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(54) Title: ENGINEERED PRIMATE CYSTINE/CYSTEINE DEGRADING ENZYMES FOR THERAPEUTIC USES

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SEQ ID NO: 3      1  MQEKDASSQGLFPHFQHFATQAIHVQDPEQWTSRAVVFPISLSTTFKQAGFGQHSSEFYSRSNGNPTKLEKAAVALLDG  60
SEQ ID NO: 4      1  MQEKDASSQGLFPHFQHFATQAIHVQDPEQWTSRAVVFPISLSTTFKQAGFGQHSSEFYSRSNGNPTKLEKAAVALLDG  60
SEQ ID NO: 5      1  MQEKDASSQGLFPHFQHFATQAIHVQDPEQWTSRAVVFPISLSTTFKQAGFGQHSSEFYSRSNGNPTKLEKAAVALLDG  60

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SEQ ID NO: 1      61  AKYCLAFASGLAATVTITLLKAGDQIICMDVYGGTNRVYFQVASEFGLKISFVDCSKIKLLEAATFETKLVNIETFT  160
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SEQ ID NO: 2      161  NPTQKVIDIEACAHIVHKGDIILVVDNTFMSPYFQRPALGADICMISATKYNMGSDVVMGLVSNVNCESLHNLEFLQ  240
SEQ ID NO: 3      161  NPTQKVIDIEACAHIVHKGDIILVVDNTFMSPYFQRPALGADICMISATKYNMGSDVVMGLVSNVNCESLHNLEFLQ  240
SEQ ID NO: 4      161  NPTQKVIDIEACAHIVHKGDIILVVDNTFMSPYFQRPALGADICMISATKYNMGSDVVMGLVSNVNCESLHNLEFLQ  240
SEQ ID NO: 5      161  NPTQKVIDIEACAHIVHKGDIILVVDNTFMSPYFQRPALGADICMISATKYNMGSDVVMGLVSNVNCESLHNLEFLQ  240

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SEQ ID NO: 1      241  NSLGAVPSFDICYLCNRGLKTLVHMEKHFENGMAYAQFLESNPVEKVIYVGLPSHFQHSILVKGQCTGCTGCTGCTGCTG  320
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SEQ ID NO: 4      241  NSLGAVPSFDICYLCNRGLKTLVHMEKHFENGMAYAQFLESNPVEKVIYVGLPSHFQHSILVKGQCTGCTGCTGCTGCTG  320
SEQ ID NO: 5      241  NSLGAVPSFDICYLCNRGLKTLVHMEKHFENGMAYAQFLESNPVEKVIYVGLPSHFQHSILVKGQCTGCTGCTGCTGCTG  320

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SEQ ID NO: 2      321  TLQHASIFLNKIKLFTLASLGGFESLASLFAIMTHASVKNDRDVLGISDTLIRLSVGLSESDLELLELDLQALKAAHFF  400
SEQ ID NO: 3      321  TLQHASIFLNKIKLFTLASLGGFESLASLFAIMTHASVKNDRDVLGISDTLIRLSVGLSESDLELLELDLQALKAAHFF  400
SEQ ID NO: 4      321  TLQHASIFLNKIKLFTLASLGGFESLASLFAIMTHASVKNDRDVLGISDTLIRLSVGLSESDLELLELDLQALKAAHFF  400
SEQ ID NO: 5      321  TLQHASIFLNKIKLFTLASLGGFESLASLFAIMTHASVKNDRDVLGISDTLIRLSVGLSESDLELLELDLQALKAAHFF  400

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SEQ ID NO: 1      401  SSSHS  405
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SEQ ID NO: 4      401  SSSHS  405
SEQ ID NO: 5      401  SSSHS  405

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FIG. 1

(57) Abstract: Methods and compositions related to the engineering of a protein with L-cyst(e)ine degrading enzyme activity are described. For example, disclosed are modified cystathionine-γ-lyases comprising one or more amino acid substitutions and capable of degrading L-cyst(e)ine. Furthermore, compositions and methods are provided for the treatment of cystinuria using the disclosed modified enzymes or nucleic acids encoding said enzymes.

[Continued on next page]

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