

1/19

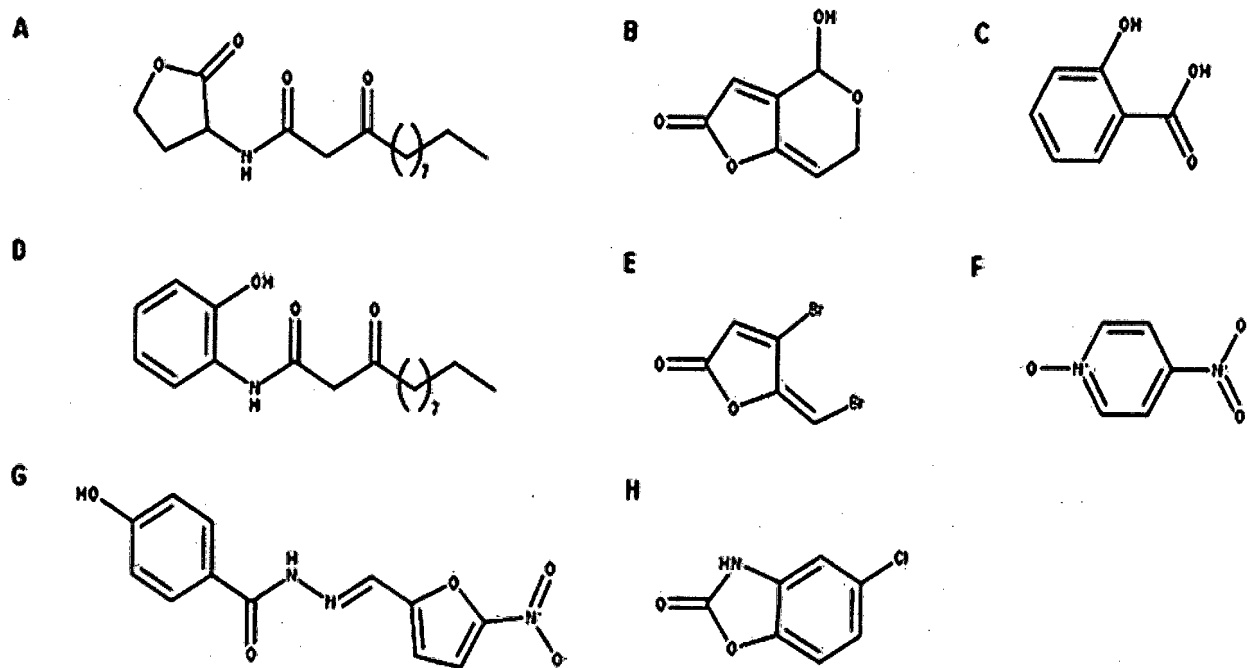
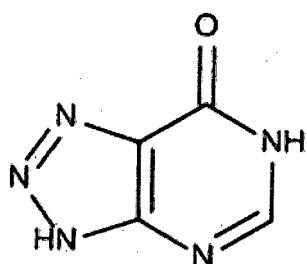


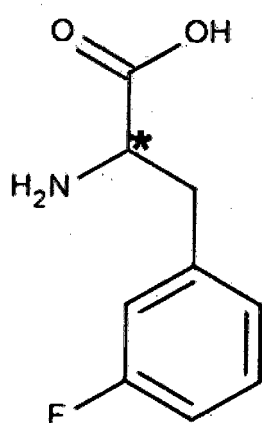
FIG. 1

2/19

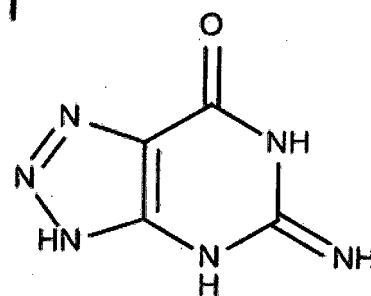
C1



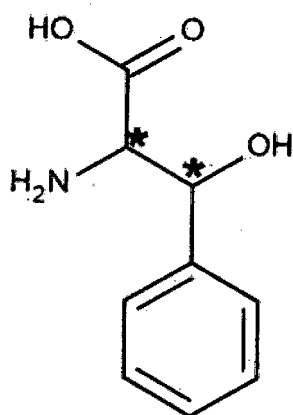
F1



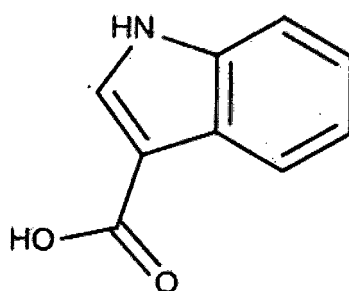
G1



H1



F2



404

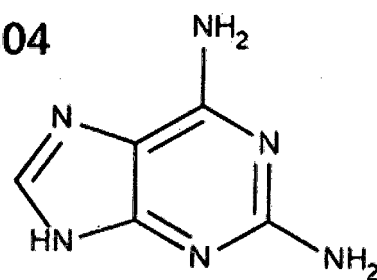


FIG. 2

3/19

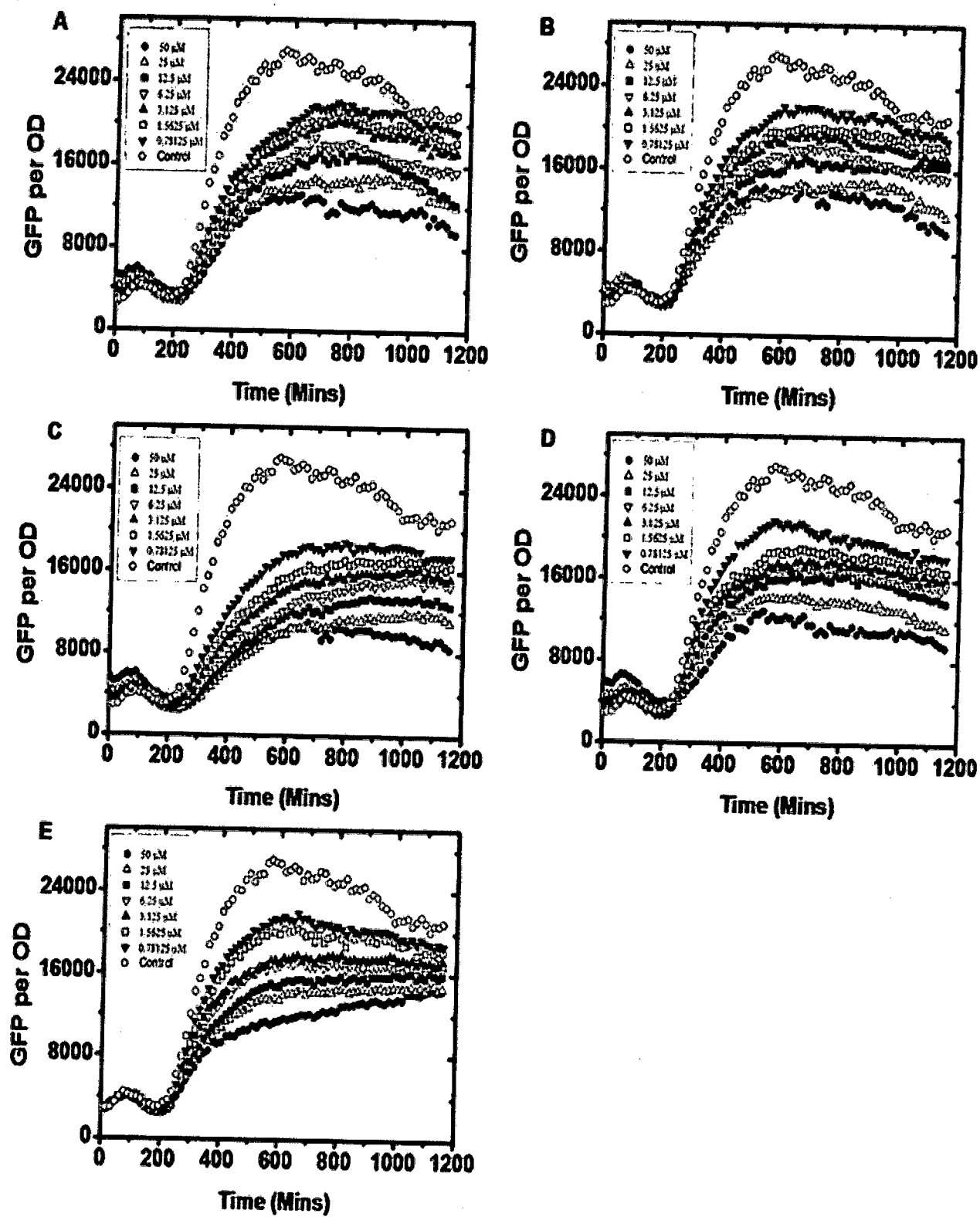


FIG. 3

4/19

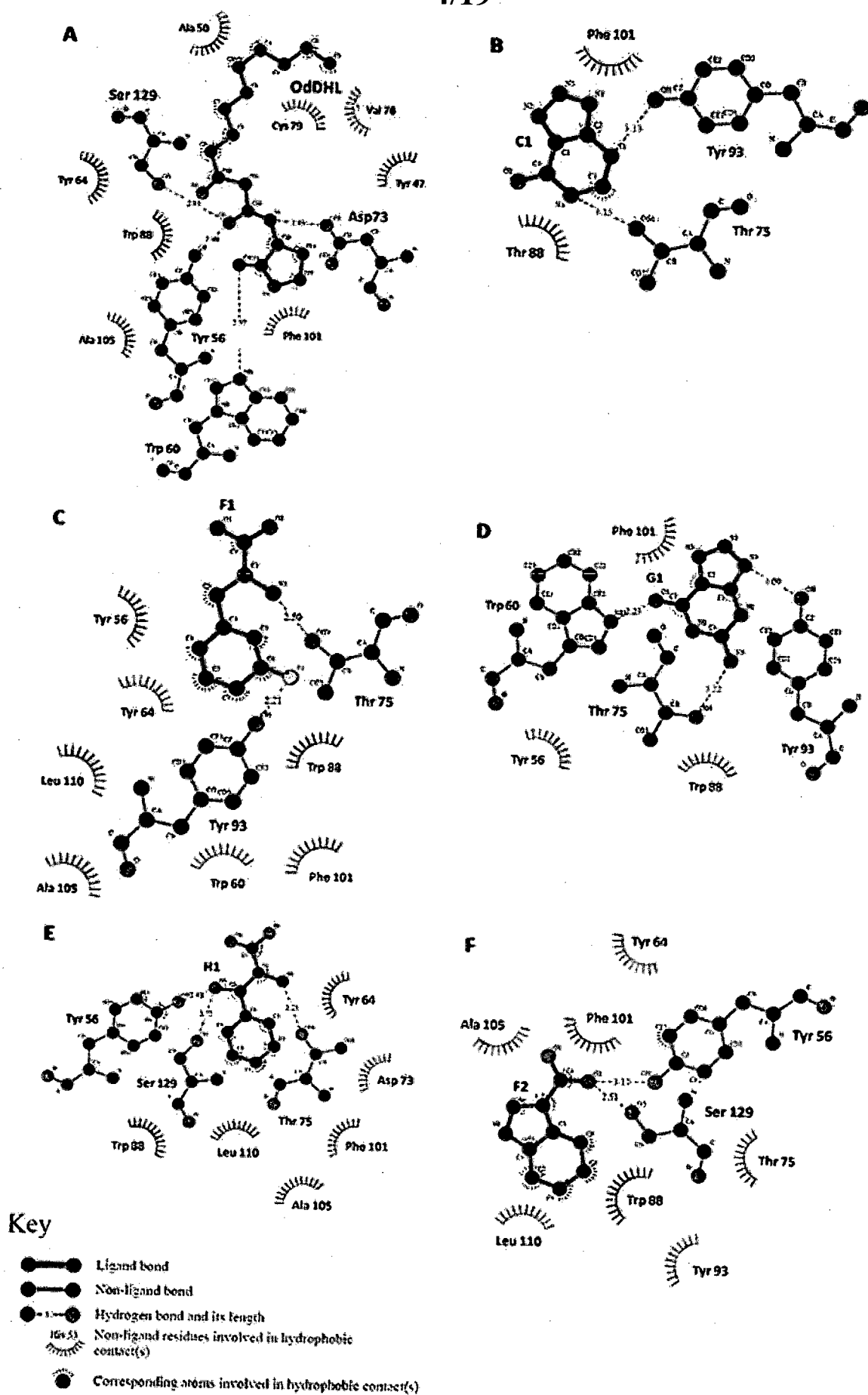


FIG. 4

5/19

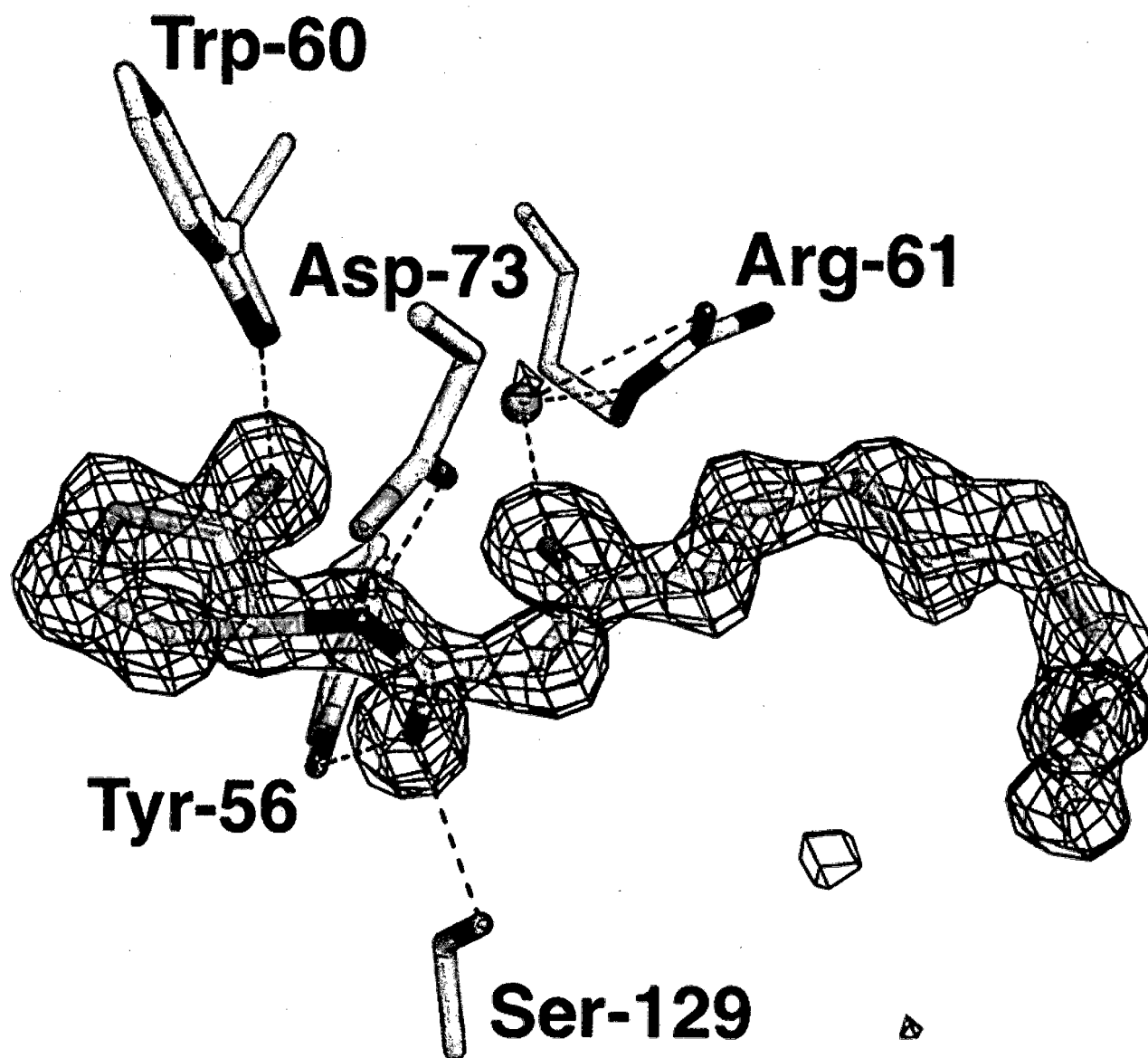


FIG. 5

6/19

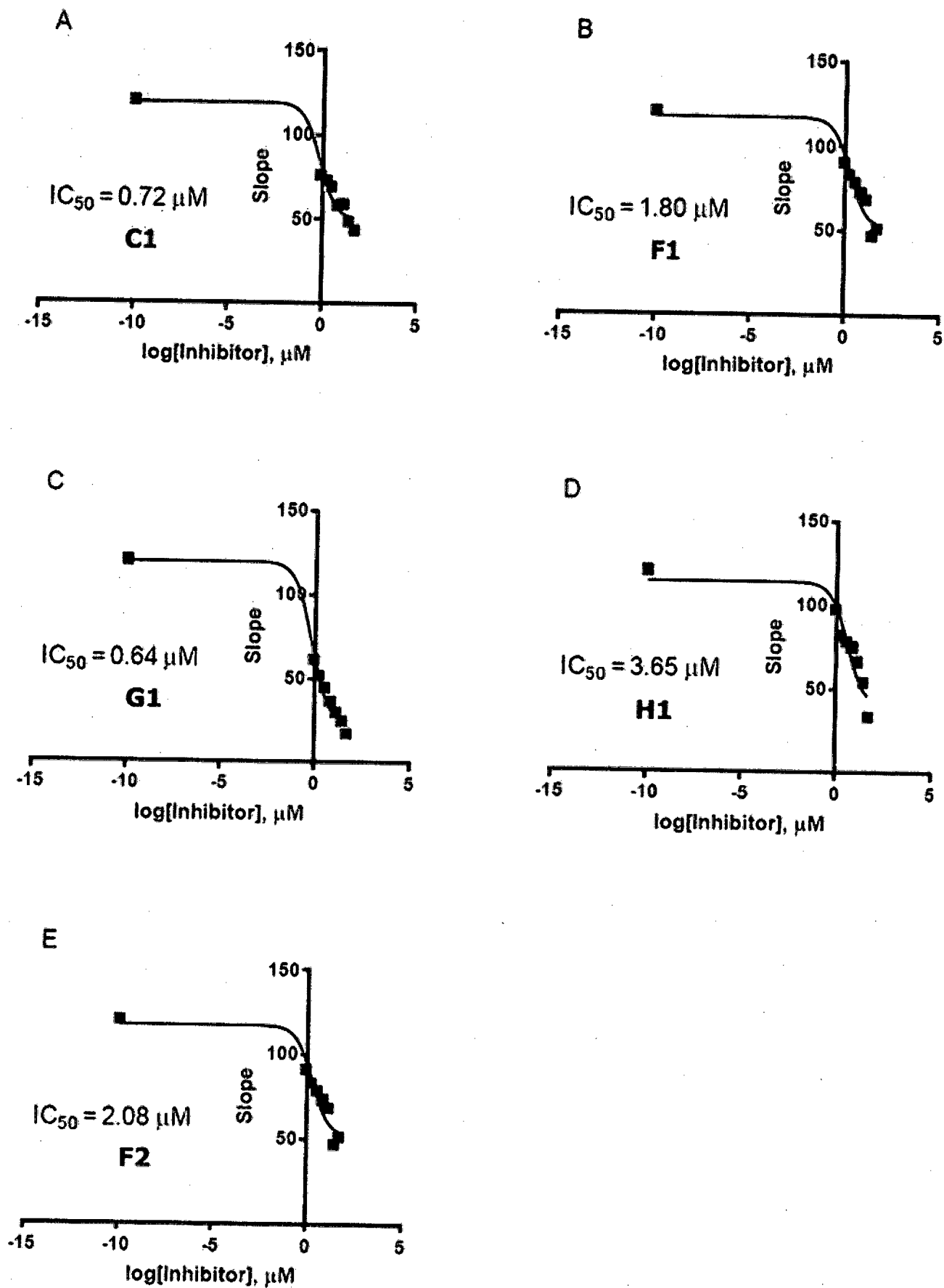


FIG. 6

7/19

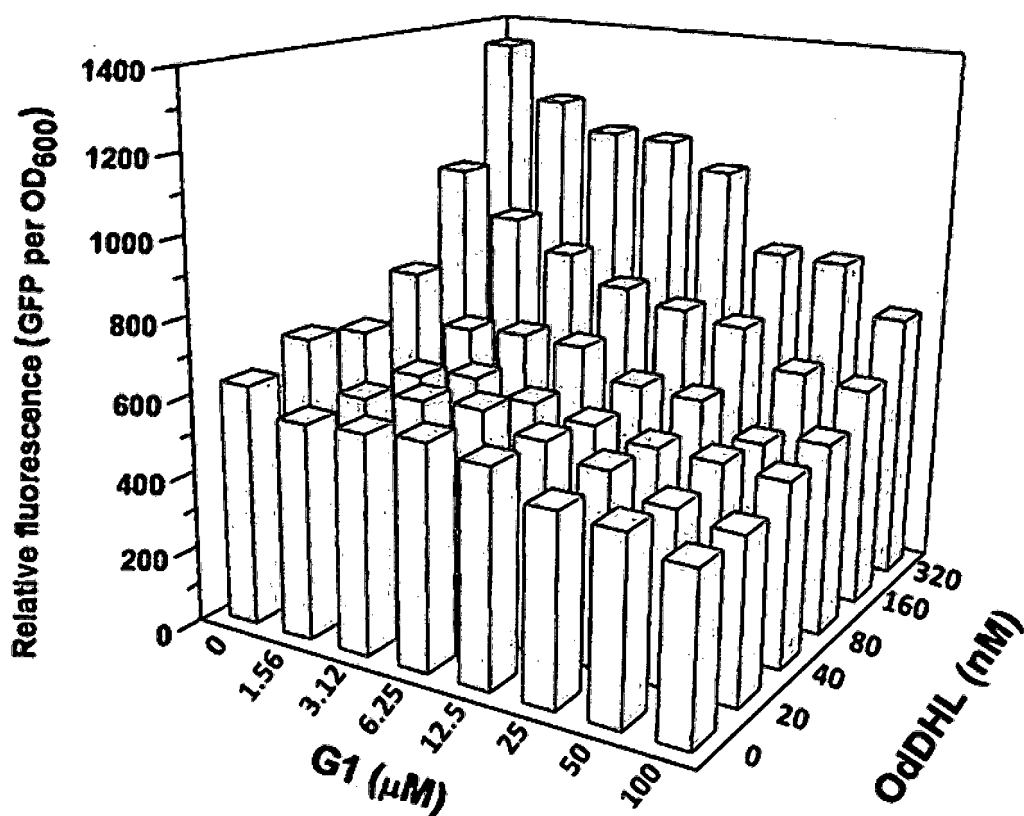


FIG. 7

8/19

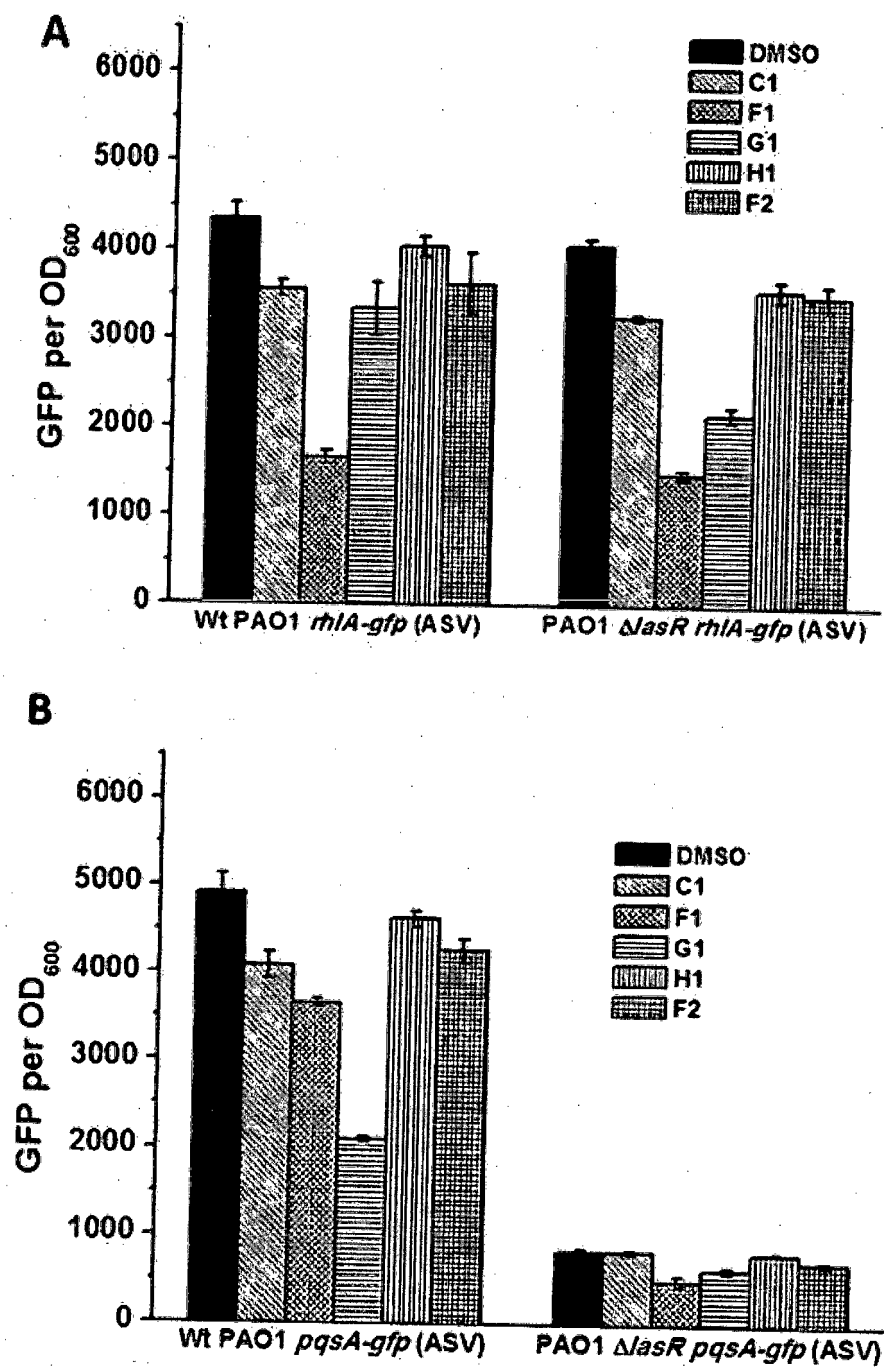


FIG. 8

9/19

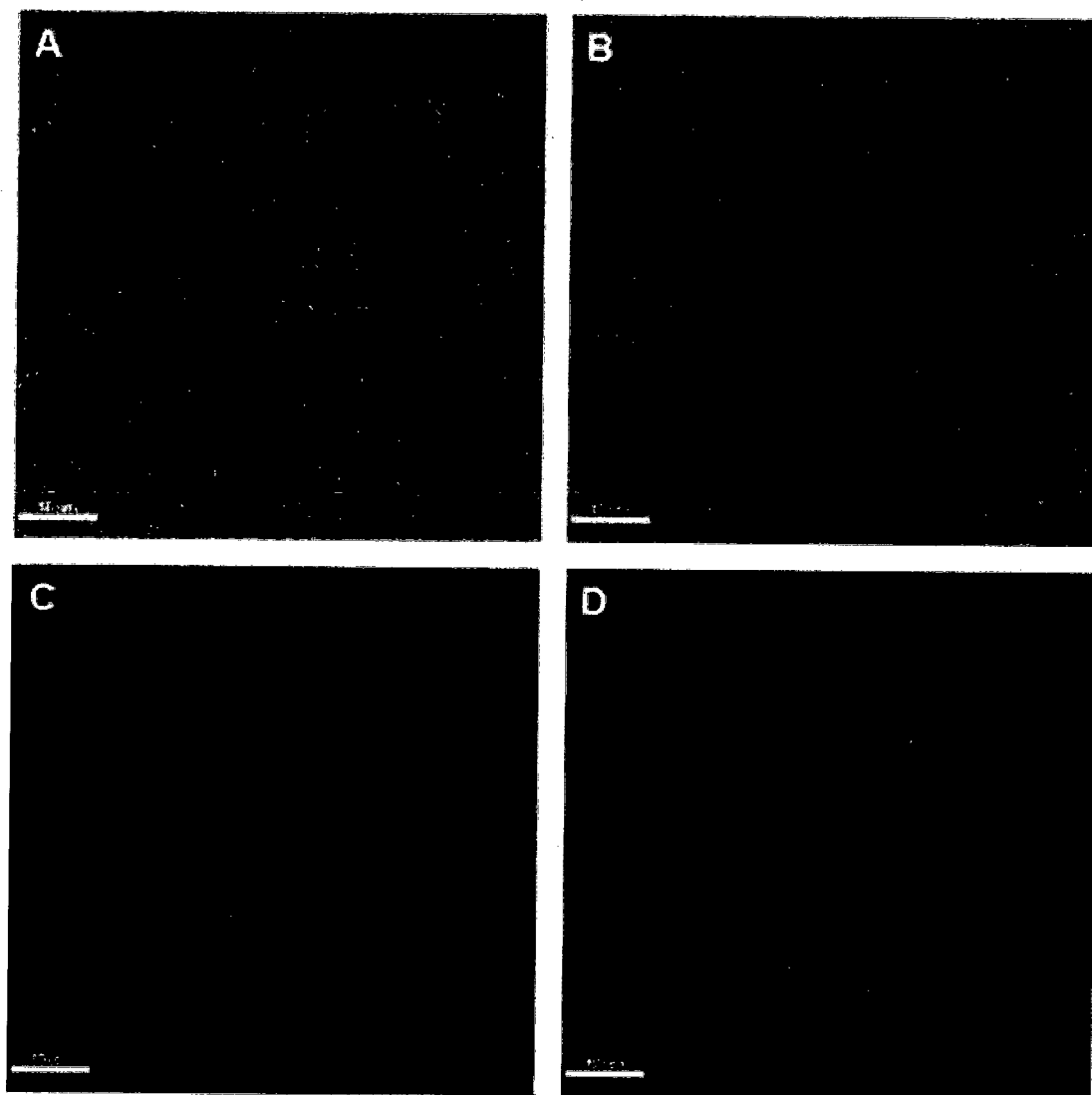


FIG. 9

10/19

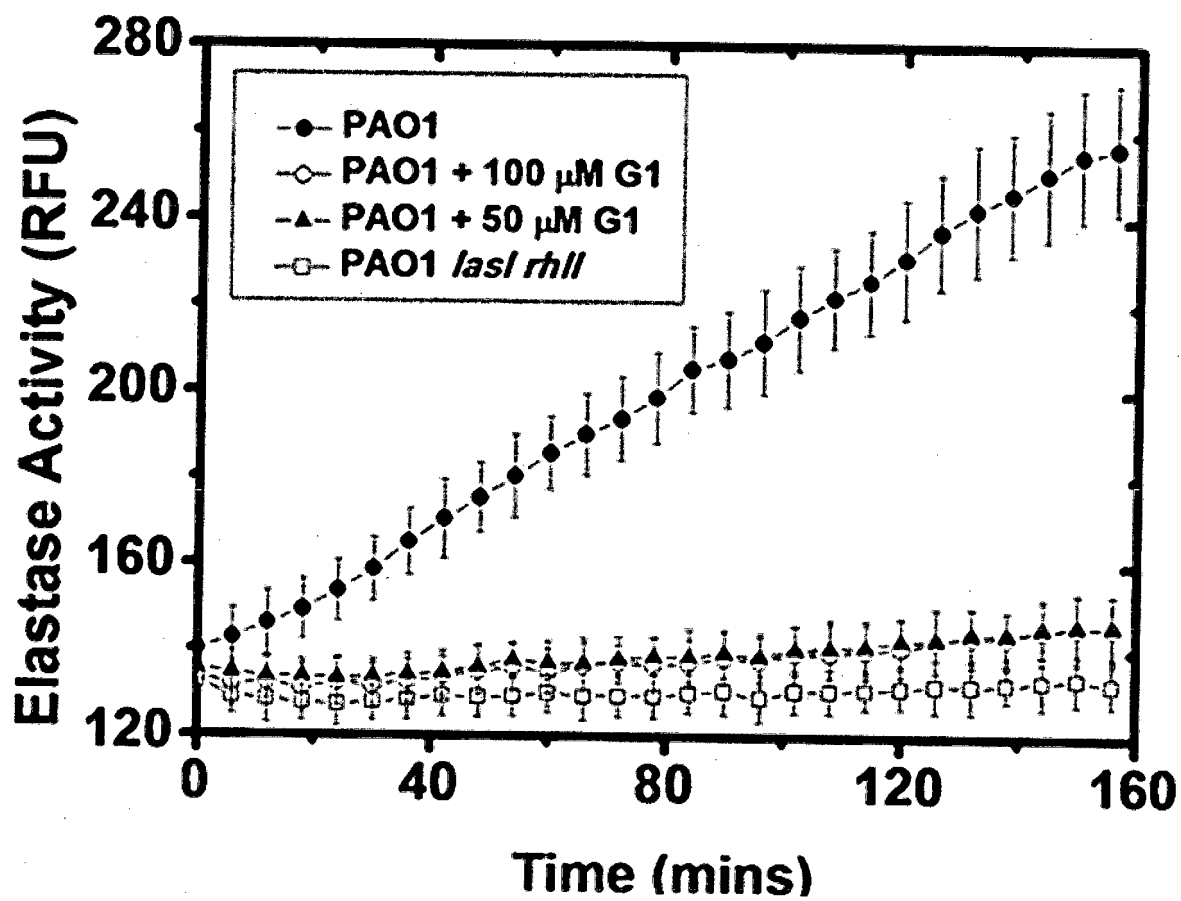


FIG. 10

11/19

Table 1. List of *P. aeruginosa* and *E. coli* strains used in the present study.

Species	Name/Genotype	Description ^a
<i>P. aeruginosa</i>	PAO1	Wild-type
	PAO1-gfp	Gfp-tagged wild-type
	PAO1/ <i>lasB</i> -gfp	Gm ^r ; PAO1 containing <i>lasB</i> -gfp(ASV) reporter fusion
	PAO1/ <i>rhlA</i> -gfp	Gm ^r ; PAO1-ATCC, <i>rhlA</i> -gfp(ASV) reporter fusion
	PAO1/ <i>pqsA</i> -gfp	Gm ^r ; PAO1-ATCC, <i>pqsA</i> -gfp(ASV) reporter fusion
	PAO1 Δ <i>lasR</i>	PAO1 <i>lasR</i> mutant
	PAO1 Δ <i>lasR</i> / <i>rhlA</i> -gfp	Gm ^r /Carb ^r ; PAO1 <i>lasR</i> mutant, <i>rhlA</i> -gfp(ASV) reporter fusion
	PAO1 Δ <i>lasR</i> / <i>pqsA</i> -gfp	Gm ^r /Carb ^r ; PAO1 <i>lasR</i> mutant, <i>rhlA</i> -gfp(ASV) reporter fusion
<i>E. coli</i>	MT102	Wild-type
	MT102/ <i>lasB</i> -gfp	MT102 containing <i>lasB</i> -gfp(ASV) reporter fusion

^aDescription of the strains' antibiotic resistance. Gm^r: gentamycin resistance. Carb^r: carbenicillin resistance.

12/19

Compound	Residues within the LasR Ligand Binding Pocket Having H-bonding interactions with Ligand
OdDHL	Tyr 56, Trp 60, Asp 73, Ser 129
C1	Thr 75, Tyr 93
F1	Thr 75, Tyr 93
G1	Trp 60, Thr 75, Tyr 93
H1	Tyr 56, Thr 75, Ser 129
F2	Tyr 56, Ser 129

FIG. 12

13/19

PA No.	Gene name	Description of Product ^a	Peptides (95%)	Coverage (95%)	115:114 ^b	p-value
PA3862	<i>dauB</i>	NAD(P)H-dependent anabolic L-arginine dehydrogenase, DauB	12	58.41	0.23	2.91E-03
PA4175	<i>piv/prpL</i>	protease IV	16	35.93	0.29	9.87E-03
PA5100	<i>hutU</i>	urocanatehydratase [<i>Pseudomonas aeruginosa</i> MPAO1/P2]	13	34.88	0.39	3.80E-04
PA3922	-	conserved hypothetical protein	10	29.23	0.42	4.90E-03
PA3919	-	conserved hypothetical protein	18	41.47	0.43	8.84E-03
PA2300	<i>chiC</i>	chitinase	16	36.85	0.44	3.65E-05
PA1372	-	hypothetical protein PA1372	12	24.47	0.45	4.52E-03
PA0572	-	hypothetical protein PA0572	12	20.26	0.46	8.03E-03
PA0792	<i>prpD</i>	propionate catabolic protein PrpD	31	51.21	0.47	2.98E-04
PA0400	<i>metBmetC</i>	probable cystathionine gamma-lyase	76	62.94	0.49	2.97E-02
PA5213	<i>gcvP1</i>	glycine cleavage system protein P1	9	15.66	0.52	2.54E-02
PA2951	<i>etfA</i>	electron transfer flavoprotein alpha-subunit	87	65.37	0.52	3.87E-02
PA0586	-	conserved hypothetical protein	9	20.89	0.53	3.21E-02
PA2399	<i>pvdD</i>	pyoverdinesynthetase D	126	45.55	0.54	2.49E-05
PA3924	-	probable medium-chain acyl-CoA ligase	10	32.32	0.54	1.24E-02
PA2290	<i>gcd</i>	glucose dehydrogenase	24	35.74	0.59	4.22E-03
PA2424	<i>pvdL</i>	pyoverdinechromophoresynthetasePvdL	368	50.25	0.60	0.00E+00
PA3148	<i>wbpI</i>	UDP-N-acetylglucosamine 2-epimerase WbpI	53	65.54	0.60	5.85E-03
PA2302	<i>ambE</i>	AmbE. Involved in L-2-amino-4-methoxy-trans-3-butenoic acid (AMB) biosynthesis	49	31.45	0.61	4.46E-07
PA2402	-	probable non-ribosomal peptide synthetase	273	41.58	0.62	2.46E-10
PA0852	-	chitin-binding protein CbpD precursor	16	36.76	0.62	1.41E-02
PA3083	<i>pepN</i>	aminopeptidase N	50	36.27	0.63	1.72E-02
-	-	putative ClpA/B protease ATP binding subunit [<i>Pseudomonas aeruginosa</i> MPAO1/P2]	30	36.05	0.63	2.90E-03
PA0588	-	conserved hypothetical protein	49	41.25	0.64	4.74E-04
PA2445	<i>gcvP2</i>	glycine cleavage system protein P2	143	51.51	0.64	9.94E-04
PA0399	-	cystathionine beta-synthase	64	68.71	0.64	4.28E-03
PA5172	-	ornithine carbamoyltransferase, catabolic	47	44.94	0.65	7.22E-03

^aDescription is obtained from the *Pseudomonas* Genome Database (Winsor et al., 2011) (<http://www.pseudomonas.org>)

^b115:114 refers to the ratio of the protein's abundance in the G1-treated sample (115) compared to the untreated control (114).

FIG. 13

14/19

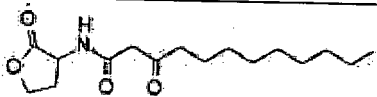
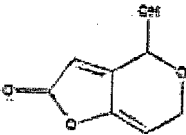
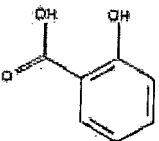
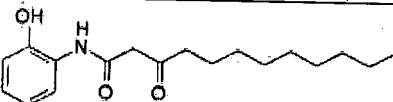
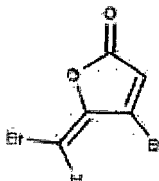
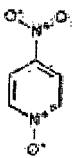
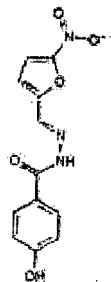
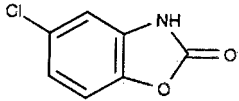
IUPAC Name	Structure	Molecular Weight	Rerank Score	Ligand Efficiency
3-Oxo-C12-HSL (OdDHL)		297.39	-81.2886	-3.87089
Patulin		154.12	-62.0131	-5.63755
Salicylic acid		137.113	-63.5007	-6.35007
3-Oxo-C12-(2-aminophenol)		305.412	-77.6409	-3.52913
Furanone C30		252.868	-62.0532	-6.89479
4-Nitropyridine-N-oxide		140.097	-63.2568	-6.32568
Nifuroxazide		275.217	-20.4001	-1.02001
Chlorzoxazone		168.557	-72.5769	-6.5979

FIG. 14

15/19

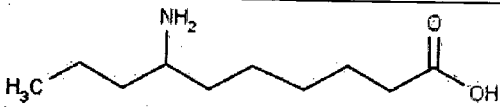
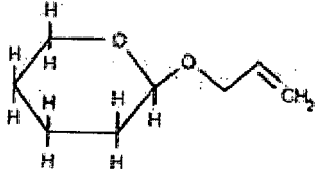
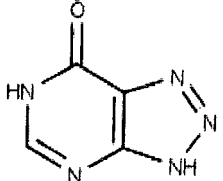
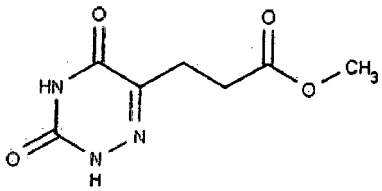
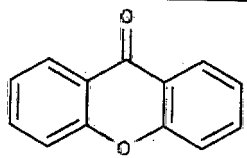
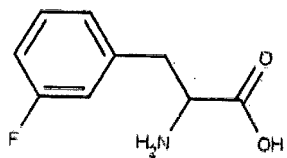
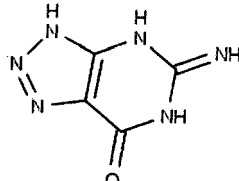
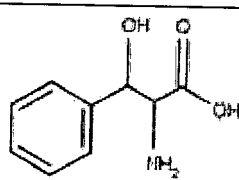
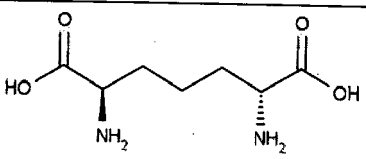
ID	IUPAC Name	Structure	Molecular Weight	Rerank Score	Ligand Efficiency
A1	7-aminodecanoic acid		186.271	- 64.26	-4.94
B1	2-prop-2-enyloxy-2H-3,4,5,6-tetrahydropyran		137.156	- 62.71	-6.27
C1	6-hydro-3H-1,2,3-triazolo[5,4-d]pyrimidin-7-one		136.092	- 64.15	-6.41
D1	methyl 3-(3,5-dioxo-2H,4H-1,2,4-triazin-6-yl)propanoate		199.164	- 69.15	-4.94
E1	xanthen-9-one		196.201	- 74.45	-4.96
F1	2-amino-3-(3-fluorophenyl)propanoic acid		182.172	- 70.69	-5.44
G1	5-imino-4,6-dihydro-3H-1,2,3-triazolo[5,4-d]pyrimidin-7-one		151.106	- 69.93	-6.36
H1	2-amino-3-hydroxy-3-phenylpropanoic acid		180.181	- 67.92	-5.22
A2	(2R,6R)-2,6-diaminoheptanedioic acid		188.181	- 68.80	-5.29

FIG. 15

16/19

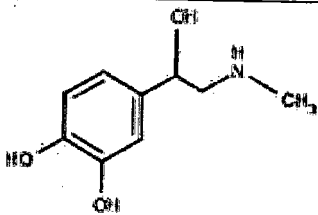
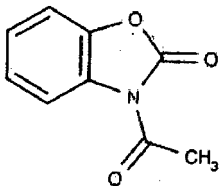
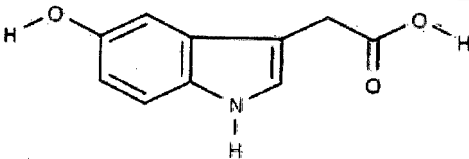
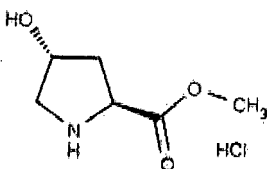
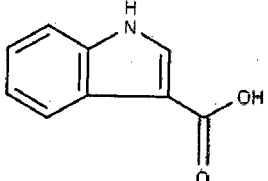
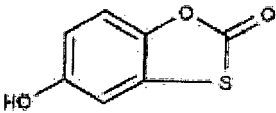
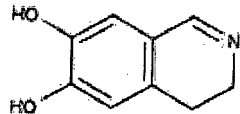
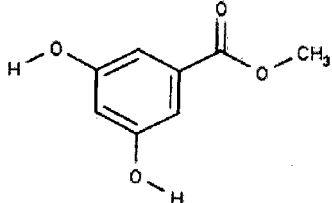
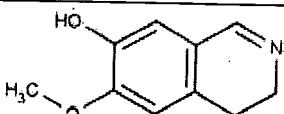
B2	4-[1-hydroxy-2-(methylamino)ethyl]benzene-1,2-diol, chloride		183.204	60.05	-4.62
C2	3-acetyl-2-oxo-3-hydrobenzoxazole		177.157	61.49	-4.73
D2	2-(5-hydroxyindol-3-yl)acetic acid		185.136	65.42	-4.67
E2	methyl (2S,4R)-4-hydroxypyrrolidine-2-carboxylate, chloride		145.156	71.23	-7.12
F2	indole-3-carboxylic acid		159.141	69.33	-5.78
G2	5-hydroxybenzo[d]1,3-oxathiolan-2-one		168.17	71.13	-6.47
H2	3,4-dihydroisoquinoline-6,7-diol		163.173	72.14	-6.01
A3	methyl 3,5-dihydroxybenzoate		162.099	67.71	-5.64
B3	6-methoxy-3,4-dihydroisoquinolin-7-ol		177.2	74.23	-5.71

FIG. 15 (continued)

17/19

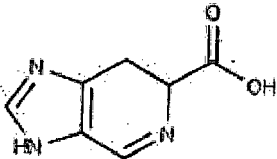
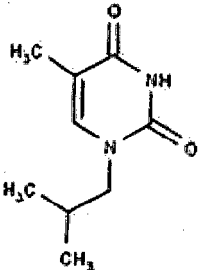
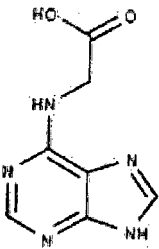
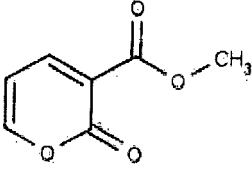
C3	6,7-dihydroimidazo[5,4-c]pyridine-6-carboxylic acid		163.133	- 75.50	-6.29
D3	5-methyl-1-(2-methylpropyl)-1,3-dihydropyrimidine-2,4-dione		182.22	- 60.08	-4.62
E3	2-(purin-6-ylamino)acetic acid		190.139	- 77.05	-5.51
F3	methyl 2-oxopyran-3-carboxylate		154.12	- 68.61	-6.24

FIG. 15 (continued)

18/19

Import Molecules	
Preparation	
Assign bonds	If missing
Assign bond orders and hybridization	If missing
Create explicit hydrogens	If missing
Assign charges (calculated by MVD)	Always
Detect flexible torsions in ligands	Always
Assign Tripos atom types	If missing
Template docking wizard	
Similarity measure	(Radius, strength, count)
Steric	1.8, 0.5, 21
Hydrogen donor	1.8, 1, 3
Hydrogen acceptor	1.8, 1, 4
Ring	1.8, 1, 5
Docking wizard	
Template docking: Docking using Ligand Template	
Scoring strength	-500.00
Energy grid resolution (Å)	0.20
Scoring function	
Score	Ligand evaluator
Steric interactions	Yes
Torsional interactions	Yes
Binding site	
Center (x,y,z)	24.07, 18.19, 77.44
Radius	9
Search algorithm	
Algorithm	MolDock Optimizer
Number of runs	10
Parameter settings	
Constrain poses to cavity	Yes
Population size	50
Max Iterations	2000
Scaling factor	0.50
Crossover rate	0.90
Offspring scheme	Scheme 1
Termination scheme	Variance-based
Pose clustering	
Multiple poses	Return one pose for each run
Tabu clustering	Yes
RMSD threshold	2.00
RMSD calculation	By atom ID (fast)
Energy penalty	100.00

FIG. 16

19/19

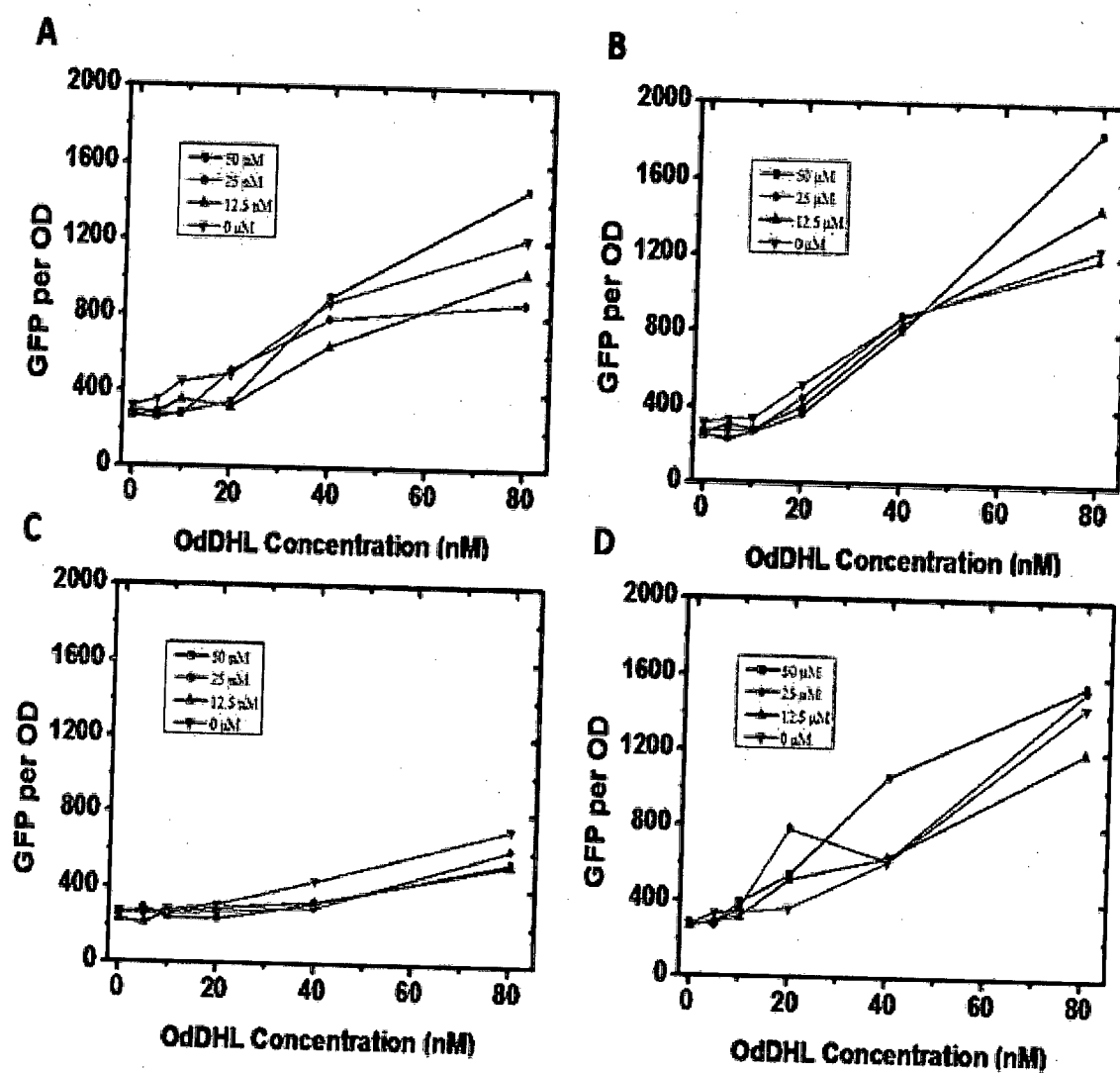


FIG. 17