	46.04	A
ATOM	373	OE1	GLN	A	63	-26.881	24.907	-13.753	1.00	47.35	A
ATOM	374	NE2	GLN	A	63	-28.386	26.526	-14.192	1.00	46.16	A
ATOM	375	C	GLN	A	63	-31.062	25.006	-16.957	1.00	40.51	A
ATOM	376	O	GLN	A	63	-31.837	25.685	-16.286	1.00	43.32	A
ATOM	377	N	THR	A	64	-31.313	24.625	-18.215	1.00	39.04	A
ATOM	378	CA	THR	A	64	-32.564	24.972	-18.904	1.00	37.15	A
ATOM	379	CB	THR	A	64	-32.539	24.536	-20.398	1.00	36.84	A
ATOM	380	OG1	THR	A	64	-31.493	25.233	-21.084	1.00	35.39	A
ATOM	381	CG2	THR	A	64	-33.872	24.834	-21.077	1.00	32.91	A
ATOM	382	C	THR	A	64	-33.714	24.265	-18.181	1.00	37.88	A
ATOM	383	O	THR	A	64	-34.827	24.791	-18.061	1.00	37.95	A
ATOM	384	N	PHE	A	65	-33.438	23.061	-17.700	1.00	37.24	A
ATOM	385	CA	PHE	A	65	-34.435	22.326	-16.951	1.00	37.39	A
ATOM	386	CB	PHE	A	65	-33.934	20.930	-16.625	1.00	37.39	A
ATOM	387	CG	PHE	A	65	-34.874	20.159	-15.749	1.00	40.42	A
ATOM	388	CD1	PHE	A	65	-35.967	19.503	-16.292	1.00	39.82	A
ATOM	389	CD2	PHE	A	65	-34.706	20.155	-14.370	1.00	40.52	A
ATOM	390	CE1	PHE	A	65	-36.871	18.861	-15.485	1.00	40.75	A
ATOM	391	CE2	PHE	A	65	-35.611	19.511	-13.556	1.00	40.34	A
ATOM	392	CZ	PHE	A	65	-36.697	18.867	-14.115	1.00	40.24	A
ATOM	393	C	PHE	A	65	-34.756	23.070	-15.639	1.00	36.83	A
ATOM	394	O	PHE	A	65	-35.918	23.289	-15.317	1.00	37.76	A
ATOM	395	N	ASN	A	66	-33.730	23.450	-14.880	1.00	35.91	A
ATOM	396	CA	ASN	A	66	-33.950	24.177	-13.633	1.00	34.39	A
ATOM	397	CB	ASN	A	66	-32.631	24.485	-12.935	1.00	32.13	A
ATOM	398	CG	ASN	A	66	-31.851	23.238	-12.606	1.00	34.28	A
ATOM	399	OD1	ASN	A	66	-32.418	22.153	-12.512	1.00	37.35	A
ATOM	400	ND2	ASN	A	66	-30.545	23.380	-12.424	1.00	33.10	A
ATOM	401	C	ASN	A	66	-34.678	25.481	-13.900	1.00	34.39	A
ATOM	402	O	ASN	A	66	-35.582	25.851	-13.163	1.00	35.59	A
ATOM	403	N	LEU	A	67	-34.299	26.172	-14.963	1.00	34.07	A
ATOM	404	CA	LEU	A	67	-34.937	27.440	-15.292	1.00	34.52	A
ATOM	405	CB	LEU	A	67	-34.189	28.135	-16.434	1.00	31.74	A
ATOM	406	CG	LEU	A	67	-34.902	29.382	-16.972	1.00	32.77	A
ATOM	407	CD1	LEU	A	67	-34.922	30.487	-15.907	1.00	29.39	A
ATOM	408	CD2	LEU	A	67	-34.216	29.848	-18.259	1.00	31.96	A
ATOM	409	C	LEU	A	67	-36.417	27.335	-15.655	1.00	34.13	A
ATOM	410	O	LEU	A	67	-37.185	28.238	-15.362	1.00	35.27	A
ATOM	411	N	PHE	A	68	-36.824	26.236	-16.280	1.00	36.35	A
ATOM	412	CA	PHE	A	68	-38.218	26.081	-16.690	1.00	37.11	A
ATOM	413	CB	PHE	A	68	-38.284	25.620	-18.150	1.00	33.91	A
ATOM	414	CG	PHE	A	68	-38.023	26.708	-19.133	1.00	31.92	A
ATOM	415	CD1	PHE	A	68	-36.724	26.985	-19.563	1.00	33.37	A
ATOM	416	CD2	PHE	A	68	-39.071	27.494	-19.607	1.00	30.01	A
ATOM	417	CE1	PHE	A	68	-36.469	28.045	-20.466	1.00	31.57	A
ATOM	418	CE2	PHE	A	68	-38.835	28.553	-20.504	1.00	30.12	A
ATOM	419	CZ	PHE	A	68	-37.534	28.830	-20.932	1.00	28.79	A

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ATOM    420  C   PHE A  68     -39.128  25.186 -15.845  1.00 39.17      A
ATOM    421  O   PHE A  68     -40.318  25.067 -16.131  1.00 39.72      A
ATOM    422  N   SER A  69     -38.592  24.558 -14.806  1.00 41.24      A
ATOM    423  CA  SER A  69     -39.424  23.709 -13.969  1.00 41.35      A
ATOM    424  CB  SER A  69     -38.721  22.398 -13.704  1.00 39.74      A
ATOM    425  OG  SER A  69     -37.509  22.664 -13.042  1.00 40.54      A
ATOM    426  C   SER A  69     -39.790  24.355 -12.635  1.00 42.76      A
ATOM    427  O   SER A  69     -40.328  23.687 -11.772  1.00 45.46      A
ATOM    428  N   THR A  70     -39.508  25.642 -12.459  1.00 44.33      A
ATOM    429  CA  THR A  70     -39.839  26.316 -11.201  1.00 47.21      A
ATOM    430  CB  THR A  70     -39.038  27.630 -10.990  1.00 47.32      A
ATOM    431  OG1 THR A  70     -39.366  28.565 -12.031  1.00 49.98      A
ATOM    432  CG2 THR A  70     -37.547  27.364 -10.977  1.00 45.16      A
ATOM    433  C   THR A  70     -41.307  26.709 -11.179  1.00 50.70      A
ATOM    434  O   THR A  70     -42.001  26.617 -12.195  1.00 50.43      A
ATOM    435  N   ARG A  71     -41.777  27.164 -10.018  1.00 53.44      A
ATOM    436  CA  ARG A  71     -43.164  27.594  -9.908  1.00 55.27      A
ATOM    437  CB  ARG A  71     -43.576  27.847  -8.449  1.00 57.92      A
ATOM    438  CG  ARG A  71     -43.186  26.760  -7.454  1.00 61.59      A
ATOM    439  CD  ARG A  71     -41.834  27.104  -6.805  1.00 64.19      A
ATOM    440  NE  ARG A  71     -40.663  26.474  -7.420  1.00 58.72      A
ATOM    441  CZ  ARG A  71     -39.469  27.046  -7.453  1.00 55.24      A
ATOM    442  NH1 ARG A  71     -39.304  28.250  -6.929  1.00 52.89      A
ATOM    443  NH2 ARG A  71     -38.435  26.399  -7.964  1.00 55.93      A
ATOM    444  C   ARG A  71     -43.298  28.891 -10.697  1.00 53.94      A
ATOM    445  O   ARG A  71     -44.382  29.232 -11.171  1.00 53.96      A
ATOM    446  N   ASP A  72     -42.196  29.619 -10.832  1.00 52.47      A
ATOM    447  CA  ASP A  72     -42.232  30.857 -11.588  1.00 53.16      A
ATOM    448  CB  ASP A  72     -40.896  31.592 -11.491  1.00 55.60      A
ATOM    449  CG  ASP A  72     -40.517  31.929 -10.069  1.00 56.39      A
ATOM    450  OD1 ASP A  72     -39.627  31.244  -9.517  1.00 57.77      A
ATOM    451  OD2 ASP A  72     -41.114  32.874  -9.510  1.00 56.32      A
ATOM    452  C   ASP A  72     -42.524  30.523 -13.050  1.00 52.84      A
ATOM    453  O   ASP A  72     -43.402  31.114 -13.672  1.00 51.84      A
ATOM    454  N   SER A  73     -41.780  29.569 -13.592  1.00 51.97      A
ATOM    455  CA  SER A  73     -41.980  29.169 -14.971  1.00 52.26      A
ATOM    456  CB  SER A  73     -40.981  28.062 -15.347  1.00 51.52      A
ATOM    457  OG  SER A  73     -41.246  27.525 -16.629  1.00 48.35      A
ATOM    458  C   SER A  73     -43.416  28.674 -15.134  1.00 53.10      A
ATOM    459  O   SER A  73     -44.097  29.008 -16.107  1.00 54.40      A
ATOM    460  N   SER A  74     -43.882  27.893 -14.165  1.00 53.63      A
ATOM    461  CA  SER A  74     -45.231  27.342 -14.222  1.00 53.33      A
ATOM    462  CB  SER A  74     -45.484  26.414 -13.041  1.00 51.87      A
ATOM    463  OG  SER A  74     -45.620  25.076 -13.494  1.00 53.40      A
ATOM    464  C   SER A  74     -46.320  28.389 -14.274  1.00 52.78      A
ATOM    465  O   SER A  74     -47.411  28.125 -14.771  1.00 54.19      A
ATOM    466  N   ALA A  75     -46.021  29.579 -13.770  1.00 51.42      A
ATOM    467  CA  ALA A  75     -46.990  30.662 -13.755  1.00 50.95      A
ATOM    468  CB  ALA A  75     -46.727  31.573 -12.556  1.00 48.85      A
ATOM    469  C   ALA A  75     -46.927  31.473 -15.041  1.00 50.90      A
ATOM    470  O   ALA A  75     -47.774  32.319 -15.292  1.00 52.54      A
ATOM    471  N   ALA A  76     -45.923  31.213 -15.860  1.00 49.86      A
ATOM    472  CA  ALA A  76     -45.769  31.969 -17.080  1.00 49.41      A
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ATOM    473  CB  ALA A  76     -44.334  32.491 -17.168  1.00 50.92      A
ATOM    474  C   ALA A  76     -46.122  31.192 -18.341  1.00 49.59      A
ATOM    475  O   ALA A  76     -46.417  31.794 -19.378  1.00 50.18      A
ATOM    476  N   TRP A  77     -46.111  29.866 -18.259  1.00 47.56      A
ATOM    477  CA  TRP A  77     -46.387  29.063 -19.438  1.00 46.48      A
ATOM    478  CB  TRP A  77     -45.110  28.355 -19.877  1.00 44.34      A
ATOM    479  CG  TRP A  77     -43.913  29.259 -19.895  1.00 42.62      A
ATOM    480  CD2 TRP A  77     -43.655  30.325 -20.813  1.00 40.67      A
ATOM    481  CE2 TRP A  77     -42.422  30.902 -20.448  1.00 40.13      A
ATOM    482  CE3 TRP A  77     -44.344  30.847 -21.914  1.00 42.24      A
ATOM    483  CD1 TRP A  77     -42.860  29.232 -19.036  1.00 40.98      A
ATOM    484  NE1 TRP A  77     -41.958  30.213 -19.360  1.00 41.31      A
ATOM    485  CZ2 TRP A  77     -41.857  31.981 -21.140  1.00 41.93      A
ATOM    486  CZ3 TRP A  77     -43.780  31.927 -22.612  1.00 42.72      A
ATOM    487  CH2 TRP A  77     -42.548  32.479 -22.218  1.00 40.65      A
ATOM    488  C   TRP A  77     -47.499  28.044 -19.317  1.00 47.54      A
ATOM    489  O   TRP A  77     -47.927  27.687 -18.228  1.00 47.95      A
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ATOM    491  CA  ASP A  78     -49.024  26.590 -20.526  1.00 52.24      A
ATOM    492  CB  ASP A  78     -49.376  26.310 -21.986  1.00 53.78      A
ATOM    493  CG  ASP A  78     -50.539  25.368 -22.128  1.00 55.91      A
ATOM    494  OD1 ASP A  78     -50.307  24.144 -22.238  1.00 57.57      A
ATOM    495  OD2 ASP A  78     -51.689  25.857 -22.115  1.00 57.70      A
ATOM    496  C   ASP A  78     -48.591  25.309 -19.815  1.00 53.52      A
ATOM    497  O   ASP A  78     -47.633  24.638 -20.217  1.00 53.27      A
ATOM    498  N   ALA A  79     -49.304  24.978 -18.746  1.00 54.38      A
ATOM    499  CA  ALA A  79     -48.983  23.797 -17.961  1.00 54.80      A
ATOM    500  CB  ALA A  79     -50.123  23.488 -16.991  1.00 54.45      A
ATOM    501  C   ALA A  79     -48.692  22.594 -18.843  1.00 54.31      A
ATOM    502  O   ALA A  79     -47.633  21.994 -18.747  1.00 55.97      A
ATOM    503  N   SER A  80     -49.619  22.255 -19.722  1.00 54.29      A
ATOM    504  CA  SER A  80     -49.438  21.096 -20.588  1.00 54.78      A
ATOM    505  CB  SER A  80     -50.677  20.900 -21.471  1.00 56.80      A
ATOM    506  OG  SER A  80     -50.573  19.708 -22.235  1.00 60.99      A
ATOM    507  C   SER A  80     -48.184  21.198 -21.453  1.00 53.08      A
ATOM    508  O   SER A  80     -47.441  20.225 -21.602  1.00 52.66      A
ATOM    509  N   LEU A  81     -47.956  22.372 -22.030  1.00 51.48      A
ATOM    510  CA  LEU A  81     -46.781  22.579 -22.858  1.00 50.28      A
ATOM    511  CB  LEU A  81     -46.848  23.939 -23.567  1.00 50.13      A
ATOM    512  CG  LEU A  81     -47.794  24.078 -24.770  1.00 52.07      A
ATOM    513  CD1 LEU A  81     -47.823  25.523 -25.274  1.00 50.96      A
ATOM    514  CD2 LEU A  81     -47.338  23.143 -25.881  1.00 51.96      A
ATOM    515  C   LEU A  81     -45.533  22.495 -21.981  1.00 49.31      A
ATOM    516  O   LEU A  81     -44.655  21.673 -22.231  1.00 49.33      A
ATOM    517  N   LEU A  82     -45.473  23.319 -20.936  1.00 47.57      A
ATOM    518  CA  LEU A  82     -44.323  23.330 -20.033  1.00 45.33      A
ATOM    519  CB  LEU A  82     -44.636  24.117 -18.770  1.00 46.40      A
ATOM    520  CG  LEU A  82     -43.611  25.158 -18.335  1.00 45.80      A
ATOM    521  CD1 LEU A  82     -43.773  25.372 -16.834  1.00 43.68      A
ATOM    522  CD2 LEU A  82     -42.207  24.705 -18.670  1.00 43.36      A
ATOM    523  C   LEU A  82     -43.864  21.945 -19.618  1.00 43.50      A
ATOM    524  O   LEU A  82     -42.689  21.626 -19.728  1.00 43.15      A
ATOM    525  N   ALA A  83     -44.785  21.114 -19.146  1.00 43.10      A
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ATOM    526  CA  ALA A  83     -44.405  19.775 -18.706  1.00 43.00      A
ATOM    527  CB  ALA A  83     -45.606  19.052 -18.090  1.00 43.77      A
ATOM    528  C   ALA A  83     -43.791  18.937 -19.826  1.00 42.10      A
ATOM    529  O   ALA A  83     -42.857  18.179 -19.591  1.00 41.05      A
ATOM    530  N   LYS A  84     -44.295  19.052 -21.049  1.00 42.19      A
ATOM    531  CA  LYS A  84     -43.688  18.251 -22.101  1.00 42.91      A
ATOM    532  CB  LYS A  84     -44.509  18.300 -23.373  1.00 44.87      A
ATOM    533  CG  LYS A  84     -45.866  17.660 -23.231  1.00 48.00      A
ATOM    534  CD  LYS A  84     -46.263  16.952 -24.500  1.00 49.01      A
ATOM    535  CE  LYS A  84     -47.734  17.105 -24.720  1.00 51.13      A
ATOM    536  NZ  LYS A  84     -48.023  18.541 -24.942  1.00 52.74      A
ATOM    537  C   LYS A  84     -42.285  18.763 -22.359  1.00 43.12      A
ATOM    538  O   LYS A  84     -41.347  17.987 -22.527  1.00 44.29      A
ATOM    539  N   PHE A  85     -42.144  20.081 -22.363  1.00 42.32      A
ATOM    540  CA  PHE A  85     -40.852  20.704 -22.571  1.00 42.58      A
ATOM    541  CB  PHE A  85     -40.964  22.222 -22.450  1.00 43.25      A
ATOM    542  CG  PHE A  85     -39.681  22.944 -22.734  1.00 42.84      A
ATOM    543  CD1 PHE A  85     -39.076  22.847 -23.982  1.00 43.39      A
ATOM    544  CD2 PHE A  85     -39.084  23.734 -21.768  1.00 42.83      A
ATOM    545  CE1 PHE A  85     -37.897  23.528 -24.265  1.00 42.40      A
ATOM    546  CE2 PHE A  85     -37.904  24.417 -22.043  1.00 43.37      A
ATOM    547  CZ  PHE A  85     -37.312  24.313 -23.295  1.00 42.70      A
ATOM    548  C   PHE A  85     -39.813  20.206 -21.572  1.00 44.30      A
ATOM    549  O   PHE A  85     -38.835  19.562 -21.964  1.00 45.07      A
ATOM    550  N   TYR A  86     -40.014  20.482 -20.282  1.00 43.21      A
ATOM    551  CA  TYR A  86     -39.018  20.055 -19.319  1.00 44.18      A
ATOM    552  CB  TYR A  86     -39.208  20.748 -17.948  1.00 45.30      A
ATOM    553  CG  TYR A  86     -40.455  20.448 -17.144  1.00 44.10      A
ATOM    554  CD1 TYR A  86     -41.328  21.474 -16.797  1.00 43.43      A
ATOM    555  CE1 TYR A  86     -42.432  21.239 -15.988  1.00 45.72      A
ATOM    556  CD2 TYR A  86     -40.720  19.163 -16.662  1.00 43.84      A
ATOM    557  CE2 TYR A  86     -41.828  18.915 -15.846  1.00 46.21      A
ATOM    558  CZ  TYR A  86     -42.678  19.963 -15.513  1.00 47.37      A
ATOM    559  OH  TYR A  86     -43.764  19.756 -14.691  1.00 49.38      A
ATOM    560  C   TYR A  86     -38.862  18.549 -19.164  1.00 44.37      A
ATOM    561  O   TYR A  86     -37.848  18.080 -18.656  1.00 44.46      A
ATOM    562  N   THR A  87     -39.846  17.785 -19.621  1.00 44.44      A
ATOM    563  CA  THR A  87     -39.752  16.330 -19.537  1.00 43.78      A
ATOM    564  CB  THR A  87     -41.129  15.644 -19.751  1.00 43.93      A
ATOM    565  OG1 THR A  87     -42.035  16.055 -18.722  1.00 42.91      A
ATOM    566  CG2 THR A  87     -40.986  14.130 -19.712  1.00 40.48      A
ATOM    567  C   THR A  87     -38.813  15.905 -20.654  1.00 43.41      A
ATOM    568  O   THR A  87     -38.040  14.962 -20.509  1.00 42.95      A
ATOM    569  N   GLU A  88     -38.898  16.620 -21.774  1.00 43.70      A
ATOM    570  CA  GLU A  88     -38.057  16.359 -22.932  1.00 42.33      A
ATOM    571  CB  GLU A  88     -38.503  17.245 -24.098  1.00 43.68      A
ATOM    572  CG  GLU A  88     -37.754  17.014 -25.394  1.00 48.37      A
ATOM    573  CD  GLU A  88     -37.718  15.546 -25.822  1.00 51.49      A
ATOM    574  OE1 GLU A  88     -38.767  14.864 -25.751  1.00 51.50      A
ATOM    575  OE2 GLU A  88     -36.634  15.083 -26.242  1.00 52.60      A
ATOM    576  C   GLU A  88     -36.616  16.664 -22.541  1.00 40.76      A
ATOM    577  O   GLU A  88     -35.695  15.921 -22.878  1.00 40.05      A
ATOM    578  N   LEU A  89     -36.428  17.756 -21.809  1.00 39.65      A
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ATOM	579	CA	LEU	A	89	-35.096	18.127	-21.373	1.00	40.05	A
ATOM	580	CB	LEU	A	89	-35.128	19.464	-20.619	1.00	39.26	A
ATOM	581	CG	LEU	A	89	-35.580	20.688	-21.432	1.00	39.90	A
ATOM	582	CD1	LEU	A	89	-35.594	21.916	-20.546	1.00	41.45	A
ATOM	583	CD2	LEU	A	89	-34.647	20.917	-22.599	1.00	37.56	A
ATOM	584	C	LEU	A	89	-34.555	17.030	-20.481	1.00	40.50	A
ATOM	585	O	LEU	A	89	-33.394	16.638	-20.598	1.00	39.83	A
ATOM	586	N	TYR	A	90	-35.412	16.520	-19.598	1.00	42.46	A
ATOM	587	CA	TYR	A	90	-35.020	15.465	-18.674	1.00	43.11	A
ATOM	588	CB	TYR	A	90	-36.154	15.134	-17.711	1.00	45.71	A
ATOM	589	CG	TYR	A	90	-35.682	14.361	-16.502	1.00	49.69	A
ATOM	590	CD1	TYR	A	90	-35.034	15.013	-15.447	1.00	50.12	A
ATOM	591	CE1	TYR	A	90	-34.535	14.307	-14.365	1.00	52.01	A
ATOM	592	CD2	TYR	A	90	-35.820	12.974	-16.435	1.00	50.69	A
ATOM	593	CE2	TYR	A	90	-35.326	12.256	-15.349	1.00	53.04	A
ATOM	594	CZ	TYR	A	90	-34.680	12.929	-14.321	1.00	53.92	A
ATOM	595	OH	TYR	A	90	-34.161	12.227	-13.256	1.00	56.71	A
ATOM	596	C	TYR	A	90	-34.643	14.217	-19.446	1.00	43.97	A
ATOM	597	O	TYR	A	90	-33.682	13.534	-19.106	1.00	44.98	A
ATOM	598	N	GLN	A	91	-35.406	13.915	-20.489	1.00	45.76	A
ATOM	599	CA	GLN	A	91	-35.116	12.748	-21.300	1.00	48.45	A
ATOM	600	CB	GLN	A	91	-36.126	12.616	-22.440	1.00	51.91	A
ATOM	601	CG	GLN	A	91	-36.964	11.363	-22.371	1.00	56.69	A
ATOM	602	CD	GLN	A	91	-36.141	10.178	-21.917	1.00	61.59	A
ATOM	603	OE1	GLN	A	91	-36.223	9.756	-20.760	1.00	63.01	A
ATOM	604	NE2	GLN	A	91	-35.322	9.648	-22.816	1.00	61.97	A
ATOM	605	C	GLN	A	91	-33.719	12.909	-21.880	1.00	48.95	A
ATOM	606	O	GLN	A	91	-32.906	11.984	-21.826	1.00	48.74	A
ATOM	607	N	GLN	A	92	-33.451	14.098	-22.419	1.00	48.30	A
ATOM	608	CA	GLN	A	92	-32.166	14.403	-23.030	1.00	49.20	A
ATOM	609	CB	GLN	A	92	-32.204	15.800	-23.666	1.00	49.21	A
ATOM	610	CG	GLN	A	92	-32.906	15.825	-25.020	1.00	50.13	A
ATOM	611	CD	GLN	A	92	-33.021	17.215	-25.621	1.00	51.05	A
ATOM	612	OE1	GLN	A	92	-32.087	18.010	-25.566	1.00	53.57	A
ATOM	613	NE2	GLN	A	92	-34.166	17.505	-26.214	1.00	52.77	A
ATOM	614	C	GLN	A	92	-30.998	14.279	-22.061	1.00	49.71	A
ATOM	615	O	GLN	A	92	-29.895	13.902	-22.462	1.00	50.06	A
ATOM	616	N	LEU	A	93	-31.223	14.602	-20.790	1.00	48.85	A
ATOM	617	CA	LEU	A	93	-30.148	14.463	-19.820	1.00	49.45	A
ATOM	618	CB	LEU	A	93	-30.545	15.025	-18.454	1.00	47.86	A
ATOM	619	CG	LEU	A	93	-30.469	16.530	-18.237	1.00	45.97	A
ATOM	620	CD1	LEU	A	93	-30.980	16.854	-16.851	1.00	45.24	A
ATOM	621	CD2	LEU	A	93	-29.042	16.997	-18.410	1.00	45.80	A
ATOM	622	C	LEU	A	93	-29.883	12.974	-19.679	1.00	51.53	A
ATOM	623	O	LEU	A	93	-28.730	12.531	-19.661	1.00	49.61	A
ATOM	624	N	ALA	A	94	-30.974	12.212	-19.585	1.00	54.03	A
ATOM	625	CA	ALA	A	94	-30.902	10.766	-19.439	1.00	56.50	A
ATOM	626	CB	ALA	A	94	-32.306	10.177	-19.305	1.00	55.64	A
ATOM	627	C	ALA	A	94	-30.161	10.139	-20.618	1.00	58.27	A
ATOM	628	O	ALA	A	94	-29.383	9.208	-20.431	1.00	60.16	A
ATOM	629	N	ASP	A	95	-30.382	10.654	-21.826	1.00	59.89	A
ATOM	630	CA	ASP	A	95	-29.696	10.115	-22.998	1.00	60.86	A
ATOM	631	CB	ASP	A	95	-30.293	10.665	-24.295	1.00	61.06	A

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ATOM    632  CG  ASP A  95     -31.745  10.259 -24.489  1.00 64.37      A
ATOM    633  OD1 ASP A  95     -32.123   9.156 -24.038  1.00 65.54      A
ATOM    634  OD2 ASP A  95     -32.513  11.034 -25.101  1.00 65.80      A
ATOM    635  C   ASP A  95     -28.208  10.424 -22.960  1.00 62.01      A
ATOM    636  O   ASP A  95     -27.396   9.594 -23.349  1.00 62.85      A
ATOM    637  N   LEU A  96     -27.840  11.612 -22.492  1.00 63.44      A
ATOM    638  CA  LEU A  96     -26.429  11.968 -22.434  1.00 65.26      A
ATOM    639  CB  LEU A  96     -26.250  13.437 -22.063  1.00 64.67      A
ATOM    640  CG  LEU A  96     -26.228  14.431 -23.223  1.00 64.38      A
ATOM    641  CD1 LEU A  96     -25.876  15.815 -22.699  1.00 63.39      A
ATOM    642  CD2 LEU A  96     -25.213  13.978 -24.256  1.00 62.74      A
ATOM    643  C   LEU A  96     -25.665  11.115 -21.444  1.00 67.97      A
ATOM    644  O   LEU A  96     -24.520  10.735 -21.693  1.00 68.62      A
ATOM    645  N   GLU A  97     -26.300  10.811 -20.321  1.00 70.13      A
ATOM    646  CA  GLU A  97     -25.657  10.017 -19.291  1.00 72.55      A
ATOM    647  CB  GLU A  97     -26.488  10.075 -18.019  1.00 71.72      A
ATOM    648  CG  GLU A  97     -26.985  11.485 -17.769  1.00 74.81      A
ATOM    649  CD  GLU A  97     -27.241  11.799 -16.314  1.00 75.51      A
ATOM    650  OE1 GLU A  97     -27.747  12.905 -16.036  1.00 74.77      A
ATOM    651  OE2 GLU A  97     -26.931  10.953 -15.451  1.00 77.73      A
ATOM    652  C   GLU A  97     -25.450   8.588 -19.762  1.00 74.96      A
ATOM    653  O   GLU A  97     -24.468   7.943 -19.390  1.00 76.46      A
ATOM    654  N   ALA A  98     -26.366   8.089 -20.586  1.00 76.86      A
ATOM    655  CA  ALA A  98     -26.223   6.737 -21.115  1.00 78.82      A
ATOM    656  CB  ALA A  98     -27.433   6.366 -21.954  1.00 77.13      A
ATOM    657  C   ALA A  98     -24.965   6.775 -21.980  1.00 81.25      A
ATOM    658  O   ALA A  98     -24.070   5.941 -21.838  1.00 81.55      A
ATOM    659  N   CYS A  99     -24.907   7.778 -22.854  1.00 83.47      A
ATOM    660  CA  CYS A  99     -23.786   7.987 -23.759  1.00 85.46      A
ATOM    661  CB  CYS A  99     -23.981   9.310 -24.517  1.00 86.41      A
ATOM    662  SG  CYS A  99     -22.959   9.545 -26.007  1.00 89.76      A
ATOM    663  C   CYS A  99     -22.462   8.000 -22.988  1.00 86.47      A
ATOM    664  O   CYS A  99     -21.478   7.415 -23.436  1.00 87.19      A
ATOM    665  N   VAL A 100     -22.438   8.659 -21.832  1.00 87.06      A
ATOM    666  CA  VAL A 100     -21.221   8.718 -21.018  1.00 88.28      A
ATOM    667  CB  VAL A 100     -21.364   9.721 -19.840  1.00 87.74      A
ATOM    668  CG1 VAL A 100     -20.109   9.704 -18.980  1.00 87.01      A
ATOM    669  CG2 VAL A 100     -21.603  11.118 -20.371  1.00 87.68      A
ATOM    670  C   VAL A 100     -20.878   7.339 -20.442  1.00 89.50      A
ATOM    671  O   VAL A 100     -19.728   6.899 -20.506  1.00 89.46      A
ATOM    672  N   ALA A 101     -21.881   6.666 -19.880  1.00 90.52      A
ATOM    673  CA  ALA A 101     -21.696   5.340 -19.294  1.00 91.37      A
ATOM    674  CB  ALA A 101     -22.924   4.958 -18.477  1.00 90.68      A
ATOM    675  C   ALA A 101     -21.448   4.305 -20.390  1.00 92.11      A
ATOM    676  O   ALA A 101     -22.144   3.290 -20.483  1.00 92.02      A
ATOM    677  N   GLY A 102     -20.445   4.572 -21.218  1.00 92.66      A
ATOM    678  CA  GLY A 102     -20.117   3.672 -22.303  1.00 93.77      A
ATOM    679  C   GLY A 102     -19.599   4.456 -23.490  1.00 94.37      A
ATOM    680  O   GLY A 102     -20.320   4.666 -24.467  1.00 94.30      A
ATOM    681  N   GLY A 103     -18.345   4.893 -23.399  1.00 94.78      A
ATOM    682  CA  GLY A 103     -17.741   5.662 -24.472  1.00 94.59      A
ATOM    683  C   GLY A 103     -17.097   6.930 -23.948  1.00 94.45      A
ATOM    684  O   GLY A 103     -17.324   7.326 -22.804  1.00 94.32      A
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ATOM    685  N   ALA A 111     -11.108  13.549 -17.360  1.00 90.11      A
ATOM    686  CA  ALA A 111     -11.032  14.851 -16.699  1.00 90.12      A
ATOM    687  CB  ALA A 111      -9.569  15.220 -16.438  1.00 89.81      A
ATOM    688  C   ALA A 111     -11.713  15.942 -17.530  1.00 89.66      A
ATOM    689  O   ALA A 111     -12.411  15.650 -18.506  1.00 90.16      A
ATOM    690  N   GLY A 112     -11.509  17.197 -17.136  1.00 88.41      A
ATOM    691  CA  GLY A 112     -12.108  18.312 -17.853  1.00 86.60      A
ATOM    692  C   GLY A 112     -11.712  19.656 -17.267  1.00 85.50      A
ATOM    693  O   GLY A 112     -10.617  19.797 -16.709  1.00 86.67      A
ATOM    694  N   ASN A 113     -12.590  20.650 -17.400  1.00 82.82      A
ATOM    695  CA  ASN A 113     -12.309  21.975 -16.860  1.00 79.24      A
ATOM    696  CB  ASN A 113     -11.567  22.843 -17.893  1.00 81.82      A
ATOM    697  CG  ASN A 113     -12.359  23.059 -19.177  1.00 83.86      A
ATOM    698  OD1 ASN A 113     -12.808  22.103 -19.818  1.00 85.28      A
ATOM    699  ND2 ASN A 113     -12.518  24.324 -19.569  1.00 83.13      A
ATOM    700  C   ASN A 113     -13.551  22.693 -16.339  1.00 75.65      A
ATOM    701  O   ASN A 113     -14.603  22.722 -16.985  1.00 74.61      A
ATOM    702  N   ALA A 114     -13.397  23.272 -15.152  1.00 71.33      A
ATOM    703  CA  ALA A 114     -14.456  23.986 -14.447  1.00 66.25      A
ATOM    704  CB  ALA A 114     -14.016  24.237 -13.002  1.00 65.33      A
ATOM    705  C   ALA A 114     -14.901  25.299 -15.078  1.00 61.91      A
ATOM    706  O   ALA A 114     -16.020  25.746 -14.859  1.00 60.64      A
ATOM    707  N   ASP A 115     -14.037  25.924 -15.858  1.00 58.78      A
ATOM    708  CA  ASP A 115     -14.404  27.197 -16.444  1.00 57.63      A
ATOM    709  CB  ASP A 115     -13.170  27.864 -17.050  1.00 58.76      A
ATOM    710  CG  ASP A 115     -12.240  28.440 -15.977  1.00 60.80      A
ATOM    711  OD1 ASP A 115     -12.644  29.410 -15.283  1.00 58.59      A
ATOM    712  OD2 ASP A 115     -11.114  27.911 -15.822  1.00 60.92      A
ATOM    713  C   ASP A 115     -15.553  27.143 -17.441  1.00 56.69      A
ATOM    714  O   ASP A 115     -16.446  27.994 -17.395  1.00 55.98      A
ATOM    715  N   SER A 116     -15.547  26.154 -18.332  1.00 54.36      A
ATOM    716  CA  SER A 116     -16.629  26.025 -19.305  1.00 51.56      A
ATOM    717  CB  SER A 116     -16.464  24.749 -20.132  1.00 51.85      A
ATOM    718  OG  SER A 116     -15.262  24.765 -20.875  1.00 52.43      A
ATOM    719  C   SER A 116     -17.957  25.964 -18.549  1.00 50.12      A
ATOM    720  O   SER A 116     -18.876  26.747 -18.798  1.00 48.52      A
ATOM    721  N   ILE A 117     -18.035  25.028 -17.612  1.00 48.20      A
ATOM    722  CA  ILE A 117     -19.234  24.839 -16.809  1.00 47.04      A
ATOM    723  CB  ILE A 117     -19.056  23.654 -15.843  1.00 45.89      A
ATOM    724  CG2 ILE A 117     -20.128  23.680 -14.771  1.00 41.04      A
ATOM    725  CG1 ILE A 117     -19.086  22.351 -16.645  1.00 44.74      A
ATOM    726  CD1 ILE A 117     -18.727  21.139 -15.847  1.00 47.83      A
ATOM    727  C   ILE A 117     -19.577  26.093 -16.029  1.00 47.34      A
ATOM    728  O   ILE A 117     -20.747  26.363 -15.755  1.00 47.25      A
ATOM    729  N   LEU A 118     -18.549  26.857 -15.676  1.00 47.11      A
ATOM    730  CA  LEU A 118     -18.743  28.095 -14.941  1.00 46.33      A
ATOM    731  CB  LEU A 118     -17.391  28.640 -14.481  1.00 46.21      A
ATOM    732  CG  LEU A 118     -17.207  29.082 -13.023  1.00 47.56      A
ATOM    733  CD1 LEU A 118     -17.864  28.110 -12.045  1.00 45.29      A
ATOM    734  CD2 LEU A 118     -15.717  29.169 -12.742  1.00 46.63      A
ATOM    735  C   LEU A 118     -19.419  29.071 -15.894  1.00 45.37      A
ATOM    736  O   LEU A 118     -20.361  29.770 -15.522  1.00 45.75      A
ATOM    737  N   ALA A 119     -18.947  29.095 -17.135  1.00 43.53      A
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ATOM    738  CA  ALA A 119     -19.515  29.980 -18.145  1.00 44.02      A
ATOM    739  CB  ALA A 119     -18.835  29.746 -19.483  1.00 43.57      A
ATOM    740  C   ALA A 119     -21.022  29.760 -18.282  1.00 44.16      A
ATOM    741  O   ALA A 119     -21.802  30.707 -18.185  1.00 43.43      A
ATOM    742  N   VAL A 120     -21.420  28.506 -18.504  1.00 43.64      A
ATOM    743  CA  VAL A 120     -22.826  28.157 -18.653  1.00 41.82      A
ATOM    744  CB  VAL A 120     -23.023  26.629 -18.940  1.00 41.05      A
ATOM    745  CG1 VAL A 120     -24.488  26.335 -19.229  1.00 38.92      A
ATOM    746  CG2 VAL A 120     -22.176  26.185 -20.109  1.00 35.59      A
ATOM    747  C   VAL A 120     -23.582  28.530 -17.378  1.00 42.89      A
ATOM    748  O   VAL A 120     -24.632  29.168 -17.443  1.00 43.59      A
ATOM    749  N   LYS A 121     -23.050  28.148 -16.218  1.00 43.62      A
ATOM    750  CA  LYS A 121     -23.713  28.470 -14.950  1.00 43.47      A
ATOM    751  CB  LYS A 121     -22.938  27.909 -13.757  1.00 42.82      A
ATOM    752  CG  LYS A 121     -23.098  26.405 -13.565  1.00 42.66      A
ATOM    753  CD  LYS A 121     -22.183  25.886 -12.463  1.00 44.00      A
ATOM    754  CE  LYS A 121     -22.464  24.418 -12.136  1.00 45.31      A
ATOM    755  NZ  LYS A 121     -23.826  24.200 -11.551  1.00 43.66      A
ATOM    756  C   LYS A 121     -23.892  29.963 -14.773  1.00 43.91      A
ATOM    757  O   LYS A 121     -24.932  30.404 -14.305  1.00 45.66      A
ATOM    758  N   LYS A 122     -22.889  30.746 -15.156  1.00 45.29      A
ATOM    759  CA  LYS A 122     -22.979  32.200 -15.028  1.00 45.49      A
ATOM    760  CB  LYS A 122     -21.584  32.824 -15.117  1.00 46.13      A
ATOM    761  CG  LYS A 122     -20.822  32.741 -13.784  1.00 49.15      A
ATOM    762  CD  LYS A 122     -19.309  32.760 -13.945  1.00 52.08      A
ATOM    763  CE  LYS A 122     -18.822  33.994 -14.692  1.00 54.97      A
ATOM    764  NZ  LYS A 122     -17.332  33.997 -14.825  1.00 58.31      A
ATOM    765  C   LYS A 122     -23.930  32.815 -16.051  1.00 44.74      A
ATOM    766  O   LYS A 122     -24.576  33.819 -15.774  1.00 44.79      A
ATOM    767  N   TYR A 123     -24.035  32.201 -17.226  1.00 43.85      A
ATOM    768  CA  TYR A 123     -24.959  32.687 -18.249  1.00 41.73      A
ATOM    769  CB  TYR A 123     -24.823  31.864 -19.534  1.00 43.00      A
ATOM    770  CG  TYR A 123     -26.012  31.914 -20.483  1.00 43.26      A
ATOM    771  CD1 TYR A 123     -26.334  33.079 -21.181  1.00 42.96      A
ATOM    772  CE1 TYR A 123     -27.375  33.096 -22.120  1.00 43.17      A
ATOM    773  CD2 TYR A 123     -26.768  30.761 -20.739  1.00 44.34      A
ATOM    774  CE2 TYR A 123     -27.808  30.764 -21.676  1.00 43.97      A
ATOM    775  CZ  TYR A 123     -28.100  31.934 -22.361  1.00 43.84      A
ATOM    776  OH  TYR A 123     -29.106  31.942 -23.289  1.00 43.65      A
ATOM    777  C   TYR A 123     -26.374  32.558 -17.718  1.00 40.54      A
ATOM    778  O   TYR A 123     -27.180  33.464 -17.886  1.00 40.80      A
ATOM    779  N   PHE A 124     -26.667  31.429 -17.076  1.00 40.17      A
ATOM    780  CA  PHE A 124     -27.993  31.187 -16.520  1.00 42.42      A
ATOM    781  CB  PHE A 124     -28.188  29.688 -16.247  1.00 41.69      A
ATOM    782  CG  PHE A 124     -28.617  28.909 -17.462  1.00 42.10      A
ATOM    783  CD1 PHE A 124     -29.922  29.007 -17.939  1.00 42.51      A
ATOM    784  CD2 PHE A 124     -27.708  28.120 -18.165  1.00 40.74      A
ATOM    785  CE1 PHE A 124     -30.317  28.332 -19.106  1.00 41.41      A
ATOM    786  CE2 PHE A 124     -28.095  27.445 -19.329  1.00 41.37      A
ATOM    787  CZ  PHE A 124     -29.400  27.554 -19.797  1.00 39.97      A
ATOM    788  C   PHE A 124     -28.242  32.023 -15.264  1.00 43.39      A
ATOM    789  O   PHE A 124     -29.378  32.322 -14.922  1.00 42.59      A
ATOM    790  N   GLN A 125     -27.179  32.421 -14.587  1.00 45.23      A
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ATOM	791	CA	GLN	A	125	-27.343	33.251	-13.415	1.00	48.87	A
ATOM	792	CB	GLN	A	125	-25.980	33.479	-12.749	1.00	52.70	A
ATOM	793	CG	GLN	A	125	-26.006	34.131	-11.371	1.00	53.89	A
ATOM	794	CD	GLN	A	125	-26.959	33.442	-10.402	1.00	58.25	A
ATOM	795	OE1	GLN	A	125	-27.117	32.216	-10.422	1.00	58.23	A
ATOM	796	NE2	GLN	A	125	-27.590	34.233	-9.534	1.00	58.44	A
ATOM	797	C	GLN	A	125	-27.942	34.565	-13.920	1.00	49.60	A
ATOM	798	O	GLN	A	125	-28.921	35.070	-13.366	1.00	50.24	A
ATOM	799	N	ARG	A	126	-27.361	35.119	-14.979	1.00	50.02	A
ATOM	800	CA	ARG	A	126	-27.883	36.362	-15.537	1.00	51.12	A
ATOM	801	CB	ARG	A	126	-27.070	36.766	-16.753	1.00	50.74	A
ATOM	802	CG	ARG	A	126	-25.703	37.248	-16.397	1.00	51.91	A
ATOM	803	CD	ARG	A	126	-24.873	37.578	-17.655	1.00	53.15	A
ATOM	804	NE	ARG	A	126	-23.567	36.942	-17.591	1.00	56.26	A
ATOM	805	CZ	ARG	A	126	-23.143	36.070	-18.500	1.00	56.88	A
ATOM	806	NH1	ARG	A	126	-21.926	35.525	-18.418	1.00	61.63	A
ATOM	807	NH2	ARG	A	126	-23.950	35.718	-19.488	1.00	57.30	A
ATOM	808	C	ARG	A	126	-29.365	36.270	-15.891	1.00	51.99	A
ATOM	809	O	ARG	A	126	-30.141	37.168	-15.542	1.00	53.15	A
ATOM	810	N	ILE	A	127	-29.758	35.181	-16.554	1.00	51.87	A
ATOM	811	CA	ILE	A	127	-31.152	34.972	-16.914	1.00	50.67	A
ATOM	812	CB	ILE	A	127	-31.403	33.556	-17.498	1.00	49.15	A
ATOM	813	CG2	ILE	A	127	-32.888	33.373	-17.759	1.00	45.24	A
ATOM	814	CG1	ILE	A	127	-30.611	33.343	-18.790	1.00	49.62	A
ATOM	815	CD1	ILE	A	127	-31.121	34.119	-19.945	1.00	50.32	A
ATOM	816	C	ILE	A	127	-31.992	35.089	-15.644	1.00	51.30	A
ATOM	817	O	ILE	A	127	-32.917	35.891	-15.579	1.00	50.89	A
ATOM	818	N	THR	A	128	-31.669	34.274	-14.644	1.00	52.07	A
ATOM	819	CA	THR	A	128	-32.412	34.277	-13.391	1.00	55.06	A
ATOM	820	CB	THR	A	128	-31.762	33.325	-12.358	1.00	54.18	A
ATOM	821	OG1	THR	A	128	-32.194	31.987	-12.618	1.00	55.56	A
ATOM	822	CG2	THR	A	128	-32.163	33.691	-10.943	1.00	56.16	A
ATOM	823	C	THR	A	128	-32.517	35.679	-12.811	1.00	56.81	A
ATOM	824	O	THR	A	128	-33.602	36.128	-12.445	1.00	56.02	A
ATOM	825	N	LEU	A	129	-31.383	36.370	-12.754	1.00	59.30	A
ATOM	826	CA	LEU	A	129	-31.321	37.718	-12.212	1.00	60.85	A
ATOM	827	CB	LEU	A	129	-29.863	38.176	-12.166	1.00	63.37	A
ATOM	828	CG	LEU	A	129	-29.428	39.036	-10.972	1.00	67.01	A
ATOM	829	CD1	LEU	A	129	-27.937	38.819	-10.757	1.00	67.40	A
ATOM	830	CD2	LEU	A	129	-29.758	40.522	-11.184	1.00	65.11	A
ATOM	831	C	LEU	A	129	-32.158	38.693	-13.037	1.00	61.24	A
ATOM	832	O	LEU	A	129	-32.768	39.610	-12.491	1.00	62.01	A
ATOM	833	N	TYR	A	130	-32.181	38.497	-14.351	1.00	60.00	A
ATOM	834	CA	TYR	A	130	-32.953	39.357	-15.243	1.00	58.99	A
ATOM	835	CB	TYR	A	130	-32.663	38.993	-16.701	1.00	58.50	A
ATOM	836	CG	TYR	A	130	-33.584	39.637	-17.715	1.00	57.74	A
ATOM	837	CD1	TYR	A	130	-33.439	40.974	-18.074	1.00	58.05	A
ATOM	838	CE1	TYR	A	130	-34.279	41.560	-19.020	1.00	58.22	A
ATOM	839	CD2	TYR	A	130	-34.594	38.901	-18.327	1.00	58.06	A
ATOM	840	CE2	TYR	A	130	-35.437	39.478	-19.272	1.00	57.76	A
ATOM	841	CZ	TYR	A	130	-35.274	40.805	-19.613	1.00	58.23	A
ATOM	842	OH	TYR	A	130	-36.113	41.378	-20.540	1.00	58.83	A
ATOM	843	C	TYR	A	130	-34.434	39.166	-14.957	1.00	59.31	A

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ATOM    844  O   TYR A 130     -35.183  40.134 -14.814  1.00 59.29      A
ATOM    845  N   LEU A 131     -34.844  37.904 -14.875  1.00 58.83      A
ATOM    846  CA  LEU A 131     -36.233  37.558 -14.617  1.00 58.58      A
ATOM    847  CB  LEU A 131     -36.390  36.037 -14.555  1.00 55.68      A
ATOM    848  CG  LEU A 131     -36.422  35.361 -15.922  1.00 53.74      A
ATOM    849  CD1 LEU A 131     -36.318  33.863 -15.755  1.00 54.07      A
ATOM    850  CD2 LEU A 131     -37.699  35.742 -16.649  1.00 52.53      A
ATOM    851  C   LEU A 131     -36.740  38.193 -13.330  1.00 59.15      A
ATOM    852  O   LEU A 131     -37.811  38.807 -13.304  1.00 57.39      A
ATOM    853  N   THR A 132     -35.966  38.041 -12.262  1.00 60.31      A
ATOM    854  CA  THR A 132     -36.342  38.608 -10.982  1.00 61.04      A
ATOM    855  CB  THR A 132     -35.474  38.034  -9.826  1.00 61.40      A
ATOM    856  OG1 THR A 132     -35.587  38.887  -8.680  1.00 64.65      A
ATOM    857  CG2 THR A 132     -34.026  37.929 -10.227  1.00 59.77      A
ATOM    858  C   THR A 132     -36.212  40.125 -11.044  1.00 61.41      A
ATOM    859  O   THR A 132     -37.112  40.853 -10.624  1.00 61.07      A
ATOM    860  N   GLY A 133     -35.102  40.598 -11.597  1.00 62.03      A
ATOM    861  CA  GLY A 133     -34.891  42.029 -11.705  1.00 62.46      A
ATOM    862  C   GLY A 133     -35.929  42.684 -12.592  1.00 62.83      A
ATOM    863  O   GLY A 133     -36.032  43.905 -12.634  1.00 63.96      A
ATOM    864  N   LYS A 134     -36.708  41.869 -13.295  1.00 62.98      A
ATOM    865  CA  LYS A 134     -37.729  42.375 -14.205  1.00 62.76      A
ATOM    866  CB  LYS A 134     -37.523  41.775 -15.595  1.00 63.31      A
ATOM    867  CG  LYS A 134     -37.830  42.712 -16.742  1.00 63.91      A
ATOM    868  CD  LYS A 134     -36.734  43.744 -16.932  1.00 64.03      A
ATOM    869  CE  LYS A 134     -37.008  44.589 -18.172  1.00 65.71      A
ATOM    870  NZ  LYS A 134     -35.986  45.656 -18.394  1.00 66.60      A
ATOM    871  C   LYS A 134     -39.122  42.026 -13.694  1.00 62.52      A
ATOM    872  O   LYS A 134     -40.118  42.159 -14.408  1.00 61.64      A
ATOM    873  N   ALA A 135     -39.175  41.558 -12.454  1.00 62.91      A
ATOM    874  CA  ALA A 135     -40.433  41.207 -11.809  1.00 62.68      A
ATOM    875  CB  ALA A 135     -41.307  42.469 -11.671  1.00 63.48      A
ATOM    876  C   ALA A 135     -41.221  40.096 -12.501  1.00 61.65      A
ATOM    877  O   ALA A 135     -42.444  40.041 -12.385  1.00 61.18      A
ATOM    878  N   TYR A 136     -40.525  39.215 -13.213  1.00 60.39      A
ATOM    879  CA  TYR A 136     -41.166  38.091 -13.908  1.00 60.51      A
ATOM    880  CB  TYR A 136     -41.622  37.024 -12.899  1.00 60.08      A
ATOM    881  CG  TYR A 136     -40.547  36.596 -11.924  1.00 62.10      A
ATOM    882  CD1 TYR A 136     -40.241  37.378 -10.807  1.00 62.66      A
ATOM    883  CE1 TYR A 136     -39.227  37.007  -9.919  1.00 63.23      A
ATOM    884  CD2 TYR A 136     -39.811  35.424 -12.131  1.00 62.49      A
ATOM    885  CE2 TYR A 136     -38.792  35.044 -11.249  1.00 64.05      A
ATOM    886  CZ  TYR A 136     -38.507  35.844 -10.146  1.00 63.71      A
ATOM    887  OH  TYR A 136     -37.495  35.495  -9.280  1.00 63.34      A
ATOM    888  C   TYR A 136     -42.359  38.479 -14.785  1.00 60.49      A
ATOM    889  O   TYR A 136     -43.334  37.731 -14.882  1.00 60.06      A
ATOM    890  N   SER A 137     -42.289  39.641 -15.425  1.00 61.06      A
ATOM    891  CA  SER A 137     -43.383  40.088 -16.284  1.00 61.14      A
ATOM    892  CB  SER A 137     -43.205  41.557 -16.650  1.00 60.90      A
ATOM    893  OG  SER A 137     -42.133  41.713 -17.559  1.00 63.48      A
ATOM    894  C   SER A 137     -43.432  39.257 -17.563  1.00 61.21      A
ATOM    895  O   SER A 137     -42.414  38.718 -18.004  1.00 59.84      A
ATOM    896  N   PRO A 138     -44.624  39.150 -18.178  1.00 61.71      A
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ATOM	897	CD	PRO	A	138	-45.906	39.727	-17.725	1.00	60.80	A
ATOM	898	CA	PRO	A	138	-44.819	38.384	-19.414	1.00	60.13	A
ATOM	899	CB	PRO	A	138	-46.238	38.773	-19.831	1.00	59.80	A
ATOM	900	CG	PRO	A	138	-46.929	38.932	-18.523	1.00	58.23	A
ATOM	901	C	PRO	A	138	-43.783	38.661	-20.506	1.00	59.03	A
ATOM	902	O	PRO	A	138	-43.361	37.737	-21.199	1.00	59.70	A
ATOM	903	N	CYS	A	139	-43.382	39.922	-20.659	1.00	57.95	A
ATOM	904	CA	CYS	A	139	-42.392	40.296	-21.666	1.00	58.35	A
ATOM	905	C	CYS	A	139	-41.024	39.758	-21.311	1.00	57.19	A
ATOM	906	O	CYS	A	139	-40.267	39.329	-22.185	1.00	57.07	A
ATOM	907	CB	CYS	A	139	-42.280	41.813	-21.798	1.00	60.88	A
ATOM	908	SG	CYS	A	139	-43.778	42.639	-22.404	1.00	68.54	A
ATOM	909	N	ALA	A	140	-40.701	39.807	-20.022	1.00	55.95	A
ATOM	910	CA	ALA	A	140	-39.420	39.318	-19.537	1.00	53.50	A
ATOM	911	CB	ALA	A	140	-39.307	39.547	-18.039	1.00	51.95	A
ATOM	912	C	ALA	A	140	-39.311	37.831	-19.857	1.00	52.02	A
ATOM	913	O	ALA	A	140	-38.249	37.350	-20.237	1.00	52.56	A
ATOM	914	N	TRP	A	141	-40.418	37.111	-19.714	1.00	50.19	A
ATOM	915	CA	TRP	A	141	-40.429	35.685	-19.990	1.00	49.75	A
ATOM	916	CB	TRP	A	141	-41.662	35.034	-19.365	1.00	48.78	A
ATOM	917	CG	TRP	A	141	-41.411	34.516	-17.981	1.00	49.84	A
ATOM	918	CD2	TRP	A	141	-40.564	33.415	-17.616	1.00	48.87	A
ATOM	919	CE2	TRP	A	141	-40.649	33.274	-16.212	1.00	48.13	A
ATOM	920	CE3	TRP	A	141	-39.744	32.534	-18.340	1.00	46.28	A
ATOM	921	CD1	TRP	A	141	-41.953	34.984	-16.814	1.00	47.90	A
ATOM	922	NE1	TRP	A	141	-41.501	34.243	-15.754	1.00	47.02	A
ATOM	923	CZ2	TRP	A	141	-39.944	32.281	-15.514	1.00	46.41	A
ATOM	924	CZ3	TRP	A	141	-39.042	31.544	-17.644	1.00	44.50	A
ATOM	925	CH2	TRP	A	141	-39.150	31.428	-16.246	1.00	46.31	A
ATOM	926	C	TRP	A	141	-40.373	35.394	-21.487	1.00	49.99	A
ATOM	927	O	TRP	A	141	-39.865	34.356	-21.908	1.00	49.91	A
ATOM	928	N	GLU	A	142	-40.902	36.314	-22.285	1.00	49.68	A
ATOM	929	CA	GLU	A	142	-40.885	36.176	-23.734	1.00	49.54	A
ATOM	930	CB	GLU	A	142	-41.879	37.161	-24.359	1.00	51.93	A
ATOM	931	CG	GLU	A	142	-42.054	37.014	-25.862	1.00	55.37	A
ATOM	932	CD	GLU	A	142	-42.079	35.566	-26.315	1.00	58.44	A
ATOM	933	OE1	GLU	A	142	-42.804	34.747	-25.698	1.00	59.65	A
ATOM	934	OE2	GLU	A	142	-41.371	35.252	-27.296	1.00	58.89	A
ATOM	935	C	GLU	A	142	-39.457	36.445	-24.235	1.00	48.12	A
ATOM	936	O	GLU	A	142	-38.990	35.830	-25.195	1.00	46.88	A
ATOM	937	N	VAL	A	143	-38.766	37.363	-23.569	1.00	46.47	A
ATOM	938	CA	VAL	A	143	-37.387	37.685	-23.918	1.00	46.26	A
ATOM	939	CB	VAL	A	143	-36.925	38.990	-23.219	1.00	46.29	A
ATOM	940	CG1	VAL	A	143	-35.505	39.327	-23.605	1.00	43.99	A
ATOM	941	CG2	VAL	A	143	-37.855	40.124	-23.594	1.00	48.07	A
ATOM	942	C	VAL	A	143	-36.471	36.532	-23.490	1.00	45.08	A
ATOM	943	O	VAL	A	143	-35.421	36.312	-24.087	1.00	46.32	A
ATOM	944	N	VAL	A	144	-36.861	35.800	-22.451	1.00	42.03	A
ATOM	945	CA	VAL	A	144	-36.051	34.680	-22.010	1.00	40.59	A
ATOM	946	CB	VAL	A	144	-36.331	34.343	-20.517	1.00	39.36	A
ATOM	947	CG1	VAL	A	144	-35.716	32.999	-20.144	1.00	38.27	A
ATOM	948	CG2	VAL	A	144	-35.722	35.421	-19.626	1.00	37.69	A
ATOM	949	C	VAL	A	144	-36.328	33.472	-22.916	1.00	41.36	A

ATOM 950 O VAL A 144 -35.419 32.715 -23.262 1.00 39.87 A
ATOM 951 N ARG A 145 -37.584 33.304 -23.311 1.00 42.03 A
ATOM 952 CA ARG A 145 -37.954 32.200 -24.178 1.00 43.63 A
ATOM 953 CB ARG A 145 -39.458 32.238 -24.485 1.00 43.53 A
ATOM 954 CG ARG A 145 -40.010 30.975 -25.172 1.00 44.12 A
ATOM 955 CD ARG A 145 -41.466 31.179 -25.671 1.00 47.31 A
ATOM 956 NE ARG A 145 -41.546 32.147 -26.772 1.00 49.05 A
ATOM 957 CZ ARG A 145 -41.087 31.924 -28.005 1.00 47.86 A
ATOM 958 NH1 ARG A 145 -40.526 30.765 -28.323 1.00 47.20 A
ATOM 959 NH2 ARG A 145 -41.141 32.882 -28.910 1.00 48.43 A
ATOM 960 C ARG A 145 -37.144 32.333 -25.474 1.00 44.89 A
ATOM 961 O ARG A 145 -36.551 31.367 -25.952 1.00 44.68 A
ATOM 962 N ALA A 146 -37.098 33.542 -26.024 1.00 45.26 A
ATOM 963 CA ALA A 146 -36.366 33.786 -27.267 1.00 44.68 A
ATOM 964 CB ALA A 146 -36.639 35.199 -27.766 1.00 41.89 A
ATOM 965 C ALA A 146 -34.865 33.564 -27.115 1.00 44.62 A
ATOM 966 O ALA A 146 -34.214 33.063 -28.028 1.00 45.73 A
ATOM 967 N GLU A 147 -34.319 33.940 -25.963 1.00 43.92 A
ATOM 968 CA GLU A 147 -32.894 33.772 -25.697 1.00 42.58 A
ATOM 969 CB GLU A 147 -32.512 34.500 -24.403 1.00 40.40 A
ATOM 970 CG GLU A 147 -31.124 34.186 -23.878 1.00 40.78 A
ATOM 971 CD GLU A 147 -30.021 34.667 -24.802 1.00 44.78 A
ATOM 972 OE1 GLU A 147 -30.039 35.853 -25.201 1.00 46.12 A
ATOM 973 OE2 GLU A 147 -29.125 33.862 -25.128 1.00 46.08 A
ATOM 974 C GLU A 147 -32.526 32.288 -25.600 1.00 42.73 A
ATOM 975 O GLU A 147 -31.490 31.871 -26.130 1.00 41.47 A
ATOM 976 N ILE A 148 -33.367 31.497 -24.929 1.00 41.27 A
ATOM 977 CA ILE A 148 -33.103 30.066 -24.794 1.00 42.00 A
ATOM 978 CB ILE A 148 -34.031 29.409 -23.715 1.00 42.87 A
ATOM 979 CG2 ILE A 148 -34.159 27.894 -23.939 1.00 41.81 A
ATOM 980 CG1 ILE A 148 -33.423 29.613 -22.331 1.00 42.77 A
ATOM 981 CD1 ILE A 148 -33.158 31.046 -21.993 1.00 47.88 A
ATOM 982 C ILE A 148 -33.284 29.382 -26.148 1.00 42.52 A
ATOM 983 O ILE A 148 -32.521 28.489 -26.510 1.00 40.95 A
ATOM 984 N MET A 149 -34.297 29.820 -26.890 1.00 43.15 A
ATOM 985 CA MET A 149 -34.594 29.288 -28.210 1.00 43.66 A
ATOM 986 CB MET A 149 -35.738 30.082 -28.840 1.00 45.34 A
ATOM 987 CG MET A 149 -36.136 29.660 -30.241 1.00 47.78 A
ATOM 988 SD MET A 149 -37.331 28.311 -30.248 1.00 53.42 A
ATOM 989 CE MET A 149 -36.351 27.036 -30.894 1.00 52.10 A
ATOM 990 C MET A 149 -33.342 29.456 -29.052 1.00 45.41 A
ATOM 991 O MET A 149 -32.924 28.543 -29.776 1.00 46.37 A
ATOM 992 N ARG A 150 -32.733 30.629 -28.945 1.00 45.61 A
ATOM 993 CA ARG A 150 -31.540 30.895 -29.709 1.00 47.17 A
ATOM 994 CB ARG A 150 -31.254 32.389 -29.720 1.00 48.49 A
ATOM 995 CG ARG A 150 -30.191 32.777 -30.712 1.00 53.95 A
ATOM 996 CD ARG A 150 -29.717 34.199 -30.516 1.00 59.85 A
ATOM 997 NE ARG A 150 -28.745 34.560 -31.546 1.00 66.19 A
ATOM 998 CZ ARG A 150 -27.975 35.644 -31.513 1.00 69.41 A
ATOM 999 NH1 ARG A 150 -28.053 36.493 -30.488 1.00 70.95 A
ATOM 1000 NH2 ARG A 150 -27.129 35.882 -32.510 1.00 69.33 A
ATOM 1001 C ARG A 150 -30.334 30.126 -29.161 1.00 48.23 A
ATOM 1002 O ARG A 150 -29.612 29.473 -29.923 1.00 48.56 A

ATOM	1003	N	SER	A	151	-30.122	30.177	-27.847	1.00	47.72	A
ATOM	1004	CA	SER	A	151	-28.973	29.492	-27.258	1.00	48.57	A
ATOM	1005	CB	SER	A	151	-28.714	29.993	-25.837	1.00	48.92	A
ATOM	1006	OG	SER	A	151	-29.880	29.900	-25.045	1.00	54.27	A
ATOM	1007	C	SER	A	151	-29.090	27.979	-27.253	1.00	48.50	A
ATOM	1008	O	SER	A	151	-28.113	27.278	-27.517	1.00	46.55	A
ATOM	1009	N	PHE	A	152	-30.277	27.468	-26.953	1.00	49.05	A
ATOM	1010	CA	PHE	A	152	-30.463	26.024	-26.938	1.00	50.72	A
ATOM	1011	CB	PHE	A	152	-31.808	25.667	-26.301	1.00	48.90	A
ATOM	1012	CG	PHE	A	152	-31.872	24.270	-25.772	1.00	47.92	A
ATOM	1013	CD1	PHE	A	152	-31.364	23.970	-24.514	1.00	48.09	A
ATOM	1014	CD2	PHE	A	152	-32.430	23.246	-26.535	1.00	48.59	A
ATOM	1015	CE1	PHE	A	152	-31.406	22.667	-24.010	1.00	47.02	A
ATOM	1016	CE2	PHE	A	152	-32.480	21.938	-26.047	1.00	49.53	A
ATOM	1017	CZ	PHE	A	152	-31.964	21.649	-24.775	1.00	48.38	A
ATOM	1018	C	PHE	A	152	-30.376	25.492	-28.387	1.00	52.04	A
ATOM	1019	O	PHE	A	152	-30.086	24.319	-28.612	1.00	51.28	A
ATOM	1020	N	ALA	A	153	-30.628	26.359	-29.366	1.00	53.53	A
ATOM	1021	CA	ALA	A	153	-30.521	25.960	-30.771	1.00	55.59	A
ATOM	1022	CB	ALA	A	153	-31.077	27.049	-31.698	1.00	53.76	A
ATOM	1023	C	ALA	A	153	-29.040	25.729	-31.060	1.00	55.66	A
ATOM	1024	O	ALA	A	153	-28.665	24.692	-31.599	1.00	55.80	A
ATOM	1025	N	LEU	A	154	-28.205	26.699	-30.696	1.00	57.44	A
ATOM	1026	CA	LEU	A	154	-26.756	26.584	-30.891	1.00	60.09	A
ATOM	1027	CB	LEU	A	154	-26.045	27.854	-30.407	1.00	57.36	A
ATOM	1028	CG	LEU	A	154	-26.306	29.106	-31.239	1.00	56.81	A
ATOM	1029	CD1	LEU	A	154	-25.681	30.305	-30.566	1.00	54.66	A
ATOM	1030	CD2	LEU	A	154	-25.746	28.915	-32.642	1.00	54.86	A
ATOM	1031	C	LEU	A	154	-26.212	25.376	-30.122	1.00	61.78	A
ATOM	1032	O	LEU	A	154	-25.251	24.730	-30.550	1.00	62.63	A
ATOM	1033	N	SER	A	155	-26.840	25.084	-28.986	1.00	62.76	A
ATOM	1034	CA	SER	A	155	-26.446	23.966	-28.146	1.00	63.82	A
ATOM	1035	CB	SER	A	155	-27.144	24.065	-26.797	1.00	63.60	A
ATOM	1036	OG	SER	A	155	-26.966	22.869	-26.066	1.00	65.69	A
ATOM	1037	C	SER	A	155	-26.779	22.627	-28.798	1.00	65.21	A
ATOM	1038	O	SER	A	155	-25.974	21.697	-28.767	1.00	65.58	A
ATOM	1039	N	THR	A	156	-27.976	22.531	-29.371	1.00	66.30	A
ATOM	1040	CA	THR	A	156	-28.422	21.319	-30.050	1.00	67.72	A
ATOM	1041	CB	THR	A	156	-29.893	21.452	-30.519	1.00	67.52	A
ATOM	1042	OG1	THR	A	156	-30.765	21.393	-29.386	1.00	69.40	A
ATOM	1043	CG2	THR	A	156	-30.262	20.339	-31.479	1.00	68.25	A
ATOM	1044	C	THR	A	156	-27.535	21.032	-31.267	1.00	69.26	A
ATOM	1045	O	THR	A	156	-27.422	19.885	-31.693	1.00	69.59	A
ATOM	1046	N	ASN	A	157	-26.915	22.076	-31.822	1.00	70.20	A
ATOM	1047	CA	ASN	A	157	-26.031	21.928	-32.979	1.00	70.93	A
ATOM	1048	CB	ASN	A	157	-25.561	23.295	-33.490	1.00	71.29	A
ATOM	1049	CG	ASN	A	157	-26.661	24.082	-34.186	1.00	71.77	A
ATOM	1050	OD1	ASN	A	157	-27.846	23.776	-34.054	1.00	71.35	A
ATOM	1051	ND2	ASN	A	157	-26.268	25.116	-34.924	1.00	72.68	A
ATOM	1052	C	ASN	A	157	-24.818	21.117	-32.560	1.00	72.23	A
ATOM	1053	O	ASN	A	157	-24.347	20.254	-33.302	1.00	73.06	A
ATOM	1054	N	LEU	A	158	-24.309	21.409	-31.367	1.00	73.17	A
ATOM	1055	CA	LEU	A	158	-23.152	20.701	-30.836	1.00	73.49	A

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ATOM   1056  CB  LEU A 158     -22.680  21.363 -29.539  1.00 73.26      A
ATOM   1057  CG  LEU A 158     -21.264  21.080 -29.018  1.00 74.00      A
ATOM   1058  CD1 LEU A 158     -21.085  21.764 -27.673  1.00 73.67      A
ATOM   1059  CD2 LEU A 158     -21.025  19.591 -28.866  1.00 74.47      A
ATOM   1060  C   LEU A 158     -23.601  19.270 -30.561  1.00 73.89      A
ATOM   1061  O   LEU A 158     -22.823  18.328 -30.663  1.00 72.76      A
ATOM   1062  N   GLN A 159     -24.875  19.120 -30.220  1.00 75.65      A
ATOM   1063  CA  GLN A 159     -25.439  17.811 -29.926  1.00 78.32      A
ATOM   1064  CB  GLN A 159     -26.861  17.972 -29.374  1.00 79.21      A
ATOM   1065  CG  GLN A 159     -27.392  16.753 -28.635  1.00 80.98      A
ATOM   1066  CD  GLN A 159     -28.629  17.063 -27.811  1.00 81.67      A
ATOM   1067  OE1 GLN A 159     -29.666  17.463 -28.347  1.00 82.31      A
ATOM   1068  NE2 GLN A 159     -28.522  16.883 -26.499  1.00 80.98      A
ATOM   1069  C   GLN A 159     -25.446  16.967 -31.198  1.00 79.66      A
ATOM   1070  O   GLN A 159     -25.157  15.769 -31.165  1.00 79.48      A
ATOM   1071  N   GLY A 160     -25.776  17.605 -32.320  1.00 81.34      A
ATOM   1072  CA  GLY A 160     -25.793  16.909 -33.592  1.00 81.32      A
ATOM   1073  C   GLY A 160     -24.383  16.471 -33.944  1.00 82.28      A
ATOM   1074  O   GLY A 160     -24.160  15.338 -34.363  1.00 82.91      A
ATOM   1075  N   ALA A 161     -23.420  17.369 -33.756  1.00 82.27      A
ATOM   1076  CA  ALA A 161     -22.023  17.071 -34.057  1.00 82.68      A
ATOM   1077  CB  ALA A 161     -21.197  18.371 -34.048  1.00 82.24      A
ATOM   1078  C   ALA A 161     -21.435  16.061 -33.067  1.00 82.41      A
ATOM   1079  O   ALA A 161     -20.248  15.738 -33.117  1.00 82.19      A
ATOM   1080  N   LEU A 162     -22.274  15.560 -32.171  1.00 82.59      A
ATOM   1081  CA  LEU A 162     -21.833  14.600 -31.169  1.00 82.81      A
ATOM   1082  CB  LEU A 162     -22.266  15.075 -29.776  1.00 81.71      A
ATOM   1083  CG  LEU A 162     -22.133  14.141 -28.573  1.00 80.63      A
ATOM   1084  CD1 LEU A 162     -21.690  14.939 -27.359  1.00 80.31      A
ATOM   1085  CD2 LEU A 162     -23.463  13.447 -28.309  1.00 79.59      A
ATOM   1086  C   LEU A 162     -22.379  13.206 -31.450  1.00 83.84      A
ATOM   1087  O   LEU A 162     -21.694  12.207 -31.222  1.00 83.86      A
ATOM   1088  N   GLY A 163     -23.606  13.142 -31.958  1.00 84.78      A
ATOM   1089  CA  GLY A 163     -24.212  11.855 -32.255  1.00 85.12      A
ATOM   1090  C   GLY A 163     -23.963  11.378 -33.671  1.00 85.32      A
ATOM   1091  O   GLY A 163     -24.939  10.958 -34.330  1.00 85.87      A
ATOM   1092  OXT GLY A 163     -22.795  11.408 -34.121  1.00 84.75      A
ATOM   1093  CB  ASN B  11     -36.003  31.054 -49.710  1.00 85.15      B
ATOM   1094  CG  ASN B  11     -35.553  29.922 -50.640  1.00 85.60      B
ATOM   1095  OD1 ASN B  11     -34.661  29.139 -50.297  1.00 84.41      B
ATOM   1096  ND2 ASN B  11     -36.172  29.834 -51.818  1.00 84.86      B
ATOM   1097  C   ASN B  11     -38.419  31.748 -49.975  1.00 83.40      B
ATOM   1098  O   ASN B  11     -38.848  32.106 -48.869  1.00 83.24      B
ATOM   1099  N   ASN B  11     -36.612  33.443 -50.017  1.00 85.25      B
ATOM   1100  CA  ASN B  11     -36.970  32.041 -50.393  1.00 84.75      B
ATOM   1101  N   ARG B  12     -39.176  31.116 -50.871  1.00 80.64      B
ATOM   1102  CA  ARG B  12     -40.566  30.781 -50.583  1.00 75.89      B
ATOM   1103  CB  ARG B  12     -41.494  31.295 -51.681  1.00 76.32      B
ATOM   1104  CG  ARG B  12     -42.957  31.189 -51.303  1.00 77.28      B
ATOM   1105  CD  ARG B  12     -43.165  31.751 -49.908  1.00 77.55      B
ATOM   1106  NE  ARG B  12     -44.512  32.270 -49.718  1.00 78.19      B
ATOM   1107  CZ  ARG B  12     -44.864  33.064 -48.715  1.00 77.18      B
ATOM   1108  NH1 ARG B  12     -43.962  33.426 -47.813  1.00 76.35      B
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ATOM	1109	NH2	ARG	B	12	-46.113	33.503	-48.622	1.00	76.77	B
ATOM	1110	C	ARG	B	12	-40.747	29.286	-50.453	1.00	72.00	B
ATOM	1111	O	ARG	B	12	-41.679	28.718	-51.024	1.00	69.87	B
ATOM	1112	N	ARG	B	13	-39.860	28.652	-49.694	1.00	68.53	B
ATOM	1113	CA	ARG	B	13	-39.940	27.215	-49.514	1.00	66.86	B
ATOM	1114	CB	ARG	B	13	-38.635	26.669	-48.944	1.00	69.00	B
ATOM	1115	CG	ARG	B	13	-38.279	27.157	-47.572	1.00	72.00	B
ATOM	1116	CD	ARG	B	13	-37.016	26.456	-47.145	1.00	75.81	B
ATOM	1117	NE	ARG	B	13	-37.112	25.019	-47.396	1.00	78.98	B
ATOM	1118	CZ	ARG	B	13	-36.088	24.176	-47.307	1.00	80.56	B
ATOM	1119	NH1	ARG	B	13	-34.886	24.632	-46.971	1.00	82.00	B
ATOM	1120	NH2	ARG	B	13	-36.263	22.882	-47.557	1.00	78.63	B
ATOM	1121	C	ARG	B	13	-41.110	26.828	-48.628	1.00	63.21	B
ATOM	1122	O	ARG	B	13	-41.297	25.660	-48.296	1.00	63.10	B
ATOM	1123	N	ALA	B	14	-41.906	27.819	-48.256	1.00	58.81	B
ATOM	1124	CA	ALA	B	14	-43.068	27.565	-47.439	1.00	56.19	B
ATOM	1125	CB	ALA	B	14	-43.667	28.874	-46.988	1.00	57.98	B
ATOM	1126	C	ALA	B	14	-44.066	26.779	-48.288	1.00	54.53	B
ATOM	1127	O	ALA	B	14	-44.438	25.651	-47.958	1.00	53.40	B
ATOM	1128	N	LEU	B	15	-44.490	27.379	-49.393	1.00	53.25	B
ATOM	1129	CA	LEU	B	15	-45.437	26.730	-50.287	1.00	51.60	B
ATOM	1130	CB	LEU	B	15	-45.868	27.717	-51.376	1.00	53.42	B
ATOM	1131	CG	LEU	B	15	-46.780	28.860	-50.918	1.00	54.05	B
ATOM	1132	CD1	LEU	B	15	-46.739	30.011	-51.905	1.00	53.59	B
ATOM	1133	CD2	LEU	B	15	-48.192	28.335	-50.780	1.00	55.07	B
ATOM	1134	C	LEU	B	15	-44.836	25.465	-50.911	1.00	49.98	B
ATOM	1135	O	LEU	B	15	-45.538	24.473	-51.136	1.00	49.36	B
ATOM	1136	N	ILE	B	16	-43.535	25.491	-51.178	1.00	46.77	B
ATOM	1137	CA	ILE	B	16	-42.883	24.334	-51.765	1.00	45.58	B
ATOM	1138	CB	ILE	B	16	-41.435	24.679	-52.164	1.00	45.17	B
ATOM	1139	CG2	ILE	B	16	-40.607	23.420	-52.375	1.00	42.57	B
ATOM	1140	CG1	ILE	B	16	-41.466	25.512	-53.448	1.00	44.62	B
ATOM	1141	CD1	ILE	B	16	-40.094	25.930	-53.945	1.00	47.42	B
ATOM	1142	C	ILE	B	16	-42.926	23.097	-50.863	1.00	46.11	B
ATOM	1143	O	ILE	B	16	-43.308	22.013	-51.309	1.00	45.20	B
ATOM	1144	N	LEU	B	17	-42.548	23.246	-49.596	1.00	46.19	B
ATOM	1145	CA	LEU	B	17	-42.584	22.105	-48.676	1.00	45.40	B
ATOM	1146	CB	LEU	B	17	-42.067	22.519	-47.303	1.00	43.77	B
ATOM	1147	CG	LEU	B	17	-40.618	22.983	-47.397	1.00	43.17	B
ATOM	1148	CD1	LEU	B	17	-40.256	23.847	-46.210	1.00	42.11	B
ATOM	1149	CD2	LEU	B	17	-39.723	21.774	-47.522	1.00	42.21	B
ATOM	1150	C	LEU	B	17	-44.007	21.566	-48.567	1.00	45.21	B
ATOM	1151	O	LEU	B	17	-44.219	20.354	-48.575	1.00	45.78	B
ATOM	1152	N	LEU	B	18	-44.983	22.464	-48.466	1.00	44.38	B
ATOM	1153	CA	LEU	B	18	-46.373	22.046	-48.391	1.00	44.44	B
ATOM	1154	CB	LEU	B	18	-47.291	23.257	-48.262	1.00	43.44	B
ATOM	1155	CG	LEU	B	18	-47.574	23.721	-46.831	1.00	43.94	B
ATOM	1156	CD1	LEU	B	18	-48.104	25.149	-46.842	1.00	42.55	B
ATOM	1157	CD2	LEU	B	18	-48.565	22.761	-46.172	1.00	40.40	B
ATOM	1158	C	LEU	B	18	-46.713	21.278	-49.654	1.00	46.61	B
ATOM	1159	O	LEU	B	18	-47.504	20.332	-49.628	1.00	47.62	B
ATOM	1160	N	ALA	B	19	-46.107	21.692	-50.764	1.00	47.27	B
ATOM	1161	CA	ALA	B	19	-46.326	21.043	-52.053	1.00	47.65	B

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ATOM   1162  CB  ALA B  19     -45.762  21.912 -53.174  1.00 47.43      B
ATOM   1163  C   ALA B  19     -45.679  19.659 -52.087  1.00 48.06      B
ATOM   1164  O   ALA B  19     -46.257  18.715 -52.620  1.00 47.48      B
ATOM   1165  N   GLN B  20     -44.474  19.553 -51.526  1.00 49.52      B
ATOM   1166  CA  GLN B  20     -43.742  18.286 -51.482  1.00 50.43      B
ATOM   1167  CB  GLN B  20     -42.266  18.521 -51.141  1.00 50.28      B
ATOM   1168  CG  GLN B  20     -41.409  19.164 -52.227  1.00 48.64      B
ATOM   1169  CD  GLN B  20     -40.000  19.484 -51.738  1.00 49.87      B
ATOM   1170  OE1 GLN B  20     -39.518  18.888 -50.778  1.00 51.73      B
ATOM   1171  NE2 GLN B  20     -39.333  20.418 -52.403  1.00 49.40      B
ATOM   1172  C   GLN B  20     -44.352  17.371 -50.428  1.00 51.95      B
ATOM   1173  O   GLN B  20     -44.020  16.199 -50.350  1.00 52.62      B
ATOM   1174  N   MET B  21     -45.249  17.915 -49.618  1.00 54.15      B
ATOM   1175  CA  MET B  21     -45.892  17.138 -48.568  1.00 56.60      B
ATOM   1176  CB  MET B  21     -46.325  18.064 -47.420  1.00 56.38      B
ATOM   1177  CG  MET B  21     -45.231  18.357 -46.394  1.00 57.01      B
ATOM   1178  SD  MET B  21     -45.690  19.612 -45.174  1.00 57.20      B
ATOM   1179  CE  MET B  21     -47.211  18.885 -44.499  1.00 57.95      B
ATOM   1180  C   MET B  21     -47.090  16.327 -49.056  1.00 58.24      B
ATOM   1181  O   MET B  21     -47.551  15.424 -48.363  1.00 58.12      B
ATOM   1182  N   ALA B  22     -47.600  16.645 -50.243  1.00 61.09      B
ATOM   1183  CA  ALA B  22     -48.754  15.922 -50.773  1.00 62.96      B
ATOM   1184  CB  ALA B  22     -49.151  16.468 -52.145  1.00 61.96      B
ATOM   1185  C   ALA B  22     -48.415  14.446 -50.872  1.00 64.38      B
ATOM   1186  O   ALA B  22     -47.323  14.086 -51.300  1.00 64.43      B
ATOM   1187  N   ARG B  23     -49.352  13.596 -50.463  1.00 67.27      B
ATOM   1188  CA  ARG B  23     -49.132  12.158 -50.508  1.00 70.44      B
ATOM   1189  CB  ARG B  23     -48.613  11.669 -49.152  1.00 71.01      B
ATOM   1190  CG  ARG B  23     -49.450  12.102 -47.968  1.00 72.18      B
ATOM   1191  CD  ARG B  23     -48.731  11.815 -46.667  1.00 73.33      B
ATOM   1192  NE  ARG B  23     -48.552  10.385 -46.450  1.00 76.38      B
ATOM   1193  CZ  ARG B  23     -47.854   9.860 -45.445  1.00 78.19      B
ATOM   1194  NH1 ARG B  23     -47.256  10.649 -44.553  1.00 77.51      B
ATOM   1195  NH2 ARG B  23     -47.760   8.538 -45.329  1.00 77.90      B
ATOM   1196  C   ARG B  23     -50.362  11.354 -50.923  1.00 72.04      B
ATOM   1197  O   ARG B  23     -50.280  10.139 -51.102  1.00 73.43      B
ATOM   1198  N   ALA B  24     -51.500  12.023 -51.077  1.00 73.32      B
ATOM   1199  CA  ALA B  24     -52.721  11.340 -51.489  1.00 75.11      B
ATOM   1200  CB  ALA B  24     -53.947  12.016 -50.872  1.00 72.05      B
ATOM   1201  C   ALA B  24     -52.817  11.370 -53.011  1.00 77.82      B
ATOM   1202  O   ALA B  24     -52.334  12.309 -53.653  1.00 78.81      B
ATOM   1203  N   SER B  25     -53.429  10.339 -53.588  1.00 79.74      B
ATOM   1204  CA  SER B  25     -53.599  10.261 -55.033  1.00 82.06      B
ATOM   1205  CB  SER B  25     -53.912   8.827 -55.442  1.00 82.21      B
ATOM   1206  OG  SER B  25     -55.044   8.348 -54.737  1.00 83.63      B
ATOM   1207  C   SER B  25     -54.746  11.178 -55.459  1.00 84.39      B
ATOM   1208  O   SER B  25     -55.633  11.492 -54.657  1.00 84.68      B
ATOM   1209  N   PRO B  26     -54.749  11.614 -56.730  1.00 85.80      B
ATOM   1210  CD  PRO B  26     -53.769  11.287 -57.779  1.00 85.92      B
ATOM   1211  CA  PRO B  26     -55.793  12.500 -57.254  1.00 87.16      B
ATOM   1212  CB  PRO B  26     -55.212  12.950 -58.588  1.00 86.58      B
ATOM   1213  CG  PRO B  26     -54.482  11.736 -59.038  1.00 86.26      B
ATOM   1214  C   PRO B  26     -57.166  11.837 -57.407  1.00 88.81      B
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ATOM	1215	O	PRO	B	26	-58.139	12.487	-57.795	1.00	89.06	B
ATOM	1216	N	PHE	B	27	-57.242	10.544	-57.108	1.00	89.93	B
ATOM	1217	CA	PHE	B	27	-58.507	9.823	-57.207	1.00	91.46	B
ATOM	1218	CB	PHE	B	27	-58.359	8.550	-58.053	1.00	91.94	B
ATOM	1219	CG	PHE	B	27	-57.967	8.801	-59.482	1.00	91.42	B
ATOM	1220	CD1	PHE	B	27	-56.659	9.137	-59.811	1.00	91.14	B
ATOM	1221	CD2	PHE	B	27	-58.909	8.695	-60.498	1.00	90.75	B
ATOM	1222	CE1	PHE	B	27	-56.294	9.361	-61.131	1.00	91.14	B
ATOM	1223	CE2	PHE	B	27	-58.555	8.917	-61.820	1.00	91.00	B
ATOM	1224	CZ	PHE	B	27	-57.245	9.252	-62.139	1.00	91.47	B
ATOM	1225	C	PHE	B	27	-58.989	9.426	-55.820	1.00	92.32	B
ATOM	1226	O	PHE	B	27	-60.192	9.267	-55.599	1.00	93.11	B
ATOM	1227	N	ALA	B	28	-58.035	9.269	-54.900	1.00	92.92	B
ATOM	1228	CA	ALA	B	28	-58.295	8.864	-53.516	1.00	92.18	B
ATOM	1229	CB	ALA	B	28	-56.996	8.915	-52.706	1.00	91.40	B
ATOM	1230	C	ALA	B	28	-59.387	9.649	-52.790	1.00	91.90	B
ATOM	1231	O	ALA	B	28	-60.199	9.057	-52.074	1.00	91.57	B
ATOM	1232	N	CYS	B	29	-59.416	10.969	-52.963	1.00	91.32	B
ATOM	1233	CA	CYS	B	29	-60.433	11.772	-52.288	1.00	91.47	B
ATOM	1234	C	CYS	B	29	-61.450	12.374	-53.243	1.00	92.66	B
ATOM	1235	O	CYS	B	29	-61.088	12.992	-54.245	1.00	92.45	B
ATOM	1236	CB	CYS	B	29	-59.780	12.887	-51.463	1.00	89.53	B
ATOM	1237	SG	CYS	B	29	-58.531	12.280	-50.282	1.00	86.39	B
ATOM	1238	N	GLY	B	30	-62.727	12.178	-52.926	1.00	93.98	B
ATOM	1239	CA	GLY	B	30	-63.784	12.716	-53.758	1.00	95.70	B
ATOM	1240	C	GLY	B	30	-63.862	14.212	-53.543	1.00	96.95	B
ATOM	1241	O	GLY	B	30	-63.276	14.727	-52.592	1.00	97.62	B
ATOM	1242	N	GLY	B	31	-64.577	14.908	-54.420	1.00	97.39	B
ATOM	1243	CA	GLY	B	31	-64.707	16.349	-54.296	1.00	97.58	B
ATOM	1244	C	GLY	B	31	-65.411	16.803	-53.027	1.00	97.64	B
ATOM	1245	O	GLY	B	31	-66.503	17.375	-53.083	1.00	98.81	B
ATOM	1246	N	GLY	B	32	-64.787	16.546	-51.880	1.00	96.79	B
ATOM	1247	CA	GLY	B	32	-65.360	16.951	-50.609	1.00	94.95	B
ATOM	1248	C	GLY	B	32	-64.893	18.350	-50.254	1.00	93.64	B
ATOM	1249	O	GLY	B	32	-64.396	18.597	-49.150	1.00	93.49	B
ATOM	1250	N	GLY	B	33	-65.052	19.265	-51.207	1.00	92.18	B
ATOM	1251	CA	GLY	B	33	-64.646	20.645	-51.009	1.00	89.82	B
ATOM	1252	C	GLY	B	33	-65.345	21.318	-49.846	1.00	88.28	B
ATOM	1253	O	GLY	B	33	-66.577	21.331	-49.762	1.00	88.34	B
ATOM	1254	N	HIS	B	34	-64.544	21.878	-48.943	1.00	85.84	B
ATOM	1255	CA	HIS	B	34	-65.053	22.571	-47.762	1.00	82.36	B
ATOM	1256	CB	HIS	B	34	-64.630	21.808	-46.496	1.00	80.60	B
ATOM	1257	CG	HIS	B	34	-65.146	22.398	-45.220	1.00	78.05	B
ATOM	1258	CD2	HIS	B	34	-65.986	21.899	-44.281	1.00	76.62	B
ATOM	1259	ND1	HIS	B	34	-64.766	23.644	-44.763	1.00	77.24	B
ATOM	1260	CE1	HIS	B	34	-65.346	23.883	-43.603	1.00	75.05	B
ATOM	1261	NE2	HIS	B	34	-66.092	22.838	-43.287	1.00	75.00	B
ATOM	1262	C	HIS	B	34	-64.472	23.983	-47.764	1.00	80.50	B
ATOM	1263	O	HIS	B	34	-63.349	24.198	-48.226	1.00	81.27	B
ATOM	1264	N	ASP	B	35	-65.246	24.947	-47.278	1.00	77.74	B
ATOM	1265	CA	ASP	B	35	-64.787	26.330	-47.225	1.00	75.78	B
ATOM	1266	CB	ASP	B	35	-65.795	27.264	-47.895	1.00	76.50	B
ATOM	1267	CG	ASP	B	35	-65.703	28.687	-47.371	1.00	77.21	B

ATOM 1268 OD1 ASP B 35 -64.578 29.227 -47.288 1.00 77.48 B
ATOM 1269 OD2 ASP B 35 -66.759 29.266 -47.040 1.00 77.57 B
ATOM 1270 C ASP B 35 -64.579 26.767 -45.784 1.00 73.69 B
ATOM 1271 O ASP B 35 -65.486 26.653 -44.956 1.00 74.03 B
ATOM 1272 N PHE B 36 -63.390 27.282 -45.484 1.00 69.71 B
ATOM 1273 CA PHE B 36 -63.097 27.707 -44.125 1.00 65.47 B
ATOM 1274 CB PHE B 36 -61.694 27.260 -43.724 1.00 63.29 B
ATOM 1275 CG PHE B 36 -61.484 25.780 -43.842 1.00 61.40 B
ATOM 1276 CD1 PHE B 36 -61.068 25.218 -45.040 1.00 60.82 B
ATOM 1277 CD2 PHE B 36 -61.722 24.942 -42.762 1.00 59.30 B
ATOM 1278 CE1 PHE B 36 -60.896 23.840 -45.157 1.00 59.96 B
ATOM 1279 CE2 PHE B 36 -61.554 23.568 -42.873 1.00 58.76 B
ATOM 1280 CZ PHE B 36 -61.139 23.018 -44.071 1.00 57.07 B
ATOM 1281 C PHE B 36 -63.254 29.195 -43.882 1.00 63.46 B
ATOM 1282 O PHE B 36 -62.813 29.701 -42.860 1.00 63.36 B
ATOM 1283 N GLY B 37 -63.892 29.889 -44.816 1.00 61.85 B
ATOM 1284 CA GLY B 37 -64.105 31.317 -44.657 1.00 60.22 B
ATOM 1285 C GLY B 37 -62.860 32.105 -44.299 1.00 59.45 B
ATOM 1286 O GLY B 37 -62.897 32.984 -43.436 1.00 59.52 B
ATOM 1287 N PHE B 38 -61.757 31.785 -44.965 1.00 58.21 B
ATOM 1288 CA PHE B 38 -60.496 32.467 -44.735 1.00 57.09 B
ATOM 1289 CB PHE B 38 -59.465 32.035 -45.776 1.00 55.16 B
ATOM 1290 CG PHE B 38 -58.169 32.774 -45.684 1.00 52.52 B
ATOM 1291 CD1 PHE B 38 -57.409 32.728 -44.523 1.00 51.16 B
ATOM 1292 CD2 PHE B 38 -57.704 33.517 -46.760 1.00 52.45 B
ATOM 1293 CE1 PHE B 38 -56.201 33.414 -44.433 1.00 50.89 B
ATOM 1294 CE2 PHE B 38 -56.492 34.207 -46.681 1.00 52.43 B
ATOM 1295 CZ PHE B 38 -55.741 34.152 -45.511 1.00 51.93 B
ATOM 1296 C PHE B 38 -60.729 33.958 -44.844 1.00 57.08 B
ATOM 1297 O PHE B 38 -61.224 34.434 -45.853 1.00 56.69 B
ATOM 1298 N PRO B 39 -60.369 34.716 -43.802 1.00 58.27 B
ATOM 1299 CD PRO B 39 -59.687 34.259 -42.581 1.00 58.11 B
ATOM 1300 CA PRO B 39 -60.542 36.168 -43.776 1.00 60.08 B
ATOM 1301 CB PRO B 39 -60.253 36.511 -42.323 1.00 59.19 B
ATOM 1302 CG PRO B 39 -59.163 35.556 -41.999 1.00 58.94 B
ATOM 1303 C PRO B 39 -59.596 36.875 -44.742 1.00 62.95 B
ATOM 1304 O PRO B 39 -58.544 37.387 -44.344 1.00 63.46 B
ATOM 1305 N GLN B 40 -59.982 36.908 -46.014 1.00 65.02 B
ATOM 1306 CA GLN B 40 -59.163 37.545 -47.031 1.00 66.34 B
ATOM 1307 CB GLN B 40 -59.705 37.224 -48.412 1.00 66.89 B
ATOM 1308 CG GLN B 40 -58.720 37.527 -49.510 1.00 69.39 B
ATOM 1309 CD GLN B 40 -59.274 37.201 -50.872 1.00 71.14 B
ATOM 1310 OE1 GLN B 40 -59.732 36.084 -51.121 1.00 71.05 B
ATOM 1311 NE2 GLN B 40 -59.235 38.174 -51.769 1.00 72.52 B
ATOM 1312 C GLN B 40 -59.085 39.056 -46.856 1.00 67.85 B
ATOM 1313 O GLN B 40 -58.107 39.678 -47.260 1.00 67.07 B
ATOM 1314 N GLU B 41 -60.110 39.643 -46.248 1.00 70.00 B
ATOM 1315 CA GLU B 41 -60.135 41.085 -46.029 1.00 73.07 B
ATOM 1316 CB GLU B 41 -61.390 41.506 -45.255 1.00 73.73 B
ATOM 1317 CG GLU B 41 -62.623 40.648 -45.473 1.00 75.45 B
ATOM 1318 CD GLU B 41 -62.636 39.399 -44.604 1.00 76.40 B
ATOM 1319 OE1 GLU B 41 -62.528 39.534 -43.363 1.00 75.97 B
ATOM 1320 OE2 GLU B 41 -62.764 38.285 -45.162 1.00 76.54 B

ATOM	1321	C	GLU	B	41	-58.914	41.562	-45.241	1.00	74.88	B
ATOM	1322	O	GLU	B	41	-58.437	42.675	-45.439	1.00	75.45	B
ATOM	1323	N	GLU	B	42	-58.414	40.722	-44.342	1.00	76.27	B
ATOM	1324	CA	GLU	B	42	-57.272	41.091	-43.515	1.00	76.77	B
ATOM	1325	CB	GLU	B	42	-57.154	40.118	-42.341	1.00	77.03	B
ATOM	1326	CG	GLU	B	42	-58.484	39.812	-41.670	1.00	76.96	B
ATOM	1327	CD	GLU	B	42	-59.135	41.036	-41.062	1.00	77.01	B
ATOM	1328	OE1	GLU	B	42	-60.354	40.980	-40.783	1.00	76.54	B
ATOM	1329	OE2	GLU	B	42	-58.428	42.047	-40.855	1.00	77.00	B
ATOM	1330	C	GLU	B	42	-55.953	41.136	-44.276	1.00	77.34	B
ATOM	1331	O	GLU	B	42	-54.978	41.721	-43.797	1.00	76.70	B
ATOM	1332	N	PHE	B	43	-55.927	40.523	-45.460	1.00	78.79	B
ATOM	1333	CA	PHE	B	43	-54.716	40.481	-46.282	1.00	79.57	B
ATOM	1334	CB	PHE	B	43	-54.354	39.030	-46.614	1.00	76.30	B
ATOM	1335	CG	PHE	B	43	-54.174	38.158	-45.407	1.00	73.38	B
ATOM	1336	CD1	PHE	B	43	-55.259	37.518	-44.827	1.00	72.32	B
ATOM	1337	CD2	PHE	B	43	-52.918	37.982	-44.846	1.00	72.34	B
ATOM	1338	CE1	PHE	B	43	-55.093	36.716	-43.708	1.00	71.63	B
ATOM	1339	CE2	PHE	B	43	-52.743	37.182	-43.727	1.00	71.80	B
ATOM	1340	CZ	PHE	B	43	-53.832	36.547	-43.158	1.00	71.86	B
ATOM	1341	C	PHE	B	43	-54.830	41.274	-47.584	1.00	81.78	B
ATOM	1342	O	PHE	B	43	-54.032	42.171	-47.855	1.00	82.37	B
ATOM	1343	N	GLY	B	44	-55.825	40.932	-48.391	1.00	84.35	B
ATOM	1344	CA	GLY	B	44	-56.013	41.619	-49.654	1.00	86.86	B
ATOM	1345	C	GLY	B	44	-56.880	42.859	-49.557	1.00	88.99	B
ATOM	1346	O	GLY	B	44	-58.085	42.785	-49.304	1.00	88.66	B
ATOM	1347	N	GLY	B	45	-56.259	44.011	-49.766	1.00	90.98	B
ATOM	1348	CA	GLY	B	45	-56.995	45.256	-49.708	1.00	93.31	B
ATOM	1349	C	GLY	B	45	-56.073	46.453	-49.679	1.00	95.02	B
ATOM	1350	O	GLY	B	45	-54.874	46.323	-49.413	1.00	95.65	B
ATOM	1351	N	GLY	B	46	-56.633	47.624	-49.967	1.00	95.75	B
ATOM	1352	CA	GLY	B	46	-55.846	48.839	-49.947	1.00	96.64	B
ATOM	1353	C	GLY	B	46	-55.513	49.204	-48.513	1.00	97.19	B
ATOM	1354	O	GLY	B	46	-55.188	50.354	-48.212	1.00	97.50	B
ATOM	1355	N	GLY	B	47	-55.602	48.218	-47.623	1.00	97.06	B
ATOM	1356	CA	GLY	B	47	-55.307	48.454	-46.223	1.00	97.22	B
ATOM	1357	C	GLY	B	47	-54.088	49.337	-46.029	1.00	97.43	B
ATOM	1358	O	GLY	B	47	-54.193	50.430	-45.463	1.00	97.59	B
ATOM	1359	N	GLY	B	48	-52.935	48.868	-46.508	1.00	96.90	B
ATOM	1360	CA	GLY	B	48	-51.700	49.623	-46.371	1.00	95.31	B
ATOM	1361	C	GLY	B	48	-51.429	50.049	-44.937	1.00	94.30	B
ATOM	1362	O	GLY	B	48	-51.772	51.165	-44.541	1.00	94.67	B
ATOM	1363	N	ALA	B	49	-50.817	49.163	-44.155	1.00	92.52	B
ATOM	1364	CA	ALA	B	49	-50.508	49.455	-42.756	1.00	90.44	B
ATOM	1365	CB	ALA	B	49	-51.795	49.488	-41.929	1.00	90.39	B
ATOM	1366	C	ALA	B	49	-49.536	48.424	-42.182	1.00	88.31	B
ATOM	1367	O	ALA	B	49	-49.944	47.366	-41.697	1.00	87.77	B
ATOM	1368	N	GLY	B	50	-48.249	48.753	-42.241	1.00	85.76	B
ATOM	1369	CA	GLY	B	50	-47.214	47.865	-41.742	1.00	82.69	B
ATOM	1370	C	GLY	B	50	-47.476	47.214	-40.396	1.00	80.16	B
ATOM	1371	O	GLY	B	50	-46.976	46.125	-40.130	1.00	80.60	B
ATOM	1372	N	ALA	B	51	-48.256	47.867	-39.543	1.00	77.39	B
ATOM	1373	CA	ALA	B	51	-48.548	47.319	-38.223	1.00	74.09	B

ATOM 1374 CB ALA B 51 -48.967 48.433 -37.273 1.00 74.25 B
ATOM 1375 C ALA B 51 -49.631 46.252 -38.287 1.00 71.65 B
ATOM 1376 O ALA B 51 -49.622 45.307 -37.499 1.00 70.67 B
ATOM 1377 N ALA B 52 -50.568 46.412 -39.220 1.00 68.72 B
ATOM 1378 CA ALA B 52 -51.652 45.450 -39.392 1.00 65.82 B
ATOM 1379 CB ALA B 52 -52.784 46.066 -40.204 1.00 65.58 B
ATOM 1380 C ALA B 52 -51.102 44.226 -40.111 1.00 63.64 B
ATOM 1381 O ALA B 52 -51.346 43.086 -39.713 1.00 63.09 B
ATOM 1382 N ALA B 53 -50.351 44.472 -41.175 1.00 60.70 B
ATOM 1383 CA ALA B 53 -49.758 43.390 -41.942 1.00 58.62 B
ATOM 1384 CB ALA B 53 -48.812 43.959 -42.994 1.00 57.63 B
ATOM 1385 C ALA B 53 -49.003 42.443 -41.014 1.00 56.79 B
ATOM 1386 O ALA B 53 -49.350 41.271 -40.897 1.00 56.46 B
ATOM 1387 N ILE B 54 -47.977 42.971 -40.350 1.00 55.35 B
ATOM 1388 CA ILE B 54 -47.139 42.197 -39.440 1.00 53.78 B
ATOM 1389 CB ILE B 54 -46.178 43.100 -38.678 1.00 53.66 B
ATOM 1390 CG2 ILE B 54 -45.360 42.267 -37.708 1.00 53.50 B
ATOM 1391 CG1 ILE B 54 -45.275 43.848 -39.665 1.00 54.89 B
ATOM 1392 CD1 ILE B 54 -44.430 44.947 -39.029 1.00 53.54 B
ATOM 1393 C ILE B 54 -47.913 41.393 -38.412 1.00 53.50 B
ATOM 1394 O ILE B 54 -47.529 40.280 -38.074 1.00 53.63 B
ATOM 1395 N SER B 55 -48.999 41.965 -37.916 1.00 53.54 B
ATOM 1396 CA SER B 55 -49.820 41.306 -36.922 1.00 53.69 B
ATOM 1397 CB SER B 55 -50.764 42.312 -36.277 1.00 55.26 B
ATOM 1398 OG SER B 55 -50.023 43.376 -35.708 1.00 58.90 B
ATOM 1399 C SER B 55 -50.615 40.161 -37.515 1.00 52.96 B
ATOM 1400 O SER B 55 -50.797 39.142 -36.867 1.00 54.85 B
ATOM 1401 N VAL B 56 -51.098 40.307 -38.738 1.00 51.44 B
ATOM 1402 CA VAL B 56 -51.849 39.210 -39.318 1.00 51.64 B
ATOM 1403 CB VAL B 56 -52.798 39.692 -40.431 1.00 51.99 B
ATOM 1404 CG1 VAL B 56 -53.812 40.643 -39.846 1.00 50.15 B
ATOM 1405 CG2 VAL B 56 -52.020 40.360 -41.536 1.00 51.94 B
ATOM 1406 C VAL B 56 -50.924 38.115 -39.849 1.00 51.00 B
ATOM 1407 O VAL B 56 -51.165 36.937 -39.613 1.00 50.59 B
ATOM 1408 N LEU B 57 -49.867 38.489 -40.560 1.00 50.84 B
ATOM 1409 CA LEU B 57 -48.943 37.479 -41.061 1.00 51.20 B
ATOM 1410 CB LEU B 57 -47.755 38.107 -41.798 1.00 51.55 B
ATOM 1411 CG LEU B 57 -47.820 38.373 -43.304 1.00 52.66 B
ATOM 1412 CD1 LEU B 57 -48.796 37.400 -43.946 1.00 52.07 B
ATOM 1413 CD2 LEU B 57 -48.221 39.805 -43.569 1.00 52.06 B
ATOM 1414 C LEU B 57 -48.410 36.699 -39.871 1.00 50.92 B
ATOM 1415 O LEU B 57 -48.392 35.462 -39.879 1.00 51.14 B
ATOM 1416 N HIS B 58 -47.983 37.427 -38.841 1.00 48.84 B
ATOM 1417 CA HIS B 58 -47.433 36.786 -37.649 1.00 48.56 B
ATOM 1418 CB HIS B 58 -47.033 37.837 -36.593 1.00 45.06 B
ATOM 1419 CG HIS B 58 -46.150 37.292 -35.510 1.00 41.60 B
ATOM 1420 CD2 HIS B 58 -44.811 37.390 -35.322 1.00 40.97 B
ATOM 1421 ND1 HIS B 58 -46.620 36.470 -34.511 1.00 41.10 B
ATOM 1422 CE1 HIS B 58 -45.605 36.077 -33.754 1.00 39.76 B
ATOM 1423 NE2 HIS B 58 -44.500 36.619 -34.225 1.00 38.18 B
ATOM 1424 C HIS B 58 -48.405 35.769 -37.035 1.00 47.89 B
ATOM 1425 O HIS B 58 -48.000 34.667 -36.652 1.00 47.61 B
ATOM 1426 N GLU B 59 -49.682 36.125 -36.955 1.00 44.67 B

ATOM	1427	CA	GLU	B	59	-50.649	35.215	-36.376	1.00	44.65	B
ATOM	1428	CB	GLU	B	59	-51.992	35.911	-36.156	1.00	45.09	B
ATOM	1429	CG	GLU	B	59	-52.996	35.078	-35.377	1.00	46.22	B
ATOM	1430	CD	GLU	B	59	-52.491	34.750	-33.994	1.00	48.75	B
ATOM	1431	OE1	GLU	B	59	-51.714	35.571	-33.474	1.00	50.15	B
ATOM	1432	OE2	GLU	B	59	-52.860	33.696	-33.422	1.00	48.92	B
ATOM	1433	C	GLU	B	59	-50.857	33.998	-37.257	1.00	44.41	B
ATOM	1434	O	GLU	B	59	-51.033	32.892	-36.757	1.00	44.67	B
ATOM	1435	N	MET	B	60	-50.842	34.196	-38.571	1.00	44.37	B
ATOM	1436	CA	MET	B	60	-51.055	33.079	-39.471	1.00	45.11	B
ATOM	1437	CB	MET	B	60	-51.331	33.559	-40.897	1.00	48.89	B
ATOM	1438	CG	MET	B	60	-51.721	32.415	-41.821	1.00	53.44	B
ATOM	1439	SD	MET	B	60	-51.754	32.856	-43.555	1.00	61.98	B
ATOM	1440	CE	MET	B	60	-50.021	33.361	-43.846	1.00	58.01	B
ATOM	1441	C	MET	B	60	-49.864	32.128	-39.465	1.00	43.04	B
ATOM	1442	O	MET	B	60	-50.039	30.909	-39.449	1.00	40.32	B
ATOM	1443	N	ILE	B	61	-48.655	32.671	-39.481	1.00	40.71	B
ATOM	1444	CA	ILE	B	61	-47.500	31.802	-39.457	1.00	42.41	B
ATOM	1445	CB	ILE	B	61	-46.170	32.608	-39.520	1.00	43.92	B
ATOM	1446	CG2	ILE	B	61	-44.975	31.667	-39.434	1.00	44.05	B
ATOM	1447	CG1	ILE	B	61	-46.094	33.395	-40.823	1.00	41.85	B
ATOM	1448	CD1	ILE	B	61	-46.283	32.551	-42.028	1.00	45.99	B
ATOM	1449	C	ILE	B	61	-47.557	30.991	-38.153	1.00	43.11	B
ATOM	1450	O	ILE	B	61	-47.413	29.762	-38.158	1.00	43.91	B
ATOM	1451	N	GLN	B	62	-47.795	31.690	-37.049	1.00	42.04	B
ATOM	1452	CA	GLN	B	62	-47.863	31.082	-35.726	1.00	43.22	B
ATOM	1453	CB	GLN	B	62	-48.229	32.140	-34.685	1.00	46.41	B
ATOM	1454	CG	GLN	B	62	-48.049	31.713	-33.245	1.00	46.91	B
ATOM	1455	CD	GLN	B	62	-46.596	31.663	-32.837	1.00	52.53	B
ATOM	1456	OE1	GLN	B	62	-45.904	30.665	-33.070	1.00	55.84	B
ATOM	1457	NE2	GLN	B	62	-46.113	32.748	-32.228	1.00	54.09	B
ATOM	1458	C	GLN	B	62	-48.880	29.960	-35.663	1.00	43.47	B
ATOM	1459	O	GLN	B	62	-48.587	28.870	-35.152	1.00	44.07	B
ATOM	1460	N	GLN	B	63	-50.083	30.228	-36.163	1.00	42.32	B
ATOM	1461	CA	GLN	B	63	-51.140	29.221	-36.158	1.00	43.14	B
ATOM	1462	CB	GLN	B	63	-52.456	29.812	-36.653	1.00	43.36	B
ATOM	1463	CG	GLN	B	63	-53.088	30.810	-35.702	1.00	45.90	B
ATOM	1464	CD	GLN	B	63	-53.432	30.220	-34.339	1.00	44.57	B
ATOM	1465	OE1	GLN	B	63	-53.643	30.956	-33.386	1.00	44.63	B
ATOM	1466	NE2	GLN	B	63	-53.497	28.896	-34.250	1.00	44.30	B
ATOM	1467	C	GLN	B	63	-50.796	28.018	-37.017	1.00	43.72	B
ATOM	1468	O	GLN	B	63	-51.089	26.880	-36.649	1.00	44.40	B
ATOM	1469	N	THR	B	64	-50.177	28.277	-38.164	1.00	42.86	B
ATOM	1470	CA	THR	B	64	-49.811	27.211	-39.073	1.00	42.63	B
ATOM	1471	CB	THR	B	64	-49.271	27.777	-40.409	1.00	42.59	B
ATOM	1472	OG1	THR	B	64	-50.275	28.599	-41.012	1.00	40.41	B
ATOM	1473	CG2	THR	B	64	-48.910	26.649	-41.368	1.00	39.23	B
ATOM	1474	C	THR	B	64	-48.762	26.343	-38.405	1.00	43.08	B
ATOM	1475	O	THR	B	64	-48.801	25.118	-38.509	1.00	45.34	B
ATOM	1476	N	PHE	B	65	-47.820	26.980	-37.724	1.00	41.85	B
ATOM	1477	CA	PHE	B	65	-46.781	26.245	-37.026	1.00	41.65	B
ATOM	1478	CB	PHE	B	65	-45.890	27.210	-36.231	1.00	39.65	B
ATOM	1479	CG	PHE	B	65	-44.753	26.533	-35.514	1.00	37.50	B

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ATOM   1480  CD1 PHE B  65     -43.503  26.448 -36.095  1.00 38.07      B
ATOM   1481  CD2 PHE B  65     -44.952  25.931 -34.285  1.00 38.71      B
ATOM   1482  CE1 PHE B  65     -42.463  25.766 -35.473  1.00 38.97      B
ATOM   1483  CE2 PHE B  65     -43.927  25.247 -33.651  1.00 40.75      B
ATOM   1484  CZ  PHE B  65     -42.674  25.163 -34.252  1.00 41.00      B
ATOM   1485  C   PHE B  65     -47.459  25.268 -36.062  1.00 42.95      B
ATOM   1486  O   PHE B  65     -47.199  24.067 -36.077  1.00 41.78      B
ATOM   1487  N   ASN B  66     -48.346  25.797 -35.228  1.00 44.10      B
ATOM   1488  CA  ASN B  66     -49.036  24.976 -34.244  1.00 45.15      B
ATOM   1489  CB  ASN B  66     -50.014  25.836 -33.444  1.00 45.22      B
ATOM   1490  CG  ASN B  66     -49.309  26.882 -32.588  1.00 45.60      B
ATOM   1491  OD1 ASN B  66     -49.917  27.866 -32.179  1.00 47.81      B
ATOM   1492  ND2 ASN B  66     -48.026  26.667 -32.310  1.00 45.74      B
ATOM   1493  C   ASN B  66     -49.758  23.802 -34.874  1.00 45.93      B
ATOM   1494  O   ASN B  66     -49.592  22.661 -34.443  1.00 46.70      B
ATOM   1495  N   LEU B  67     -50.545  24.087 -35.906  1.00 46.78      B
ATOM   1496  CA  LEU B  67     -51.314  23.072 -36.614  1.00 45.25      B
ATOM   1497  CB  LEU B  67     -52.027  23.708 -37.802  1.00 44.17      B
ATOM   1498  CG  LEU B  67     -52.943  22.848 -38.673  1.00 44.83      B
ATOM   1499  CD1 LEU B  67     -54.221  22.524 -37.908  1.00 43.33      B
ATOM   1500  CD2 LEU B  67     -53.269  23.609 -39.950  1.00 43.75      B
ATOM   1501  C   LEU B  67     -50.465  21.914 -37.109  1.00 46.02      B
ATOM   1502  O   LEU B  67     -50.888  20.763 -37.037  1.00 47.59      B
ATOM   1503  N   PHE B  68     -49.270  22.209 -37.606  1.00 45.93      B
ATOM   1504  CA  PHE B  68     -48.407  21.165 -38.142  1.00 48.01      B
ATOM   1505  CB  PHE B  68     -47.690  21.674 -39.400  1.00 47.07      B
ATOM   1506  CG  PHE B  68     -48.573  21.725 -40.623  1.00 47.28      B
ATOM   1507  CD1 PHE B  68     -49.374  22.834 -40.879  1.00 47.40      B
ATOM   1508  CD2 PHE B  68     -48.629  20.643 -41.497  1.00 45.54      B
ATOM   1509  CE1 PHE B  68     -50.217  22.863 -41.985  1.00 45.20      B
ATOM   1510  CE2 PHE B  68     -49.463  20.660 -42.598  1.00 45.58      B
ATOM   1511  CZ  PHE B  68     -50.261  21.772 -42.843  1.00 45.21      B
ATOM   1512  C   PHE B  68     -47.385  20.564 -37.174  1.00 50.56      B
ATOM   1513  O   PHE B  68     -46.660  19.625 -37.519  1.00 50.22      B
ATOM   1514  N   SER B  69     -47.333  21.093 -35.959  1.00 52.03      B
ATOM   1515  CA  SER B  69     -46.397  20.592 -34.963  1.00 51.91      B
ATOM   1516  CB  SER B  69     -45.844  21.762 -34.145  1.00 50.79      B
ATOM   1517  OG  SER B  69     -46.861  22.698 -33.850  1.00 50.68      B
ATOM   1518  C   SER B  69     -47.098  19.559 -34.071  1.00 52.49      B
ATOM   1519  O   SER B  69     -46.471  18.877 -33.263  1.00 51.65      B
ATOM   1520  N   THR B  70     -48.406  19.437 -34.256  1.00 53.35      B
ATOM   1521  CA  THR B  70     -49.220  18.485 -33.519  1.00 54.95      B
ATOM   1522  CB  THR B  70     -50.715  18.667 -33.892  1.00 54.32      B
ATOM   1523  OG1 THR B  70     -51.292  19.672 -33.051  1.00 53.43      B
ATOM   1524  CG2 THR B  70     -51.491  17.378 -33.749  1.00 53.28      B
ATOM   1525  C   THR B  70     -48.816  17.024 -33.764  1.00 57.60      B
ATOM   1526  O   THR B  70     -48.196  16.683 -34.775  1.00 56.59      B
ATOM   1527  N   ARG B  71     -49.183  16.177 -32.806  1.00 60.45      B
ATOM   1528  CA  ARG B  71     -48.931  14.739 -32.839  1.00 63.09      B
ATOM   1529  CB  ARG B  71     -49.445  14.131 -31.527  1.00 66.17      B
ATOM   1530  CG  ARG B  71     -50.748  14.806 -31.033  1.00 71.66      B
ATOM   1531  CD  ARG B  71     -50.651  15.471 -29.626  1.00 74.28      B
ATOM   1532  NE  ARG B  71     -49.626  16.519 -29.495  1.00 75.60      B
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ATOM	1533	CZ	ARG	B	71	-48.406	16.325	-28.982	1.00	76.64	B
ATOM	1534	NH1	ARG	B	71	-48.039	15.122	-28.548	1.00	76.04	B
ATOM	1535	NH2	ARG	B	71	-47.551	17.338	-28.891	1.00	75.84	B
ATOM	1536	C	ARG	B	71	-49.654	14.119	-34.046	1.00	62.93	B
ATOM	1537	O	ARG	B	71	-49.156	13.186	-34.684	1.00	62.66	B
ATOM	1538	N	ASP	B	72	-50.834	14.654	-34.344	1.00	62.27	B
ATOM	1539	CA	ASP	B	72	-51.642	14.201	-35.465	1.00	61.32	B
ATOM	1540	CB	ASP	B	72	-53.017	14.844	-35.398	1.00	63.05	B
ATOM	1541	CG	ASP	B	72	-53.745	14.517	-34.121	1.00	65.14	B
ATOM	1542	OD1	ASP	B	72	-54.164	13.350	-33.973	1.00	66.97	B
ATOM	1543	OD2	ASP	B	72	-53.894	15.425	-33.270	1.00	65.14	B
ATOM	1544	C	ASP	B	72	-50.973	14.600	-36.768	1.00	60.42	B
ATOM	1545	O	ASP	B	72	-51.034	13.882	-37.762	1.00	61.00	B
ATOM	1546	N	SER	B	73	-50.341	15.762	-36.758	1.00	59.06	B
ATOM	1547	CA	SER	B	73	-49.657	16.238	-37.938	1.00	58.72	B
ATOM	1548	CB	SER	B	73	-49.126	17.654	-37.704	1.00	57.83	B
ATOM	1549	OG	SER	B	73	-48.578	18.194	-38.892	1.00	58.48	B
ATOM	1550	C	SER	B	73	-48.509	15.281	-38.262	1.00	58.75	B
ATOM	1551	O	SER	B	73	-48.355	14.859	-39.408	1.00	58.86	B
ATOM	1552	N	SER	B	74	-47.718	14.927	-37.250	1.00	57.50	B
ATOM	1553	CA	SER	B	74	-46.582	14.026	-37.443	1.00	56.83	B
ATOM	1554	CB	SER	B	74	-45.849	13.794	-36.127	1.00	55.68	B
ATOM	1555	OG	SER	B	74	-45.131	14.949	-35.737	1.00	59.88	B
ATOM	1556	C	SER	B	74	-47.000	12.686	-38.020	1.00	55.92	B
ATOM	1557	O	SER	B	74	-46.286	12.097	-38.837	1.00	54.81	B
ATOM	1558	N	ALA	B	75	-48.154	12.201	-37.583	1.00	54.52	B
ATOM	1559	CA	ALA	B	75	-48.658	10.929	-38.069	1.00	54.44	B
ATOM	1560	CB	ALA	B	75	-49.870	10.520	-37.268	1.00	53.67	B
ATOM	1561	C	ALA	B	75	-49.029	11.043	-39.540	1.00	54.05	B
ATOM	1562	O	ALA	B	75	-48.835	10.114	-40.323	1.00	53.83	B
ATOM	1563	N	ALA	B	76	-49.542	12.211	-39.905	1.00	53.41	B
ATOM	1564	CA	ALA	B	76	-49.996	12.477	-41.255	1.00	52.31	B
ATOM	1565	CB	ALA	B	76	-51.042	13.580	-41.208	1.00	52.11	B
ATOM	1566	C	ALA	B	76	-48.946	12.810	-42.315	1.00	52.55	B
ATOM	1567	O	ALA	B	76	-49.114	12.443	-43.477	1.00	52.41	B
ATOM	1568	N	TRP	B	77	-47.862	13.481	-41.941	1.00	51.98	B
ATOM	1569	CA	TRP	B	77	-46.879	13.868	-42.947	1.00	51.34	B
ATOM	1570	CB	TRP	B	77	-46.887	15.391	-43.126	1.00	50.88	B
ATOM	1571	CG	TRP	B	77	-48.248	15.994	-43.099	1.00	52.09	B
ATOM	1572	CD2	TRP	B	77	-49.187	16.052	-44.178	1.00	53.10	B
ATOM	1573	CE2	TRP	B	77	-50.347	16.691	-43.689	1.00	53.99	B
ATOM	1574	CE3	TRP	B	77	-49.163	15.624	-45.512	1.00	52.69	B
ATOM	1575	CD1	TRP	B	77	-48.858	16.579	-42.032	1.00	53.81	B
ATOM	1576	NE1	TRP	B	77	-50.119	17.002	-42.375	1.00	54.33	B
ATOM	1577	CZ2	TRP	B	77	-51.476	16.916	-44.490	1.00	54.45	B
ATOM	1578	CZ3	TRP	B	77	-50.287	15.845	-46.309	1.00	50.90	B
ATOM	1579	CH2	TRP	B	77	-51.427	16.486	-45.794	1.00	51.54	B
ATOM	1580	C	TRP	B	77	-45.450	13.425	-42.722	1.00	50.67	B
ATOM	1581	O	TRP	B	77	-45.053	13.094	-41.620	1.00	49.80	B
ATOM	1582	N	ASP	B	78	-44.672	13.436	-43.796	1.00	52.39	B
ATOM	1583	CA	ASP	B	78	-43.278	13.064	-43.711	1.00	53.40	B
ATOM	1584	CB	ASP	B	78	-42.578	13.257	-45.050	1.00	55.50	B
ATOM	1585	CG	ASP	B	78	-41.104	12.936	-44.966	1.00	59.62	B

ATOM 1586 OD1 ASP B 78 -40.273 13.875 -45.018 1.00 62.42 B
ATOM 1587 OD2 ASP B 78 -40.777 11.738 -44.820 1.00 59.99 B
ATOM 1588 C ASP B 78 -42.602 13.933 -42.663 1.00 53.04 B
ATOM 1589 O ASP B 78 -42.706 15.160 -42.700 1.00 53.12 B
ATOM 1590 N ALA B 79 -41.901 13.287 -41.738 1.00 52.08 B
ATOM 1591 CA ALA B 79 -41.220 13.983 -40.662 1.00 52.01 B
ATOM 1592 CB ALA B 79 -40.643 12.968 -39.675 1.00 50.85 B
ATOM 1593 C ALA B 79 -40.128 14.917 -41.179 1.00 51.80 B
ATOM 1594 O ALA B 79 -40.008 16.050 -40.723 1.00 52.56 B
ATOM 1595 N SER B 80 -39.341 14.453 -42.138 1.00 51.82 B
ATOM 1596 CA SER B 80 -38.273 15.277 -42.687 1.00 51.59 B
ATOM 1597 CB SER B 80 -37.511 14.507 -43.764 1.00 53.55 B
ATOM 1598 OG SER B 80 -36.317 15.188 -44.120 1.00 57.70 B
ATOM 1599 C SER B 80 -38.818 16.577 -43.280 1.00 50.52 B
ATOM 1600 O SER B 80 -38.223 17.649 -43.113 1.00 51.02 B
ATOM 1601 N LEU B 81 -39.937 16.487 -43.990 1.00 47.40 B
ATOM 1602 CA LEU B 81 -40.521 17.684 -44.574 1.00 46.68 B
ATOM 1603 CB LEU B 81 -41.665 17.327 -45.531 1.00 44.63 B
ATOM 1604 CG LEU B 81 -41.253 16.605 -46.824 1.00 43.12 B
ATOM 1605 CD1 LEU B 81 -42.433 16.565 -47.792 1.00 40.61 B
ATOM 1606 CD2 LEU B 81 -40.080 17.329 -47.467 1.00 38.50 B
ATOM 1607 C LEU B 81 -41.021 18.607 -43.464 1.00 47.01 B
ATOM 1608 O LEU B 81 -40.806 19.823 -43.507 1.00 46.43 B
ATOM 1609 N LEU B 82 -41.668 18.019 -42.462 1.00 45.79 B
ATOM 1610 CA LEU B 82 -42.184 18.790 -41.344 1.00 44.38 B
ATOM 1611 CB LEU B 82 -42.915 17.881 -40.355 1.00 43.65 B
ATOM 1612 CG LEU B 82 -44.350 17.506 -40.712 1.00 42.39 B
ATOM 1613 CD1 LEU B 82 -44.969 16.779 -39.542 1.00 41.48 B
ATOM 1614 CD2 LEU B 82 -45.148 18.764 -41.040 1.00 40.02 B
ATOM 1615 C LEU B 82 -41.106 19.579 -40.608 1.00 43.60 B
ATOM 1616 O LEU B 82 -41.306 20.748 -40.294 1.00 43.44 B
ATOM 1617 N ALA B 83 -39.968 18.958 -40.326 1.00 41.84 B
ATOM 1618 CA ALA B 83 -38.920 19.686 -39.617 1.00 42.47 B
ATOM 1619 CB ALA B 83 -37.732 18.749 -39.241 1.00 42.87 B
ATOM 1620 C ALA B 83 -38.442 20.857 -40.466 1.00 40.93 B
ATOM 1621 O ALA B 83 -38.074 21.898 -39.930 1.00 41.51 B
ATOM 1622 N LYS B 84 -38.458 20.693 -41.785 1.00 39.80 B
ATOM 1623 CA LYS B 84 -38.041 21.770 -42.680 1.00 40.20 B
ATOM 1624 CB LYS B 84 -37.916 21.257 -44.121 1.00 42.21 B
ATOM 1625 CG LYS B 84 -36.919 20.117 -44.326 1.00 44.38 B
ATOM 1626 CD LYS B 84 -36.542 20.019 -45.799 1.00 45.90 B
ATOM 1627 CE LYS B 84 -35.545 18.920 -46.068 1.00 45.47 B
ATOM 1628 NZ LYS B 84 -36.209 17.606 -45.922 1.00 49.90 B
ATOM 1629 C LYS B 84 -39.076 22.902 -42.631 1.00 39.06 B
ATOM 1630 O LYS B 84 -38.743 24.087 -42.678 1.00 39.36 B
ATOM 1631 N PHE B 85 -40.338 22.512 -42.539 1.00 37.58 B
ATOM 1632 CA PHE B 85 -41.449 23.442 -42.475 1.00 38.00 B
ATOM 1633 CB PHE B 85 -42.749 22.644 -42.492 1.00 38.99 B
ATOM 1634 CG PHE B 85 -43.959 23.458 -42.811 1.00 39.63 B
ATOM 1635 CD1 PHE B 85 -43.942 24.366 -43.866 1.00 38.44 B
ATOM 1636 CD2 PHE B 85 -45.137 23.276 -42.099 1.00 38.81 B
ATOM 1637 CE1 PHE B 85 -45.076 25.079 -44.211 1.00 39.59 B
ATOM 1638 CE2 PHE B 85 -46.288 23.986 -42.439 1.00 41.20 B

ATOM	1639	CZ	PHE	B	85	-46.255	24.891	-43.501	1.00	41.17	B
ATOM	1640	C	PHE	B	85	-41.387	24.331	-41.223	1.00	38.99	B
ATOM	1641	O	PHE	B	85	-41.419	25.557	-41.334	1.00	39.44	B
ATOM	1642	N	TYR	B	86	-41.299	23.709	-40.044	1.00	38.21	B
ATOM	1643	CA	TYR	B	86	-41.217	24.435	-38.769	1.00	37.40	B
ATOM	1644	CB	TYR	B	86	-40.998	23.493	-37.574	1.00	35.90	B
ATOM	1645	CG	TYR	B	86	-41.920	22.311	-37.450	1.00	33.12	B
ATOM	1646	CD1	TYR	B	86	-43.276	22.428	-37.721	1.00	32.96	B
ATOM	1647	CE1	TYR	B	86	-44.138	21.343	-37.563	1.00	35.08	B
ATOM	1648	CD2	TYR	B	86	-41.435	21.077	-37.019	1.00	30.36	B
ATOM	1649	CE2	TYR	B	86	-42.276	19.992	-36.861	1.00	30.76	B
ATOM	1650	CZ	TYR	B	86	-43.628	20.133	-37.129	1.00	34.57	B
ATOM	1651	OH	TYR	B	86	-44.491	19.085	-36.932	1.00	37.86	B
ATOM	1652	C	TYR	B	86	-40.044	25.403	-38.776	1.00	38.65	B
ATOM	1653	O	TYR	B	86	-40.156	26.527	-38.300	1.00	40.78	B
ATOM	1654	N	THR	B	87	-38.905	24.948	-39.289	1.00	38.79	B
ATOM	1655	CA	THR	B	87	-37.712	25.778	-39.347	1.00	38.38	B
ATOM	1656	CB	THR	B	87	-36.538	25.026	-39.984	1.00	35.81	B
ATOM	1657	OG1	THR	B	87	-36.316	23.803	-39.276	1.00	35.27	B
ATOM	1658	CG2	THR	B	87	-35.280	25.870	-39.946	1.00	28.02	B
ATOM	1659	C	THR	B	87	-37.976	27.029	-40.165	1.00	40.34	B
ATOM	1660	O	THR	B	87	-37.600	28.136	-39.768	1.00	42.58	B
ATOM	1661	N	GLU	B	88	-38.629	26.849	-41.308	1.00	41.62	B
ATOM	1662	CA	GLU	B	88	-38.948	27.962	-42.196	1.00	41.56	B
ATOM	1663	CB	GLU	B	88	-39.541	27.428	-43.498	1.00	41.09	B
ATOM	1664	CG	GLU	B	88	-39.850	28.487	-44.526	1.00	43.87	B
ATOM	1665	CD	GLU	B	88	-38.622	29.295	-44.906	1.00	47.13	B
ATOM	1666	OE1	GLU	B	88	-37.542	28.689	-45.046	1.00	48.15	B
ATOM	1667	OE2	GLU	B	88	-38.728	30.528	-45.078	1.00	48.87	B
ATOM	1668	C	GLU	B	88	-39.941	28.907	-41.523	1.00	41.37	B
ATOM	1669	O	GLU	B	88	-39.719	30.120	-41.441	1.00	42.84	B
ATOM	1670	N	LEU	B	89	-41.037	28.342	-41.032	1.00	39.06	B
ATOM	1671	CA	LEU	B	89	-42.049	29.144	-40.380	1.00	38.27	B
ATOM	1672	CB	LEU	B	89	-43.214	28.255	-39.938	1.00	34.88	B
ATOM	1673	CG	LEU	B	89	-43.971	27.575	-41.087	1.00	32.56	B
ATOM	1674	CD1	LEU	B	89	-45.074	26.700	-40.540	1.00	29.69	B
ATOM	1675	CD2	LEU	B	89	-44.519	28.629	-42.014	1.00	29.86	B
ATOM	1676	C	LEU	B	89	-41.475	29.923	-39.199	1.00	39.22	B
ATOM	1677	O	LEU	B	89	-41.707	31.125	-39.070	1.00	38.24	B
ATOM	1678	N	TYR	B	90	-40.703	29.257	-38.351	1.00	39.74	B
ATOM	1679	CA	TYR	B	90	-40.153	29.951	-37.214	1.00	41.05	B
ATOM	1680	CB	TYR	B	90	-39.453	28.987	-36.256	1.00	43.39	B
ATOM	1681	CG	TYR	B	90	-39.363	29.572	-34.863	1.00	45.73	B
ATOM	1682	CD1	TYR	B	90	-40.479	29.577	-34.019	1.00	44.72	B
ATOM	1683	CE1	TYR	B	90	-40.446	30.218	-32.789	1.00	46.68	B
ATOM	1684	CD2	TYR	B	90	-38.203	30.219	-34.429	1.00	45.13	B
ATOM	1685	CE2	TYR	B	90	-38.160	30.863	-33.193	1.00	46.07	B
ATOM	1686	CZ	TYR	B	90	-39.287	30.863	-32.379	1.00	46.81	B
ATOM	1687	OH	TYR	B	90	-39.272	31.538	-31.177	1.00	46.41	B
ATOM	1688	C	TYR	B	90	-39.193	31.047	-37.639	1.00	42.36	B
ATOM	1689	O	TYR	B	90	-39.092	32.086	-36.986	1.00	43.93	B
ATOM	1690	N	GLN	B	91	-38.487	30.831	-38.738	1.00	43.52	B
ATOM	1691	CA	GLN	B	91	-37.557	31.844	-39.217	1.00	45.08	B

ATOM	1692	CB	GLN	B	91	-36.684	31.262	-40.330	1.00	44.47	B
ATOM	1693	CG	GLN	B	91	-35.262	31.826	-40.377	1.00	48.72	B
ATOM	1694	CD	GLN	B	91	-34.471	31.656	-39.068	1.00	49.14	B
ATOM	1695	OE1	GLN	B	91	-34.568	30.634	-38.385	1.00	49.61	B
ATOM	1696	NE2	GLN	B	91	-33.669	32.660	-38.735	1.00	49.34	B
ATOM	1697	C	GLN	B	91	-38.382	33.040	-39.721	1.00	45.99	B
ATOM	1698	O	GLN	B	91	-38.042	34.204	-39.472	1.00	44.12	B
ATOM	1699	N	GLN	B	92	-39.482	32.753	-40.412	1.00	45.91	B
ATOM	1700	CA	GLN	B	92	-40.340	33.821	-40.904	1.00	47.21	B
ATOM	1701	CB	GLN	B	92	-41.514	33.244	-41.698	1.00	47.99	B
ATOM	1702	CG	GLN	B	92	-41.191	32.841	-43.123	1.00	51.32	B
ATOM	1703	CD	GLN	B	92	-42.447	32.523	-43.905	1.00	55.62	B
ATOM	1704	OE1	GLN	B	92	-43.411	33.290	-43.885	1.00	57.55	B
ATOM	1705	NE2	GLN	B	92	-42.448	31.390	-44.602	1.00	56.89	B
ATOM	1706	C	GLN	B	92	-40.873	34.654	-39.733	1.00	47.67	B
ATOM	1707	O	GLN	B	92	-41.157	35.838	-39.880	1.00	48.06	B
ATOM	1708	N	LEU	B	93	-41.011	34.017	-38.575	1.00	48.22	B
ATOM	1709	CA	LEU	B	93	-41.502	34.663	-37.366	1.00	46.33	B
ATOM	1710	CB	LEU	B	93	-41.793	33.606	-36.312	1.00	44.07	B
ATOM	1711	CG	LEU	B	93	-43.211	33.418	-35.790	1.00	42.19	B
ATOM	1712	CD1	LEU	B	93	-44.271	33.719	-36.855	1.00	40.20	B
ATOM	1713	CD2	LEU	B	93	-43.303	31.992	-35.296	1.00	38.45	B
ATOM	1714	C	LEU	B	93	-40.454	35.629	-36.848	1.00	47.84	B
ATOM	1715	O	LEU	B	93	-40.772	36.740	-36.439	1.00	47.68	B
ATOM	1716	N	ASN	B	94	-39.196	35.201	-36.857	1.00	49.68	B
ATOM	1717	CA	ASN	B	94	-38.118	36.067	-36.396	1.00	50.86	B
ATOM	1718	CB	ASN	B	94	-36.797	35.295	-36.302	1.00	49.93	B
ATOM	1719	CG	ASN	B	94	-36.741	34.372	-35.097	1.00	49.12	B
ATOM	1720	OD1	ASN	B	94	-37.613	34.402	-34.228	1.00	48.85	B
ATOM	1721	ND2	ASN	B	94	-35.699	33.555	-35.035	1.00	50.25	B
ATOM	1722	C	ASN	B	94	-37.957	37.256	-37.339	1.00	52.00	B
ATOM	1723	O	ASN	B	94	-37.673	38.362	-36.902	1.00	52.28	B
ATOM	1724	N	ASP	B	95	-38.144	37.038	-38.635	1.00	54.31	B
ATOM	1725	CA	ASP	B	95	-38.016	38.147	-39.574	1.00	55.94	B
ATOM	1726	CB	ASP	B	95	-38.055	37.651	-41.021	1.00	56.73	B
ATOM	1727	CG	ASP	B	95	-36.892	36.737	-41.344	1.00	59.74	B
ATOM	1728	OD1	ASP	B	95	-35.823	36.923	-40.721	1.00	60.29	B
ATOM	1729	OD2	ASP	B	95	-37.037	35.844	-42.216	1.00	60.62	B
ATOM	1730	C	ASP	B	95	-39.114	39.167	-39.340	1.00	55.97	B
ATOM	1731	O	ASP	B	95	-38.849	40.357	-39.328	1.00	55.88	B
ATOM	1732	N	LEU	B	96	-40.343	38.701	-39.145	1.00	57.37	B
ATOM	1733	CA	LEU	B	96	-41.460	39.602	-38.898	1.00	59.48	B
ATOM	1734	CB	LEU	B	96	-42.762	38.813	-38.735	1.00	57.57	B
ATOM	1735	CG	LEU	B	96	-43.302	38.114	-39.984	1.00	56.36	B
ATOM	1736	CD1	LEU	B	96	-44.553	37.313	-39.654	1.00	53.91	B
ATOM	1737	CD2	LEU	B	96	-43.607	39.163	-41.034	1.00	57.46	B
ATOM	1738	C	LEU	B	96	-41.201	40.436	-37.644	1.00	62.45	B
ATOM	1739	O	LEU	B	96	-41.511	41.628	-37.601	1.00	62.77	B
ATOM	1740	N	GLU	B	97	-40.628	39.812	-36.622	1.00	65.05	B
ATOM	1741	CA	GLU	B	97	-40.338	40.528	-35.392	1.00	68.23	B
ATOM	1742	CB	GLU	B	97	-39.952	39.540	-34.277	1.00	68.89	B
ATOM	1743	CG	GLU	B	97	-41.097	38.626	-33.830	1.00	71.87	B
ATOM	1744	CD	GLU	B	97	-40.668	37.539	-32.849	1.00	73.15	B

ATOM 1745 OE1 GLU B 97 -40.181 37.886 -31.756 1.00 76.25 B
ATOM 1746 OE2 GLU B 97 -40.820 36.337 -33.164 1.00 72.83 B
ATOM 1747 C GLU B 97 -39.214 41.532 -35.651 1.00 70.40 B
ATOM 1748 O GLU B 97 -39.135 42.571 -34.998 1.00 71.54 B
ATOM 1749 N ALA B 98 -38.349 41.229 -36.614 1.00 73.00 B
ATOM 1750 CA ALA B 98 -37.248 42.128 -36.952 1.00 75.20 B
ATOM 1751 CB ALA B 98 -36.322 41.474 -37.970 1.00 75.82 B
ATOM 1752 C ALA B 98 -37.808 43.423 -37.523 1.00 76.99 B
ATOM 1753 O ALA B 98 -37.160 44.467 -37.448 1.00 77.06 B
ATOM 1754 N CYS B 99 -39.015 43.337 -38.088 1.00 79.24 B
ATOM 1755 CA CYS B 99 -39.711 44.478 -38.691 1.00 81.14 B
ATOM 1756 CB CYS B 99 -40.765 44.002 -39.695 1.00 81.56 B
ATOM 1757 SG CYS B 99 -40.126 43.247 -41.210 1.00 84.65 B
ATOM 1758 C CYS B 99 -40.397 45.359 -37.658 1.00 82.14 B
ATOM 1759 O CYS B 99 -40.290 46.582 -37.715 1.00 82.34 B
ATOM 1760 N VAL B 100 -41.116 44.740 -36.725 1.00 83.70 B
ATOM 1761 CA VAL B 100 -41.814 45.493 -35.684 1.00 85.68 B
ATOM 1762 CB VAL B 100 -42.619 44.556 -34.740 1.00 85.07 B
ATOM 1763 CG1 VAL B 100 -41.688 43.602 -34.020 1.00 84.36 B
ATOM 1764 CG2 VAL B 100 -43.405 45.381 -33.741 1.00 85.62 B
ATOM 1765 C VAL B 100 -40.801 46.287 -34.863 1.00 87.06 B
ATOM 1766 O VAL B 100 -41.162 47.202 -34.115 1.00 87.20 B
ATOM 1767 N ALA B 101 -39.529 45.927 -35.023 1.00 88.22 B
ATOM 1768 CA ALA B 101 -38.434 46.582 -34.323 1.00 89.09 B
ATOM 1769 CB ALA B 101 -37.497 45.533 -33.730 1.00 88.54 B
ATOM 1770 C ALA B 101 -37.666 47.498 -35.276 1.00 89.84 B
ATOM 1771 O ALA B 101 -37.324 48.626 -34.925 1.00 90.61 B
ATOM 1772 N GLY B 102 -37.401 47.010 -36.484 1.00 90.46 B
ATOM 1773 CA GLY B 102 -36.678 47.808 -37.457 1.00 91.07 B
ATOM 1774 C GLY B 102 -37.577 48.761 -38.223 1.00 92.05 B
ATOM 1775 O GLY B 102 -37.266 49.135 -39.351 1.00 92.33 B
ATOM 1776 N GLY B 103 -38.692 49.157 -37.612 1.00 92.84 B
ATOM 1777 CA GLY B 103 -39.616 50.069 -38.266 1.00 92.74 B
ATOM 1778 C GLY B 103 -40.887 50.291 -37.465 1.00 92.62 B
ATOM 1779 O GLY B 103 -41.047 51.321 -36.807 1.00 92.47 B
ATOM 1780 N ALA B 111 -51.414 47.696 -31.869 1.00 93.96 B
ATOM 1781 CA ALA B 111 -51.666 47.368 -33.267 1.00 93.85 B
ATOM 1782 CB ALA B 111 -51.378 45.889 -33.516 1.00 92.71 B
ATOM 1783 C ALA B 111 -53.105 47.697 -33.661 1.00 93.95 B
ATOM 1784 O ALA B 111 -53.906 46.792 -33.916 1.00 94.29 B
ATOM 1785 N GLY B 112 -53.424 48.993 -33.708 1.00 92.98 B
ATOM 1786 CA GLY B 112 -54.760 49.429 -34.080 1.00 91.20 B
ATOM 1787 C GLY B 112 -55.854 48.615 -33.416 1.00 90.66 B
ATOM 1788 O GLY B 112 -56.271 48.924 -32.298 1.00 91.11 B
ATOM 1789 N ASN B 113 -56.328 47.575 -34.101 1.00 88.98 B
ATOM 1790 CA ASN B 113 -57.368 46.715 -33.546 1.00 86.63 B
ATOM 1791 CB ASN B 113 -58.702 46.922 -34.275 1.00 88.02 B
ATOM 1792 CG ASN B 113 -58.597 46.693 -35.770 1.00 88.87 B
ATOM 1793 OD1 ASN B 113 -57.973 45.729 -36.226 1.00 88.93 B
ATOM 1794 ND2 ASN B 113 -59.225 47.573 -36.545 1.00 89.31 B
ATOM 1795 C ASN B 113 -56.988 45.237 -33.586 1.00 84.10 B
ATOM 1796 O ASN B 113 -56.396 44.750 -34.559 1.00 82.68 B
ATOM 1797 N ALA B 114 -57.333 44.538 -32.507 1.00 80.69 B

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ATOM   1798  CA  ALA B 114     -57.053  43.117 -32.365  1.00 77.04      B
ATOM   1799  CB  ALA B 114     -57.060  42.734 -30.885  1.00 74.97      B
ATOM   1800  C   ALA B 114     -58.094  42.307 -33.129  1.00 75.04      B
ATOM   1801  O   ALA B 114     -58.167  41.092 -32.987  1.00 75.09      B
ATOM   1802  N   ASP B 115     -58.898  42.993 -33.935  1.00 73.04      B
ATOM   1803  CA  ASP B 115     -59.940  42.354 -34.739  1.00 71.39      B
ATOM   1804  CB  ASP B 115     -60.755  43.408 -35.493  1.00 75.02      B
ATOM   1805  CG  ASP B 115     -61.440  44.387 -34.573  1.00 77.51      B
ATOM   1806  OD1 ASP B 115     -61.719  45.520 -35.022  1.00 77.99      B
ATOM   1807  OD2 ASP B 115     -61.707  44.019 -33.408  1.00 80.45      B
ATOM   1808  C   ASP B 115     -59.318  41.429 -35.766  1.00 68.05      B
ATOM   1809  O   ASP B 115     -59.626  40.245 -35.834  1.00 67.22      B
ATOM   1810  N   SER B 116     -58.451  42.002 -36.585  1.00 65.47      B
ATOM   1811  CA  SER B 116     -57.775  41.259 -37.628  1.00 62.95      B
ATOM   1812  CB  SER B 116     -56.707  42.137 -38.277  1.00 63.58      B
ATOM   1813  OG  SER B 116     -57.268  43.350 -38.753  1.00 63.46      B
ATOM   1814  C   SER B 116     -57.140  39.998 -37.062  1.00 61.42      B
ATOM   1815  O   SER B 116     -57.296  38.917 -37.626  1.00 62.05      B
ATOM   1816  N   ILE B 117     -56.430  40.137 -35.946  1.00 58.31      B
ATOM   1817  CA  ILE B 117     -55.772  38.999 -35.313  1.00 54.83      B
ATOM   1818  CB  ILE B 117     -54.966  39.423 -34.076  1.00 53.03      B
ATOM   1819  CG2 ILE B 117     -54.366  38.202 -33.414  1.00 51.47      B
ATOM   1820  CG1 ILE B 117     -53.871  40.404 -34.477  1.00 52.17      B
ATOM   1821  CD1 ILE B 117     -53.280  41.161 -33.307  1.00 50.94      B
ATOM   1822  C   ILE B 117     -56.772  37.944 -34.870  1.00 54.11      B
ATOM   1823  O   ILE B 117     -56.565  36.761 -35.091  1.00 56.60      B
ATOM   1824  N   LEU B 118     -57.854  38.370 -34.235  1.00 52.88      B
ATOM   1825  CA  LEU B 118     -58.862  37.430 -33.766  1.00 50.60      B
ATOM   1826  CB  LEU B 118     -59.955  38.167 -32.984  1.00 51.65      B
ATOM   1827  CG  LEU B 118     -61.046  37.271 -32.391  1.00 54.03      B
ATOM   1828  CD1 LEU B 118     -60.591  36.760 -31.040  1.00 54.61      B
ATOM   1829  CD2 LEU B 118     -62.343  38.044 -32.249  1.00 53.11      B
ATOM   1830  C   LEU B 118     -59.470  36.716 -34.966  1.00 49.21      B
ATOM   1831  O   LEU B 118     -59.797  35.534 -34.900  1.00 47.90      B
ATOM   1832  N   ALA B 119     -59.611  37.436 -36.072  1.00 48.72      B
ATOM   1833  CA  ALA B 119     -60.183  36.852 -37.278  1.00 49.24      B
ATOM   1834  CB  ALA B 119     -60.323  37.916 -38.343  1.00 48.04      B
ATOM   1835  C   ALA B 119     -59.339  35.674 -37.793  1.00 50.65      B
ATOM   1836  O   ALA B 119     -59.884  34.667 -38.270  1.00 51.27      B
ATOM   1837  N   VAL B 120     -58.016  35.795 -37.691  1.00 49.50      B
ATOM   1838  CA  VAL B 120     -57.130  34.727 -38.130  1.00 50.37      B
ATOM   1839  CB  VAL B 120     -55.657  35.188 -38.178  1.00 49.79      B
ATOM   1840  CG1 VAL B 120     -54.746  33.979 -38.348  1.00 47.60      B
ATOM   1841  CG2 VAL B 120     -55.455  36.190 -39.315  1.00 47.48      B
ATOM   1842  C   VAL B 120     -57.235  33.546 -37.170  1.00 52.26      B
ATOM   1843  O   VAL B 120     -57.177  32.377 -37.582  1.00 51.97      B
ATOM   1844  N   LYS B 121     -57.382  33.855 -35.883  1.00 53.62      B
ATOM   1845  CA  LYS B 121     -57.501  32.811 -34.875  1.00 54.59      B
ATOM   1846  CB  LYS B 121     -57.508  33.413 -33.475  1.00 54.64      B
ATOM   1847  CG  LYS B 121     -56.148  33.911 -33.017  1.00 58.06      B
ATOM   1848  CD  LYS B 121     -56.232  34.584 -31.650  1.00 60.35      B
ATOM   1849  CE  LYS B 121     -54.864  35.021 -31.140  1.00 60.35      B
ATOM   1850  NZ  LYS B 121     -53.990  33.861 -30.842  1.00 61.51      B
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ATOM 1851 C LYS B 121 -58.769 32.005 -35.108 1.00 55.58 B
ATOM 1852 O LYS B 121 -58.744 30.780 -35.065 1.00 55.57 B
ATOM 1853 N LYS B 122 -59.876 32.689 -35.378 1.00 56.77 B
ATOM 1854 CA LYS B 122 -61.140 31.997 -35.618 1.00 58.18 B
ATOM 1855 CB LYS B 122 -62.275 33.014 -35.811 1.00 60.88 B
ATOM 1856 CG LYS B 122 -62.628 33.807 -34.545 1.00 63.85 B
ATOM 1857 CD LYS B 122 -63.785 34.770 -34.784 1.00 67.04 B
ATOM 1858 CE LYS B 122 -65.079 34.020 -35.089 1.00 70.23 B
ATOM 1859 NZ LYS B 122 -66.260 34.925 -35.259 1.00 71.84 B
ATOM 1860 C LYS B 122 -61.036 31.078 -36.835 1.00 57.34 B
ATOM 1861 O LYS B 122 -61.588 29.975 -36.846 1.00 57.39 B
ATOM 1862 N TYR B 123 -60.316 31.540 -37.852 1.00 55.98 B
ATOM 1863 CA TYR B 123 -60.117 30.774 -39.080 1.00 54.34 B
ATOM 1864 CB TYR B 123 -59.252 31.593 -40.050 1.00 54.18 B
ATOM 1865 CG TYR B 123 -58.689 30.830 -41.226 1.00 53.30 B
ATOM 1866 CD1 TYR B 123 -59.524 30.175 -42.130 1.00 53.39 B
ATOM 1867 CE1 TYR B 123 -59.001 29.474 -43.217 1.00 53.48 B
ATOM 1868 CD2 TYR B 123 -57.315 30.767 -41.436 1.00 53.09 B
ATOM 1869 CE2 TYR B 123 -56.781 30.069 -42.518 1.00 53.78 B
ATOM 1870 CZ TYR B 123 -57.627 29.426 -43.404 1.00 53.93 B
ATOM 1871 OH TYR B 123 -57.097 28.736 -44.471 1.00 52.16 B
ATOM 1872 C TYR B 123 -59.458 29.430 -38.773 1.00 53.07 B
ATOM 1873 O TYR B 123 -59.994 28.369 -39.100 1.00 51.67 B
ATOM 1874 N PHE B 124 -58.296 29.487 -38.133 1.00 52.86 B
ATOM 1875 CA PHE B 124 -57.555 28.283 -37.775 1.00 53.45 B
ATOM 1876 CB PHE B 124 -56.200 28.665 -37.186 1.00 50.18 B
ATOM 1877 CG PHE B 124 -55.177 29.018 -38.228 1.00 48.40 B
ATOM 1878 CD1 PHE B 124 -54.460 28.019 -38.880 1.00 43.87 B
ATOM 1879 CD2 PHE B 124 -54.958 30.345 -38.590 1.00 46.73 B
ATOM 1880 CE1 PHE B 124 -53.553 28.327 -39.865 1.00 41.12 B
ATOM 1881 CE2 PHE B 124 -54.040 30.659 -39.587 1.00 44.49 B
ATOM 1882 CZ PHE B 124 -53.338 29.641 -40.223 1.00 41.38 B
ATOM 1883 C PHE B 124 -58.336 27.440 -36.796 1.00 55.05 B
ATOM 1884 O PHE B 124 -58.134 26.234 -36.695 1.00 54.37 B
ATOM 1885 N GLN B 125 -59.238 28.094 -36.076 1.00 59.25 B
ATOM 1886 CA GLN B 125 -60.081 27.421 -35.106 1.00 60.57 B
ATOM 1887 CB GLN B 125 -60.883 28.445 -34.307 1.00 64.50 B
ATOM 1888 CG GLN B 125 -61.759 27.839 -33.227 1.00 70.78 B
ATOM 1889 CD GLN B 125 -60.960 27.038 -32.212 1.00 74.51 B
ATOM 1890 OE1 GLN B 125 -60.071 27.575 -31.540 1.00 76.71 B
ATOM 1891 NE2 GLN B 125 -61.272 25.744 -32.095 1.00 75.37 B
ATOM 1892 C GLN B 125 -61.014 26.525 -35.894 1.00 59.74 B
ATOM 1893 O GLN B 125 -61.124 25.336 -35.608 1.00 60.48 B
ATOM 1894 N ARG B 126 -61.672 27.096 -36.901 1.00 58.55 B
ATOM 1895 CA ARG B 126 -62.591 26.332 -37.740 1.00 58.45 B
ATOM 1896 CB ARG B 126 -63.192 27.230 -38.819 1.00 58.22 B
ATOM 1897 CG ARG B 126 -64.322 28.135 -38.334 1.00 56.82 B
ATOM 1898 CD ARG B 126 -64.632 29.227 -39.348 1.00 55.96 B
ATOM 1899 NE ARG B 126 -64.100 30.523 -38.925 1.00 56.75 B
ATOM 1900 CZ ARG B 126 -63.490 31.379 -39.738 1.00 57.05 B
ATOM 1901 NH1 ARG B 126 -63.333 31.072 -41.013 1.00 56.86 B
ATOM 1902 NH2 ARG B 126 -63.039 32.541 -39.282 1.00 57.49 B
ATOM 1903 C ARG B 126 -61.874 25.151 -38.384 1.00 59.08 B

ATOM	1904	O	ARG	B	126	-62.406	24.043	-38.425	1.00	58.89	B
ATOM	1905	N	ILE	B	127	-60.667	25.396	-38.888	1.00	59.70	B
ATOM	1906	CA	ILE	B	127	-59.862	24.351	-39.514	1.00	59.95	B
ATOM	1907	CB	ILE	B	127	-58.472	24.891	-39.914	1.00	59.73	B
ATOM	1908	CG2	ILE	B	127	-57.508	23.745	-40.190	1.00	57.13	B
ATOM	1909	CG1	ILE	B	127	-58.609	25.809	-41.126	1.00	60.37	B
ATOM	1910	CD1	ILE	B	127	-57.338	26.563	-41.468	1.00	62.06	B
ATOM	1911	C	ILE	B	127	-59.675	23.199	-38.538	1.00	60.89	B
ATOM	1912	O	ILE	B	127	-59.904	22.041	-38.884	1.00	60.80	B
ATOM	1913	N	THR	B	128	-59.264	23.543	-37.319	1.00	61.84	B
ATOM	1914	CA	THR	B	128	-59.012	22.583	-36.241	1.00	63.43	B
ATOM	1915	CB	THR	B	128	-58.598	23.320	-34.940	1.00	64.67	B
ATOM	1916	OG1	THR	B	128	-57.481	24.172	-35.212	1.00	67.07	B
ATOM	1917	CG2	THR	B	128	-58.204	22.331	-33.853	1.00	65.28	B
ATOM	1918	C	THR	B	128	-60.209	21.690	-35.918	1.00	63.22	B
ATOM	1919	O	THR	B	128	-60.045	20.515	-35.585	1.00	61.95	B
ATOM	1920	N	LEU	B	129	-61.407	22.256	-36.008	1.00	64.24	B
ATOM	1921	CA	LEU	B	129	-62.630	21.524	-35.716	1.00	66.29	B
ATOM	1922	CB	LEU	B	129	-63.771	22.505	-35.454	1.00	66.59	B
ATOM	1923	CG	LEU	B	129	-64.722	22.138	-34.313	1.00	67.84	B
ATOM	1924	CD1	LEU	B	129	-65.736	23.255	-34.140	1.00	67.06	B
ATOM	1925	CD2	LEU	B	129	-65.409	20.796	-34.595	1.00	67.62	B
ATOM	1926	C	LEU	B	129	-62.986	20.619	-36.886	1.00	68.37	B
ATOM	1927	O	LEU	B	129	-63.672	19.613	-36.720	1.00	70.05	B
ATOM	1928	N	TYR	B	130	-62.530	20.994	-38.077	1.00	69.17	B
ATOM	1929	CA	TYR	B	130	-62.780	20.208	-39.273	1.00	68.74	B
ATOM	1930	CB	TYR	B	130	-62.296	20.973	-40.507	1.00	69.94	B
ATOM	1931	CG	TYR	B	130	-62.397	20.200	-41.803	1.00	71.43	B
ATOM	1932	CD1	TYR	B	130	-63.627	19.990	-42.425	1.00	71.95	B
ATOM	1933	CE1	TYR	B	130	-63.719	19.273	-43.624	1.00	72.25	B
ATOM	1934	CD2	TYR	B	130	-61.258	19.671	-42.409	1.00	72.21	B
ATOM	1935	CE2	TYR	B	130	-61.340	18.950	-43.607	1.00	72.56	B
ATOM	1936	CZ	TYR	B	130	-62.571	18.756	-44.207	1.00	72.07	B
ATOM	1937	OH	TYR	B	130	-62.649	18.044	-45.383	1.00	71.77	B
ATOM	1938	C	TYR	B	130	-61.996	18.911	-39.115	1.00	69.00	B
ATOM	1939	O	TYR	B	130	-62.556	17.821	-39.175	1.00	68.44	B
ATOM	1940	N	LEU	B	131	-60.691	19.044	-38.896	1.00	68.64	B
ATOM	1941	CA	LEU	B	131	-59.821	17.890	-38.724	1.00	68.04	B
ATOM	1942	CB	LEU	B	131	-58.422	18.345	-38.310	1.00	66.02	B
ATOM	1943	CG	LEU	B	131	-57.471	18.856	-39.391	1.00	65.04	B
ATOM	1944	CD1	LEU	B	131	-56.264	19.481	-38.719	1.00	63.94	B
ATOM	1945	CD2	LEU	B	131	-57.043	17.716	-40.313	1.00	63.38	B
ATOM	1946	C	LEU	B	131	-60.347	16.891	-37.698	1.00	68.93	B
ATOM	1947	O	LEU	B	131	-60.523	15.714	-38.006	1.00	68.61	B
ATOM	1948	N	THR	B	132	-60.594	17.363	-36.478	1.00	70.61	B
ATOM	1949	CA	THR	B	132	-61.083	16.495	-35.406	1.00	71.92	B
ATOM	1950	CB	THR	B	132	-60.841	17.131	-34.008	1.00	71.89	B
ATOM	1951	OG1	THR	B	132	-61.250	16.214	-32.987	1.00	70.43	B
ATOM	1952	CG2	THR	B	132	-61.623	18.429	-33.860	1.00	72.59	B
ATOM	1953	C	THR	B	132	-62.565	16.161	-35.562	1.00	72.74	B
ATOM	1954	O	THR	B	132	-63.170	15.549	-34.683	1.00	73.16	B
ATOM	1955	N	GLY	B	133	-63.141	16.576	-36.687	1.00	73.71	B
ATOM	1956	CA	GLY	B	133	-64.539	16.301	-36.968	1.00	73.91	B

ATOM 1957 C GLY B 133 -64.582 15.208 -38.019 1.00 74.32 B
ATOM 1958 O GLY B 133 -65.606 14.556 -38.236 1.00 74.32 B
ATOM 1959 N LYS B 134 -63.442 15.015 -38.676 1.00 74.07 B
ATOM 1960 CA LYS B 134 -63.296 14.001 -39.708 1.00 73.57 B
ATOM 1961 CB LYS B 134 -62.847 14.629 -41.028 1.00 72.93 B
ATOM 1962 CG LYS B 134 -63.976 14.926 -42.004 1.00 73.33 B
ATOM 1963 CD LYS B 134 -64.905 16.035 -41.525 1.00 74.01 B
ATOM 1964 CE LYS B 134 -65.972 16.349 -42.583 1.00 74.15 B
ATOM 1965 NZ LYS B 134 -66.745 17.600 -42.317 1.00 72.79 B
ATOM 1966 C LYS B 134 -62.282 12.962 -39.262 1.00 73.93 B
ATOM 1967 O LYS B 134 -61.676 12.278 -40.082 1.00 72.76 B
ATOM 1968 N LYS B 135 -62.093 12.867 -37.951 1.00 75.07 B
ATOM 1969 CA LYS B 135 -61.184 11.890 -37.367 1.00 76.77 B
ATOM 1970 CB LYS B 135 -61.808 10.496 -37.485 1.00 77.37 B
ATOM 1971 CG LYS B 135 -63.245 10.428 -36.990 1.00 78.83 B
ATOM 1972 CD LYS B 135 -63.856 9.057 -37.231 1.00 81.28 B
ATOM 1973 CE LYS B 135 -63.278 8.000 -36.295 1.00 83.54 B
ATOM 1974 NZ LYS B 135 -63.708 8.200 -34.876 1.00 84.34 B
ATOM 1975 C LYS B 135 -59.773 11.878 -37.967 1.00 77.31 B
ATOM 1976 O LYS B 135 -59.174 10.815 -38.135 1.00 78.04 B
ATOM 1977 N TYR B 136 -59.246 13.056 -38.283 1.00 77.23 B
ATOM 1978 CA TYR B 136 -57.902 13.181 -38.845 1.00 76.63 B
ATOM 1979 CB TYR B 136 -56.861 12.989 -37.748 1.00 78.09 B
ATOM 1980 CG TYR B 136 -57.053 13.907 -36.564 1.00 82.10 B
ATOM 1981 CD1 TYR B 136 -58.076 13.685 -35.638 1.00 83.03 B
ATOM 1982 CE1 TYR B 136 -58.244 14.522 -34.529 1.00 84.37 B
ATOM 1983 CD2 TYR B 136 -56.204 14.992 -36.359 1.00 83.46 B
ATOM 1984 CE2 TYR B 136 -56.362 15.837 -35.255 1.00 85.30 B
ATOM 1985 CZ TYR B 136 -57.382 15.596 -34.341 1.00 85.81 B
ATOM 1986 OH TYR B 136 -57.524 16.419 -33.237 1.00 85.88 B
ATOM 1987 C TYR B 136 -57.615 12.202 -39.980 1.00 75.70 B
ATOM 1988 O TYR B 136 -56.528 11.625 -40.057 1.00 74.43 B
ATOM 1989 N SER B 137 -58.592 12.039 -40.867 1.00 75.24 B
ATOM 1990 CA SER B 137 -58.477 11.131 -42.001 1.00 74.25 B
ATOM 1991 CB SER B 137 -59.860 10.845 -42.580 1.00 73.68 B
ATOM 1992 OG SER B 137 -60.451 12.033 -43.072 1.00 73.31 B
ATOM 1993 C SER B 137 -57.578 11.668 -43.106 1.00 74.57 B
ATOM 1994 O SER B 137 -57.476 12.880 -43.312 1.00 73.85 B
ATOM 1995 N PRO B 138 -56.921 10.758 -43.842 1.00 74.56 B
ATOM 1996 CD PRO B 138 -56.984 9.296 -43.668 1.00 74.19 B
ATOM 1997 CA PRO B 138 -56.021 11.103 -44.940 1.00 74.13 B
ATOM 1998 CB PRO B 138 -55.832 9.771 -45.643 1.00 73.66 B
ATOM 1999 CG PRO B 138 -55.810 8.822 -44.486 1.00 73.91 B
ATOM 2000 C PRO B 138 -56.579 12.177 -45.859 1.00 74.15 B
ATOM 2001 O PRO B 138 -55.832 13.016 -46.362 1.00 74.48 B
ATOM 2002 N CYS B 139 -57.887 12.156 -46.081 1.00 74.19 B
ATOM 2003 CA CYS B 139 -58.488 13.163 -46.943 1.00 75.46 B
ATOM 2004 C CYS B 139 -58.702 14.457 -46.178 1.00 74.04 B
ATOM 2005 O CYS B 139 -58.472 15.545 -46.705 1.00 73.77 B
ATOM 2006 CB CYS B 139 -59.814 12.665 -47.538 1.00 79.16 B
ATOM 2007 SG CYS B 139 -59.600 11.373 -48.809 1.00 82.68 B
ATOM 2008 N ALA B 140 -59.136 14.342 -44.930 1.00 72.55 B
ATOM 2009 CA ALA B 140 -59.346 15.529 -44.115 1.00 71.12 B

ATOM 2010 CB ALA B 140 -59.704 15.128 -42.704 1.00 71.98 B
ATOM 2011 C ALA B 140 -58.063 16.364 -44.117 1.00 70.40 B
ATOM 2012 O ALA B 140 -58.104 17.576 -44.354 1.00 70.21 B
ATOM 2013 N TRP B 141 -56.929 15.706 -43.862 1.00 68.06 B
ATOM 2014 CA TRP B 141 -55.630 16.379 -43.839 1.00 66.09 B
ATOM 2015 CB TRP B 141 -54.511 15.405 -43.429 1.00 65.31 B
ATOM 2016 CG TRP B 141 -54.188 15.447 -41.954 1.00 64.66 B
ATOM 2017 CD2 TRP B 141 -53.698 16.570 -41.215 1.00 63.91 B
ATOM 2018 CE2 TRP B 141 -53.587 16.171 -39.868 1.00 63.61 B
ATOM 2019 CE3 TRP B 141 -53.333 17.879 -41.564 1.00 63.30 B
ATOM 2020 CD1 TRP B 141 -54.351 14.438 -41.046 1.00 64.31 B
ATOM 2021 NE1 TRP B 141 -53.995 14.864 -39.793 1.00 63.47 B
ATOM 2022 CZ2 TRP B 141 -53.140 17.031 -38.864 1.00 63.01 B
ATOM 2023 CZ3 TRP B 141 -52.887 18.735 -40.566 1.00 63.15 B
ATOM 2024 CH2 TRP B 141 -52.792 18.305 -39.231 1.00 62.58 B
ATOM 2025 C TRP B 141 -55.293 16.999 -45.190 1.00 65.08 B
ATOM 2026 O TRP B 141 -54.775 18.118 -45.263 1.00 64.05 B
ATOM 2027 N GLU B 142 -55.592 16.268 -46.259 1.00 63.17 B
ATOM 2028 CA GLU B 142 -55.324 16.750 -47.603 1.00 60.88 B
ATOM 2029 CB GLU B 142 -55.801 15.725 -48.635 1.00 59.86 B
ATOM 2030 CG GLU B 142 -55.595 16.126 -50.094 1.00 58.69 B
ATOM 2031 CD GLU B 142 -54.176 16.583 -50.414 1.00 57.82 B
ATOM 2032 OE1 GLU B 142 -53.198 15.912 -50.004 1.00 58.06 B
ATOM 2033 OE2 GLU B 142 -54.045 17.617 -51.096 1.00 54.99 B
ATOM 2034 C GLU B 142 -56.005 18.092 -47.825 1.00 60.14 B
ATOM 2035 O GLU B 142 -55.367 19.042 -48.265 1.00 61.06 B
ATOM 2036 N VAL B 143 -57.288 18.184 -47.505 1.00 58.83 B
ATOM 2037 CA VAL B 143 -58.006 19.437 -47.692 1.00 60.46 B
ATOM 2038 CB VAL B 143 -59.473 19.312 -47.217 1.00 63.38 B
ATOM 2039 CG1 VAL B 143 -60.189 20.652 -47.353 1.00 64.93 B
ATOM 2040 CG2 VAL B 143 -60.194 18.259 -48.044 1.00 62.82 B
ATOM 2041 C VAL B 143 -57.324 20.584 -46.937 1.00 60.05 B
ATOM 2042 O VAL B 143 -57.199 21.703 -47.453 1.00 60.09 B
ATOM 2043 N VAL B 144 -56.881 20.301 -45.716 1.00 58.84 B
ATOM 2044 CA VAL B 144 -56.207 21.307 -44.905 1.00 56.80 B
ATOM 2045 CB VAL B 144 -55.901 20.779 -43.475 1.00 56.37 B
ATOM 2046 CG1 VAL B 144 -54.933 21.720 -42.756 1.00 53.83 B
ATOM 2047 CG2 VAL B 144 -57.195 20.655 -42.688 1.00 53.78 B
ATOM 2048 C VAL B 144 -54.907 21.723 -45.570 1.00 55.71 B
ATOM 2049 O VAL B 144 -54.580 22.907 -45.619 1.00 56.30 B
ATOM 2050 N ARG B 145 -54.166 20.748 -46.083 1.00 54.57 B
ATOM 2051 CA ARG B 145 -52.904 21.039 -46.746 1.00 53.98 B
ATOM 2052 CB ARG B 145 -52.290 19.755 -47.301 1.00 54.48 B
ATOM 2053 CG ARG B 145 -50.776 19.805 -47.398 1.00 57.53 B
ATOM 2054 CD ARG B 145 -50.189 18.656 -48.226 1.00 59.32 B
ATOM 2055 NE ARG B 145 -50.007 19.028 -49.627 1.00 60.85 B
ATOM 2056 CZ ARG B 145 -51.000 19.146 -50.497 1.00 61.21 B
ATOM 2057 NH1 ARG B 145 -52.245 18.912 -50.113 1.00 63.40 B
ATOM 2058 NH2 ARG B 145 -50.750 19.516 -51.741 1.00 61.96 B
ATOM 2059 C ARG B 145 -53.163 22.034 -47.884 1.00 53.44 B
ATOM 2060 O ARG B 145 -52.508 23.072 -47.982 1.00 51.98 B
ATOM 2061 N ALA B 146 -54.141 21.724 -48.729 1.00 52.37 B
ATOM 2062 CA ALA B 146 -54.474 22.596 -49.844 1.00 52.73 B

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ATOM   2063  CB  ALA B 146     -55.476  21.927 -50.752  1.00 53.23       B
ATOM   2064  C   ALA B 146     -55.013  23.937 -49.375  1.00 52.70       B
ATOM   2065  O   ALA B 146     -54.678  24.964 -49.964  1.00 53.35       B
ATOM   2066  N   GLU B 147     -55.841  23.937 -48.328  1.00 52.05       B
ATOM   2067  CA  GLU B 147     -56.401  25.191 -47.799  1.00 51.29       B
ATOM   2068  CB  GLU B 147     -57.351  24.913 -46.626  1.00 52.80       B
ATOM   2069  CG  GLU B 147     -57.846  26.161 -45.865  1.00 56.59       B
ATOM   2070  CD  GLU B 147     -58.780  27.066 -46.685  1.00 60.42       B
ATOM   2071  OE1 GLU B 147     -59.760  26.554 -47.274  1.00 63.21       B
ATOM   2072  OE2 GLU B 147     -58.546  28.294 -46.732  1.00 61.56       B
ATOM   2073  C   GLU B 147     -55.295  26.129 -47.325  1.00 50.23       B
ATOM   2074  O   GLU B 147     -55.338  27.332 -47.575  1.00 48.90       B
ATOM   2075  N   ILE B 148     -54.308  25.561 -46.638  1.00 49.88       B
ATOM   2076  CA  ILE B 148     -53.187  26.320 -46.099  1.00 48.21       B
ATOM   2077  CB  ILE B 148     -52.368  25.443 -45.110  1.00 47.14       B
ATOM   2078  CG2 ILE B 148     -51.030  26.118 -44.755  1.00 44.12       B
ATOM   2079  CG1 ILE B 148     -53.223  25.162 -43.870  1.00 44.09       B
ATOM   2080  CD1 ILE B 148     -53.734  26.429 -43.164  1.00 42.93       B
ATOM   2081  C   ILE B 148     -52.292  26.883 -47.196  1.00 48.42       B
ATOM   2082  O   ILE B 148     -51.653  27.925 -47.014  1.00 47.29       B
ATOM   2083  N   MET B 149     -52.243  26.199 -48.335  1.00 49.13       B
ATOM   2084  CA  MET B 149     -51.442  26.686 -49.452  1.00 51.23       B
ATOM   2085  CB  MET B 149     -51.230  25.600 -50.494  1.00 51.00       B
ATOM   2086  CG  MET B 149     -49.910  24.895 -50.350  1.00 53.30       B
ATOM   2087  SD  MET B 149     -49.527  23.955 -51.813  1.00 56.01       B
ATOM   2088  CE  MET B 149     -50.453  22.505 -51.485  1.00 54.85       B
ATOM   2089  C   MET B 149     -52.176  27.855 -50.082  1.00 51.95       B
ATOM   2090  O   MET B 149     -51.568  28.851 -50.492  1.00 52.45       B
ATOM   2091  N   ARG B 150     -53.495  27.724 -50.150  1.00 51.47       B
ATOM   2092  CA  ARG B 150     -54.333  28.767 -50.707  1.00 52.51       B
ATOM   2093  CB  ARG B 150     -55.790  28.312 -50.658  1.00 55.92       B
ATOM   2094  CG  ARG B 150     -56.784  29.125 -51.454  1.00 60.87       B
ATOM   2095  CD  ARG B 150     -58.038  28.271 -51.662  1.00 67.39       B
ATOM   2096  NE  ARG B 150     -59.207  29.025 -52.117  1.00 73.67       B
ATOM   2097  CZ  ARG B 150     -59.231  29.827 -53.180  1.00 76.78       B
ATOM   2098  NH1 ARG B 150     -58.140  30.001 -53.922  1.00 78.58       B
ATOM   2099  NH2 ARG B 150     -60.354  30.456 -53.506  1.00 77.37       B
ATOM   2100  C   ARG B 150     -54.109  30.009 -49.851  1.00 51.57       B
ATOM   2101  O   ARG B 150     -53.689  31.046 -50.355  1.00 52.44       B
ATOM   2102  N   SER B 151     -54.354  29.887 -48.549  1.00 50.14       B
ATOM   2103  CA  SER B 151     -54.168  30.999 -47.633  1.00 49.46       B
ATOM   2104  CB  SER B 151     -54.458  30.559 -46.207  1.00 48.27       B
ATOM   2105  OG  SER B 151     -55.742  29.986 -46.112  1.00 48.71       B
ATOM   2106  C   SER B 151     -52.760  31.574 -47.705  1.00 50.79       B
ATOM   2107  O   SER B 151     -52.584  32.791 -47.687  1.00 50.33       B
ATOM   2108  N   PHE B 152     -51.749  30.716 -47.778  1.00 52.18       B
ATOM   2109  CA  PHE B 152     -50.380  31.225 -47.861  1.00 55.34       B
ATOM   2110  CB  PHE B 152     -49.365  30.087 -47.739  1.00 55.53       B
ATOM   2111  CG  PHE B 152     -48.768  29.954 -46.366  1.00 54.12       B
ATOM   2112  CD1 PHE B 152     -49.502  29.406 -45.320  1.00 54.49       B
ATOM   2113  CD2 PHE B 152     -47.476  30.391 -46.114  1.00 53.65       B
ATOM   2114  CE1 PHE B 152     -48.954  29.297 -44.039  1.00 53.70       B
ATOM   2115  CE2 PHE B 152     -46.925  30.286 -44.834  1.00 55.29       B
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ATOM   2116  CZ  PHE B 152     -47.668  29.737 -43.799  1.00 53.15      B
ATOM   2117  C   PHE B 152     -50.095  32.024 -49.145  1.00 55.94      B
ATOM   2118  O   PHE B 152     -49.423  33.062 -49.115  1.00 54.62      B
ATOM   2119  N   ALA B 153     -50.603  31.541 -50.271  1.00 57.38      B
ATOM   2120  CA  ALA B 153     -50.381  32.238 -51.526  1.00 59.97      B
ATOM   2121  CB  ALA B 153     -50.910  31.408 -52.700  1.00 59.69      B
ATOM   2122  C   ALA B 153     -51.083  33.587 -51.460  1.00 61.25      B
ATOM   2123  O   ALA B 153     -50.514  34.607 -51.841  1.00 62.94      B
ATOM   2124  N   LEU B 154     -52.312  33.588 -50.953  1.00 62.12      B
ATOM   2125  CA  LEU B 154     -53.112  34.804 -50.833  1.00 63.13      B
ATOM   2126  CB  LEU B 154     -54.510  34.437 -50.340  1.00 60.76      B
ATOM   2127  CG  LEU B 154     -55.360  33.639 -51.331  1.00 59.42      B
ATOM   2128  CD1 LEU B 154     -56.627  33.136 -50.660  1.00 58.68      B
ATOM   2129  CD2 LEU B 154     -55.698  34.523 -52.513  1.00 57.64      B
ATOM   2130  C   LEU B 154     -52.518  35.899 -49.932  1.00 65.86      B
ATOM   2131  O   LEU B 154     -52.951  37.052 -49.982  1.00 65.99      B
ATOM   2132  N   SER B 155     -51.525  35.546 -49.121  1.00 68.63      B
ATOM   2133  CA  SER B 155     -50.899  36.509 -48.219  1.00 71.66      B
ATOM   2134  CB  SER B 155     -50.675  35.871 -46.845  1.00 71.59      B
ATOM   2135  OG  SER B 155     -49.726  34.820 -46.920  1.00 71.04      B
ATOM   2136  C   SER B 155     -49.562  37.032 -48.750  1.00 74.34      B
ATOM   2137  O   SER B 155     -48.873  37.802 -48.071  1.00 74.13      B
ATOM   2138  N   THR B 156     -49.193  36.611 -49.958  1.00 76.74      B
ATOM   2139  CA  THR B 156     -47.930  37.037 -50.556  1.00 78.25      B
ATOM   2140  CB  THR B 156     -47.659  36.302 -51.909  1.00 78.41      B
ATOM   2141  OG1 THR B 156     -48.703  36.602 -52.847  1.00 78.59      B
ATOM   2142  CG2 THR B 156     -47.600  34.791 -51.697  1.00 77.83      B
ATOM   2143  C   THR B 156     -47.930  38.547 -50.784  1.00 78.96      B
ATOM   2144  O   THR B 156     -46.955  39.233 -50.479  1.00 77.97      B
ATOM   2145  N   ASN B 157     -49.035  39.062 -51.313  1.00 80.60      B
ATOM   2146  CA  ASN B 157     -49.146  40.489 -51.576  1.00 82.39      B
ATOM   2147  CB  ASN B 157     -50.574  40.847 -52.011  1.00 83.54      B
ATOM   2148  CG  ASN B 157     -50.923  40.286 -53.382  1.00 85.98      B
ATOM   2149  OD1 ASN B 157     -50.166  40.449 -54.344  1.00 86.88      B
ATOM   2150  ND2 ASN B 157     -52.075  39.628 -53.481  1.00 87.40      B
ATOM   2151  C   ASN B 157     -48.752  41.307 -50.351  1.00 82.41      B
ATOM   2152  O   ASN B 157     -48.015  42.290 -50.459  1.00 83.08      B
ATOM   2153  N   LEU B 158     -49.234  40.889 -49.185  1.00 81.77      B
ATOM   2154  CA  LEU B 158     -48.936  41.585 -47.941  1.00 80.56      B
ATOM   2155  CB  LEU B 158     -49.732  40.974 -46.785  1.00 80.09      B
ATOM   2156  CG  LEU B 158     -50.412  41.950 -45.821  1.00 79.10      B
ATOM   2157  CD1 LEU B 158     -51.452  42.765 -46.569  1.00 79.09      B
ATOM   2158  CD2 LEU B 158     -51.078  41.183 -44.702  1.00 79.49      B
ATOM   2159  C   LEU B 158     -47.447  41.501 -47.647  1.00 80.15      B
ATOM   2160  O   LEU B 158     -46.772  42.520 -47.568  1.00 80.43      B
ATOM   2161  N   GLN B 159     -46.935  40.286 -47.494  1.00 80.14      B
ATOM   2162  CA  GLN B 159     -45.519  40.095 -47.210  1.00 81.12      B
ATOM   2163  CB  GLN B 159     -45.171  38.603 -47.275  1.00 81.69      B
ATOM   2164  CG  GLN B 159     -45.683  37.807 -46.067  1.00 83.74      B
ATOM   2165  CD  GLN B 159     -45.782  36.306 -46.320  1.00 84.02      B
ATOM   2166  OE1 GLN B 159     -46.586  35.853 -47.141  1.00 84.95      B
ATOM   2167  NE2 GLN B 159     -44.969  35.531 -45.611  1.00 81.86      B
ATOM   2168  C   GLN B 159     -44.662  40.899 -48.189  1.00 81.34      B
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ATOM   2169  O   GLN B 159     -43.627  41.459 -47.813  1.00 80.91       B
ATOM   2170  N   GLY B 160     -45.115  40.973 -49.438  1.00 81.50       B
ATOM   2171  CA  GLY B 160     -44.389  41.716 -50.453  1.00 82.03       B
ATOM   2172  C   GLY B 160     -44.444  43.224 -50.261  1.00 82.52       B
ATOM   2173  O   GLY B 160     -43.401  43.875 -50.197  1.00 83.21       B
ATOM   2174  N   ALA B 161     -45.652  43.783 -50.174  1.00 82.63       B
ATOM   2175  CA  ALA B 161     -45.832  45.225 -49.989  1.00 82.61       B
ATOM   2176  CB  ALA B 161     -47.318  45.575 -49.991  1.00 81.89       B
ATOM   2177  C   ALA B 161     -45.193  45.672 -48.681  1.00 82.81       B
ATOM   2178  O   ALA B 161     -44.989  46.865 -48.444  1.00 82.18       B
ATOM   2179  N   LEU B 162     -44.892  44.691 -47.836  1.00 83.61       B
ATOM   2180  CA  LEU B 162     -44.262  44.918 -46.542  1.00 83.73       B
ATOM   2181  CB  LEU B 162     -44.569  43.741 -45.608  1.00 81.75       B
ATOM   2182  CG  LEU B 162     -44.375  43.877 -44.097  1.00 80.23       B
ATOM   2183  CD1 LEU B 162     -44.889  42.617 -43.433  1.00 79.72       B
ATOM   2184  CD2 LEU B 162     -42.912  44.096 -43.755  1.00 80.03       B
ATOM   2185  C   LEU B 162     -42.760  45.014 -46.802  1.00 84.64       B
ATOM   2186  O   LEU B 162     -42.053  45.804 -46.167  1.00 84.99       B
ATOM   2187  N   GLY B 163     -42.288  44.206 -47.752  1.00 84.65       B
ATOM   2188  CA  GLY B 163     -40.881  44.207 -48.107  1.00 84.77       B
ATOM   2189  C   GLY B 163     -40.469  45.480 -48.828  1.00 85.10       B
ATOM   2190  O   GLY B 163     -39.592  46.201 -48.300  1.00 84.53       B
ATOM   2191  OXT GLY B 163     -41.021  45.762 -49.918  1.00 84.32       B
ATOM   2192  S   CXS $1001     -37.007   7.286 -12.909  1.00 89.60       $
ATOM   2193  O1  CXS $1001     -37.722   7.642 -11.758  1.00 90.92       $
ATOM   2194  O2  CXS $1001     -37.206   7.283 -14.330  1.00 90.52       $
ATOM   2195  O3  CXS $1001     -35.476   7.404 -12.678  1.00 90.21       $
ATOM   2196  C1  CXS $1001     -36.878   9.113 -13.140  1.00 86.35       $
ATOM   2197  C2  CXS $1001     -38.280   9.714 -13.449  1.00 82.21       $
ATOM   2198  C3  CXS $1001     -38.308  11.211 -13.660  1.00 78.87       $
ATOM   2199  N   CXS $1001     -39.730  11.610 -13.907  1.00 74.83       $
ATOM   2200  C4  CXS $1001     -39.806  13.069 -14.118  1.00 72.04       $
ATOM   2201  C5  CXS $1001     -38.946  13.813 -13.094  1.00 71.28       $
ATOM   2202  C6  CXS $1001     -38.989  15.336 -13.308  1.00 70.38       $
ATOM   2203  C7  CXS $1001     -38.608  15.704 -14.767  1.00 70.92       $
ATOM   2204  C8  CXS $1001     -39.501  14.945 -15.785  1.00 69.52       $
ATOM   2205  C9  CXS $1001     -39.379  13.417 -15.567  1.00 71.02       $
ATOM   2206  S   CXS $1002     -33.172  31.213 -33.664  1.00 59.12       $
ATOM   2207  O1  CXS $1002     -33.303  31.719 -34.982  1.00 61.00       $
ATOM   2208  O2  CXS $1002     -31.915  30.813 -33.130  1.00 59.84       $
ATOM   2209  O3  CXS $1002     -33.679  32.294 -32.738  1.00 61.33       $
ATOM   2210  C1  CXS $1002     -34.407  29.954 -33.375  1.00 56.21       $
ATOM   2211  C2  CXS $1002     -34.146  28.753 -34.253  1.00 51.82       $
ATOM   2212  C3  CXS $1002     -35.236  27.757 -33.951  1.00 52.23       $
ATOM   2213  N   CXS $1002     -35.098  26.561 -34.782  1.00 53.07       $
ATOM   2214  C4  CXS $1002     -36.180  25.616 -34.422  1.00 50.12       $
ATOM   2215  C5  CXS $1002     -37.574  26.289 -34.439  1.00 47.85       $
ATOM   2216  C6  CXS $1002     -38.645  25.266 -34.045  1.00 47.93       $
ATOM   2217  C7  CXS $1002     -38.644  24.095 -35.046  1.00 49.65       $
ATOM   2218  C8  CXS $1002     -37.263  23.410 -35.077  1.00 49.27       $
ATOM   2219  C9  CXS $1002     -36.157  24.435 -35.413  1.00 50.51       $
ATOM   2220  O   HOH S   1     -55.089  30.721 -29.788  1.00 42.32       S
ATOM   2221  O   HOH S   2     -51.354  16.117 -54.214  1.00 66.49       S
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ATOM	2222	O	HOH	S	3	-35.292	43.228	-45.412	1.00	70.66	S
ATOM	2223	O	HOH	S	6	-36.194	33.341	-31.023	1.00	62.49	S
ATOM	2224	O	HOH	S	8	-42.460	34.031	-31.211	1.00	52.51	S
ATOM	2225	O	HOH	S	11	-51.117	14.500	-24.316	1.00	63.19	S
ATOM	2226	O	HOH	S	13	-34.186	35.241	-31.749	1.00	69.73	S
ATOM	2227	O	HOH	S	14	-46.886	23.354	-15.063	1.00	62.91	S
ATOM	2228	O	HOH	S	15	-67.379	16.745	-38.051	1.00	74.92	S
ATOM	2229	O	HOH	S	16	-48.149	52.600	-41.809	1.00	65.55	S
ATOM	2230	O	HOH	S	20	-37.533	46.814	-44.158	1.00	63.62	S
ATOM	2231	O	HOH	S	23	-26.090	20.564	-40.954	1.00	64.92	S
ATOM	2232	O	HOH	S	33	-66.641	27.143	-35.990	1.00	64.70	S
ATOM	2233	O	HOH	S	34	-34.278	43.389	-42.980	1.00	66.36	S
ATOM	2234	O	HOH	S	35	-40.575	14.233	-23.786	1.00	68.23	S
ATOM	2235	O	HOH	S	36	-26.941	28.813	-12.491	1.00	61.13	S
ATOM	2236	O	HOH	S	37	-30.827	27.593	-14.316	1.00	59.11	S
ATOM	2237	O	HOH	S	39	-44.040	36.979	-30.178	1.00	56.62	S
ATOM	2238	O	HOH	S	40	-33.347	44.688	-11.256	1.00	77.43	S
ATOM	2239	O	HOH	S	42	-64.966	36.711	-39.384	1.00	64.46	S
ATOM	2240	O	HOH	S	43	-14.994	28.360	-34.554	1.00	79.56	S
ATOM	2241	O	HOH	S	45	-58.115	31.298	-30.300	1.00	73.59	S
ATOM	2242	O	HOH	S	46	-36.924	25.549	-50.937	1.00	62.92	S
ATOM	2243	O	HOH	S	49	-20.930	37.291	-14.901	1.00	62.70	S
ATOM	2244	O	HOH	S	55	-35.088	9.503	-41.169	1.00	56.66	S
ATOM	2245	O	HOH	S	58	-45.523	36.927	-10.019	1.00	53.41	S
ATOM	2246	O	HOH	S	60	-24.940	43.426	-34.908	1.00	64.11	S
ATOM	2247	O	HOH	S	61	-43.094	16.769	-33.268	1.00	88.80	S
ATOM	2248	O	HOH	S	64	-52.392	52.632	-34.025	1.00	92.27	S
ATOM	2249	O	HOH	S	66	-14.474	29.522	-20.678	1.00	73.76	S
ATOM	2250	O	HOH	S	67	-61.923	12.568	-56.894	1.00	71.78	S
ATOM	2251	O	HOH	S	68	-17.930	11.026	-27.010	1.00	57.62	S
ATOM	2252	O	HOH	S	69	-26.009	23.821	-38.215	1.00	56.83	S
ATOM	2253	O	HOH	S	70	-34.979	17.848	-41.915	1.00	57.66	S
ATOM	2254	O	HOH	S	73	-53.375	25.113	-34.332	1.00	67.17	S
ATOM	2255	O	HOH	S	78	-3.369	14.903	-39.536	1.00	76.47	S
ATOM	2256	O	HOH	S	79	-49.809	52.012	-53.024	1.00	74.16	S
ATOM	2257	O	HOH	S	80	-52.873	32.569	-23.870	1.00	59.72	S
ATOM	2258	O	HOH	S	81	-69.907	24.040	-37.219	1.00	59.30	S
ATOM	2259	O	HOH	S	82	-42.669	56.555	-30.390	1.00	65.30	S
ATOM	2260	O	HOH	S	85	-29.842	34.315	-33.948	1.00	62.56	S
ATOM	2261	O	HOH	S	96	-54.795	49.118	-60.472	1.00	72.94	S
ATOM	2262	O	HOH	S	100	-16.120	34.824	-29.084	1.00	73.72	S
ATOM	2263	O	HOH	S	103	-41.801	10.188	-41.652	1.00	59.23	S
ATOM	2264	O	HOH	S	108	-72.826	20.167	-44.484	1.00	75.51	S
ATOM	2265	O	HOH	S	111	-31.210	25.257	-37.321	1.00	71.53	S
ATOM	2266	O	HOH	S	113	-35.456	11.432	-29.314	1.00	64.29	S
ATOM	2267	O	HOH	S	114	-14.615	14.030	-42.236	1.00	64.98	S
ATOM	2268	O	HOH	S	116	-30.150	46.628	-35.936	1.00	67.88	S
ATOM	2269	O	HOH	S	117	-33.711	52.716	-21.422	1.00	75.50	S
ATOM	2270	O	HOH	S	122	-42.524	31.582	-56.165	1.00	60.35	S
ATOM	2271	O	HOH	S	124	-57.788	19.390	-20.057	1.00	80.05	S
ATOM	2272	O	HOH	S	127	-8.352	21.156	-33.703	1.00	72.60	S
ATOM	2273	O	HOH	S	131	-65.658	4.703	-48.301	1.00	67.75	S
ATOM	2274	O	HOH	S	136	-31.961	29.091	-37.073	1.00	65.98	S

ATOM	2275	O	HOH	S	144	-32.295	17.761	-36.053	1.00	61.82	S
ATOM	2276	O	HOH	S	145	-16.099	20.782	-27.246	1.00	62.57	S
ATOM	2277	O	HOH	S	152	-40.098	47.171	-61.867	1.00	70.18	S
ATOM	2278	O	HOH	S	153	-16.949	16.723	-30.701	1.00	72.82	S
ATOM	2279	O	HOH	S	154	-49.102	54.760	-44.857	1.00	74.87	S
ATOM	2280	O	HOH	S	155	-33.241	36.181	-28.893	1.00	53.26	S
ATOM	2281	O	HOH	S	157	-28.846	4.566	-28.970	1.00	65.48	S
ATOM	2282	O	HOH	S	159	-18.078	6.979	-32.388	1.00	62.25	S
ATOM	2283	O	HOH	S	160	-49.927	12.224	-25.999	1.00	83.57	S
ATOM	2284	O	HOH	S	161	-35.384	38.748	-45.921	1.00	78.38	S
ATOM	2285	O	HOH	S	164	-19.431	9.631	-42.561	1.00	83.75	S
ATOM	2286	O	HOH	S	165	-24.757	7.452	-28.428	1.00	62.83	S
ATOM	2287	O	HOH	S	166	-26.095	40.110	-19.029	1.00	71.51	S
ATOM	2288	O	HOH	S	167	-33.517	28.875	-11.950	1.00	65.15	S
ATOM	2289	O	HOH	S	169	-23.559	26.637	-34.978	1.00	69.82	S
ATOM	2290	O	HOH	S	171	-35.911	32.089	-11.426	1.00	70.81	S
ATOM	2291	O	HOH	S	173	-29.541	39.675	-27.861	1.00	73.58	S
ATOM	2292	O	HOH	S	174	-42.366	9.773	-12.564	1.00	75.10	S
ATOM	2293	O	HOH	S	179	-37.615	36.321	-6.575	1.00	60.84	S
ATOM	2294	O	HOH	S	185	-37.396	54.966	-35.497	1.00	66.51	S
ATOM	2295	O	HOH	S	186	-34.811	40.197	-42.025	1.00	78.57	S
ATOM	2296	O	HOH	S	189	-41.472	38.031	-56.357	1.00	76.56	S
ATOM	2297	O	HOH	S	193	-31.145	43.929	-38.718	1.00	64.82	S
ATOM	2298	O	HOH	S	197	-44.621	37.091	-53.919	1.00	74.57	S
ATOM	2299	O	HOH	S	200	-26.601	47.858	-27.412	1.00	73.60	S
ATOM	2300	O	HOH	S	204	-34.070	22.759	-42.394	1.00	64.86	S
ATOM	2301	O	HOH	S	206	-56.104	23.451	-54.858	1.00	63.95	S
ATOM	2302	O	HOH	S	207	-42.623	14.939	-36.850	1.00	58.12	S
ATOM	2303	O	HOH	S	215	-57.916	20.611	-53.534	1.00	65.65	S
ATOM	2304	O	HOH	S	217	-68.703	19.492	-32.308	1.00	66.71	S
ATOM	2305	O	HOH	S	218	-34.288	47.462	-17.190	1.00	87.83	S
ATOM	2306	O	HOH	S	219	-47.023	49.480	-49.463	1.00	80.36	S
ATOM	2307	O	HOH	S	221	-36.167	35.091	-46.526	1.00	82.36	S
ATOM	2308	O	HOH	S	229	-5.120	14.056	-34.382	1.00	80.88	S
ATOM	2309	O	HOH	S	234	-61.102	28.009	-56.501	1.00	73.87	S
ATOM	2310	O	HOH	S	236	-50.038	53.208	-31.379	1.00	80.66	S
ATOM	2311	O	HOH	S	238	-63.210	5.594	-33.656	1.00	73.31	S
ATOM	2312	O	HOH	S	239	-18.979	25.474	-40.262	1.00	65.13	S
ATOM	2313	O	HOH	S	241	-9.247	22.473	-40.473	1.00	62.01	S
ATOM	2314	O	HOH	S	242	-23.581	0.874	-22.639	1.00	79.48	S
ATOM	2315	O	HOH	S	244	-37.921	9.795	-41.267	1.00	71.07	S
ATOM	2316	O	HOH	S	245	-68.213	16.294	-47.338	1.00	66.37	S
ATOM	2317	O	HOH	S	259	-54.297	15.702	-29.864	1.00	69.25	S
ATOM	2318	O	HOH	S	260	-53.332	29.741	-10.004	1.00	79.52	S
ATOM	2319	O	HOH	S	261	-58.281	47.179	-58.668	1.00	71.63	S
ATOM	2320	O	HOH	S	262	-61.633	19.952	-25.923	1.00	74.21	S
ATOM	2321	O	HOH	S	264	-59.854	24.019	-57.410	1.00	84.87	S
ATOM	2322	O	HOH	S	265	-34.910	13.726	-35.043	1.00	75.92	S
ATOM	2323	O	HOH	S	266	-65.206	-1.041	-22.378	1.00	67.71	S
ATOM	2324	O	HOH	S	267	-30.825	12.386	-15.339	1.00	53.22	S
ATOM	2325	O	HOH	S	268	-23.141	25.046	-40.085	1.00	77.62	S
ATOM	2326	O	HOH	S	273	-64.261	24.028	-29.410	1.00	61.30	S
ATOM	2327	O	HOH	S	281	-45.175	18.432	-30.051	1.00	88.80	S

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ATOM   2328  O   HOH S 285     -44.514  56.451 -43.099  1.00 73.84      S
ATOM   2329  O   HOH S 298     -41.747  37.900  -7.567  1.00 67.96      S
ATOM   2330  O   HOH S 301     -51.187  22.922 -27.202  1.00 59.87      S
ATOM   2331  O   HOH S 308     -56.697  51.798 -45.311  1.00 76.39      S
ATOM   2332  O   HOH S 310     -30.921  48.271 -19.130  1.00 67.15      S
ATOM   2333  O   HOH S 315     -26.247   3.171 -24.345  1.00 70.11      S
ATOM   2334  O   HOH S 317      -7.989  11.928 -10.219  1.00 69.93      S
ATOM   2335  O   HOH S 323     -67.469   1.840 -28.352  1.00 73.34      S
ATOM   2336  O   HOH S 327      -1.519   7.683 -30.620  1.00 68.63      S
ATOM   2337  O   HOH S 330     -13.341  11.540 -27.689  1.00 66.95      S
ATOM   2338  O   HOH S 334     -31.782  46.438 -31.042  1.00 84.75      S
ATOM   2339  O   HOH S 337     -14.963  25.917 -41.978  1.00 64.34      S
ATOM   2340  O   HOH S 341     -55.975  23.392 -31.423  1.00 74.05      S
ATOM   2341  O   HOH S 347     -30.795  46.682 -44.519  1.00 85.03      S
ATOM   2342  O   HOH S 348     -40.398  44.400 -17.941  1.00 78.54      S
ATOM   2343  O   HOH S 351     -63.588  34.580 -53.000  1.00 64.83      S
ATOM   2344  O   HOH S 352     -52.859  26.925 -10.393  1.00 76.36      S
ATOM   2345  O   HOH S 360     -66.994  13.614 -58.601  1.00 80.08      S
ATOM   2346  O   HOH S 362      -6.728   7.392 -14.487  1.00 66.11      S
ATOM   2347  O   HOH S 363     -45.315  52.345 -44.599  1.00 70.94      S
ATOM   2348  O   HOH S 364     -27.723  55.681 -25.949  1.00 80.92      S
ATOM   2349  O   HOH S 365      -0.192   8.761 -14.858  1.00 65.43      S
ATOM   2350  O   HOH S 366     -33.943  48.435  -9.023  1.00 73.21      S
ATOM   2351  O   HOH S 369     -23.185  39.615 -20.816  1.00 75.14      S
ATOM   2352  O   HOH S 371     -47.369   8.811 -24.333  1.00 90.58      S
ATOM   2353  O   HOH S 378     -72.215  16.093 -37.276  1.00 79.02      S
ATOM   2354  O   HOH S 382     -62.101  39.118 -53.345  1.00 91.47      S
ATOM   2355  O   HOH S 399      -5.346   7.993 -18.480  1.00 82.98      S
ATOM   2356  O   HOH S 404     -48.898  52.763 -34.937  1.00 79.67      S
ATOM   2357  O   HOH S 408     -58.332  50.605 -57.798  1.00 73.84      S
ATOM   2358  O   HOH S 414     -16.594  33.677 -18.292  1.00 67.72      S
ATOM   2359  O   HOH S 421     -14.075   7.273 -31.446  1.00 75.74      S
ATOM   2360  O   HOH S 425     -52.456  25.670 -30.099  1.00 68.36      S
ATOM   2361  O   HOH S 429     -34.829  54.773 -17.284  1.00 73.77      S
ATOM   2362  O   HOH S 438     -25.176  29.403 -40.958  1.00 77.48      S
ATOM   2363  O   HOH S 444     -42.956  49.806 -10.829  1.00 87.00      S
ATOM   2364  O   HOH S 458     -70.377  23.808 -46.086  1.00 78.30      S
ATOM   2365  O   HOH S 476     -33.612  35.694 -43.631  1.00 66.61      S
ATOM   2366  O   HOH S 488     -43.909  38.988 -59.269  1.00 90.04      S
ATOM   2367  O   HOH S 490     -55.112  12.025 -28.305  1.00 69.08      S
ATOM   2368  O   HOH S 497     -52.018  36.590 -59.300  1.00 73.00      S
ATOM   2369  O   HOH S 498     -67.080   8.456 -47.025  1.00 77.54      S
ATOM   2370  O   HOH S 501     -33.375  45.638 -46.606  1.00 67.04      S
ATOM   2371  O   HOH S 504     -17.519  40.287 -29.824  1.00 75.48      S
ATOM   2372  O   HOH S 508     -38.469  54.630 -22.566  1.00 81.92      S
ATOM   2373  O   HOH S 548      -7.619  13.490 -18.323  1.00 80.70      S
ATOM   2374  O   HOH S 562     -52.127   9.380 -31.442  1.00 93.77      S
ATOM   2375  O   HOH S 574     -71.476  15.001 -51.047  1.00 83.08      S
ATOM   2376  O   HOH S 581     -35.133  54.715 -54.265  1.00 79.21      S
ATOM   2377  O   HOH S 598     -38.686  54.511 -51.645  1.00 83.16      S
END
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What is claimed is:

1. A crystalline recombinant interferon comprising the amino acid sequence of SEQ ID NO: 1.

2. The crystalline interferon of claim 1, wherein the space group of this crystal is $P3_121$.

3. The crystalline interferon of any one of claims 1-2, wherein the unit cell parameters of the crystal are a=b=77.92 Å, c=125.935 Å, $\alpha=\beta=90^{o}$, $\gamma=120^{o}$, with a variability of at most 5% in all cell parameters.

4. The crystalline interferon of any one of claims 1-3, wherein said crystal contains two molecules in an asymmetric unit.

5. The crystalline interferon of any one of claims 1-4, wherein the crystal further comprises covalently or non-covalently bound metal ions.

6. The crystalline interferon of any one of claims 1-5, wherein said recombinant interferon is encoded by the nucleotide sequence comprising SEQ ID NO: 2.

7. A composition comprising the crystalline interferon of any one of claims 1-6.

8. The composition of claim 7, wherein the composition is a pharmaceutical composition.

9. The composition of claim 8, further comprises a pharmaceutically acceptable carrier.

10. A computer-based method for identifying candidate compound that could interact with recombinant interferon, said method comprises the steps of:
    (a) providing a three-dimensional structure comprising atomic coordinate of recombinant interferon as shown in table 7, said atomic coordinates optionally have a variability of root mean square deviation from the conserved backbone atoms (Cα) of less than about 0.65 Å, or about 0.5 Å, or about 0.35 Å; and
    (b) selecting a candidate compound that comprises structural features capable of interacting with said three-dimensional structure or selected portion thereof, thereby identifying a candidate compound that could interact with said recombinant interferon.

11. The method of claim 10, wherein said structural features are selected from the group consisting of antigenic sites, hydrophilic properties, surface accessibility, and structural motifs.

12. The method of any one of claims 10-11, wherein the selection of candidate compound in step (b) comprises:
    (i) generating three-dimensional structures for a plurality of candidate compounds; and
    (ii) fitting each of the three-dimensional structures of step (i) against the three-dimensional structure of step (a) or selected portion thereof to find the most energetically favorable interaction, thereby identifying a candidate compound that could interact with the recombinant interferon.

13. The method of any one of claims 10-12, further comprises the steps of:
    (c) obtaining or synthesizing the candidate compound; and
    (d) contacting the candidate compound with said recombinant interferon to determine the ability of the candidate compound to interact with said recombinant interferon.

14. The method of claim 13, wherein the step of determining the ability of the candidate compound to interact with said recombinant interferon further comprises measuring an activity of said recombinant interferon when contacted with the candidate compound.

15. The method of claim 14, wherein said activity is selected from the group consisting of antivirus activity, antitumor activity, anti-proliferation activity, natural killer cell activation, and immunomodulatory activity.

16. The method of any one of claims 10-15, wherein said candidate compound is a ligand bound to said recombinant interferon or selected portion thereof.

17. The method of claim 16, wherein said ligand is selected from the group consisting of receptor, modifier, agonist, antagonist, and said selected portion comprises one or more amino acid residues of amino acid residues 25-33 and/or 45-52 of said recombinant interferon.

18. The method of claim 17, wherein said selected portion comprises amino acid residues 25-33 and/or 44-52 of said recombinant interferon.

19. A computer-based method for designing a mimetic of a recombinant interferon, comprising the steps of:
    (a) generating three-dimensional structures for a plurality of mimetics; and
    (b) fitting each of the three-dimensional structures of step (a) against a three-dimensional structure comprising atomic coordinate of recombinant interferon as shown in table 7 or selected portion thereof to find the best fitting mimetic of said recombinant interferon, said atomic coordinates optionally have a variability of root mean square deviation from the conserved backbone atoms (Cα) of less than about 0.65 Å, or about 0.5 Å, or about 0.35 Å.

20. A computer-based method of rational drug design, comprising the steps of:
    (a) providing a three-dimensional structure comprising atomic coordinate of recombinant interferon as shown in table 7, said atomic coordinates optionally have a variability of root mean square deviation from the conserved backbone atoms (Cα) of less than about 0.65 Å, or about 0.5 Å, or about 0.35 Å;
    (b) providing three-dimensional structures for a plurality of molecular fragments;
    (c) fitting each of the three-dimensional structures of step (b) against the three-dimensional structure of step (a) or selected portion thereof; and
    (d) assembling the selected molecular fragments into a molecule to form a candidate drug.

21. The method of claim 20, further comprises the following steps:
    (e) obtaining or synthesizing the candidate drug; and
    (f) contacting the candidate drug with said recombinant interferon to determine the ability of the candidate drug to interact with said recombinant interferon.

22. The method of any one of claims 10-21, wherein the selected portion of said three-dimensional structure comprises atomic coordinates of one or more amino acid residues of amino acid residues 25-33 and/or 45-52 of said recombinant interferon, said atomic coordinates optionally have a variability of root mean square deviation from the conserved backbone atoms (Cα) of less than about 0.65 Å, or about 0.5 Å, or about 0.35 Å.

23. The method of claim 22, wherein the selected portion of said three-dimensional structure comprises atomic coordinates of amino acid residues 25-33 and/or 45-52 in table 7, said atomic coordinates optionally have a variability of root mean square deviation from the conserved backbone atoms (Cα) of less than about 0.65 Å, or about 0.5 Å, or about 0.35 Å.

24. A mimetic of an interferon which comprises amino acid sequence as shown in SEQ ID NO: 4 and/or SEQ ID NO: 5.

25. The mimetic of claim 24, wherein after superimposition of the Cα-backbone of the three-dimensional structure of said interferon mimetic with the Cα-backbone of the three-dimensional structure of IFN-α2b protein using the least squares method, the location root-mean-square deviation of Cα in the 25-33 residues of said interferon mimetic and Cα in the corresponding residues of IFN-α2b protein is 3.63Å±5%.

26. The mimetic of claim 25, wherein in comparison with the corresponding residues of IFN-α2b, the deviations of α carbons of residues 25-33 of said mimetic are 3.291Å±5%, 4.779Å±5%, 5.090Å±5%, 3.588Å±5%, 2.567Å±5%, 2.437Å±5%, 3.526Å±5%, 4.820Å±5% and 2.756Å±5% respectively.

27. The mimetic of any one of claims 24-26, wherein after superimposition of the Cα-backbone of three-dimensional structure of said mimetic and the Cα-backbone of three-dimensional structure of IFN-α2b protein using the least squares method, the location root-mean-square deviation of Cα in the 44-52 residues of said mimetic and Cα in the corresponding residues of IFN-α2b protein is 2.90Å±5%.

28. The mimetic of claim 27, in comparison with the corresponding residues of IFN-α2b, the deviations of α carbons of residues 44-52 of said mimetic are 1.614Å±5%, 1.383Å±5%, 2.735Å±5%, 2.709Å±5%, 5.018Å±5%, 4.140Å±5%, 3.809Å±5%, 2.970Å±5%, and 0.881Å±5% respectively.

29. The mimetic of any one of claims 24-28, which is a functional mimetic or a structural mimetic.

30. The mimetic of any one of claims 24-29, wherein said interferon is recombinant interferon (rSIFN-co).

31. A composition comprising the mimetic of any one of claims 24-30.

32. The composition of claim 31, which is a pharmaceutical composition.

33. The composition of claim 32, further comprises a pharmaceutically acceptable carrier.

34. A method for the treatment of viral disease and/or tumor, said method comprises administering to the subject an effective amount of the crystal of any one of claims 1-6, mimetic of any one of claims 24-30 or composition of any one of claims 7-9 and 31-33.

35. Use of the crystal of any one of claims 1-6, mimetic of any one of claims 24-30 or composition of any one of claims 7-9 and 31-33 for preparation of medicament for treating viral diseases and/or tumors.

36. The method of claim 34 or use of claim 35, wherein said viral diseases include: hepatitis A, hepatitis B, hepatitis C, other types of hepatitis, viral infections caused by Epstein-Barr virus, human immunodeficiency virus (HIV), Ebola virus, severe acute respiratory syndrome (SARS) virus, influenza virus, cytomegalovirus, herpes simplex virus, or other types of herpes virus, papovavirus, pox virus, picornavirus, adenovirus, rhinovirus, human T-cell leukemia viruses type I, human T-cell leukemia viruses type II, or human T-cell leukemia virus type III.

37. The method of claim 34 or use of claim 35, wherein said tumor is cancerous.

38. The method of claim 34 or use of claim 35, wherein said tumor is solid tumor.

39. The method of claim 34 or use of claim 35, wherein said tumors include: skin cancer, basal cell carcinoma and malignant melanoma, renal cell carcinoma, liver cancer, thyroid cancer, nasopharyngeal cancer, solid tumors, prostate cancer, stomach/abdominal cancer, esophageal cancer, rectal cancer, pancreatic cancer, breast cancer, ovarian cancer, superficial bladder cancer, hemangioma, epidermoid cancer, cervical cancer, non-small cell lung cancer, small cell lung cancer, glial stromal tumors, leukemia, acute leukemia, chronic leukemia, chronic myelogenous leukemia, hairy cell leukemia, lymphadenoma, multiple myeloma, polycythemia, Kaposi's sarcoma.