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(54) Title: **CONDITIONALLY ACTIVE PROTEINS WITH pH SELECTIVITY**

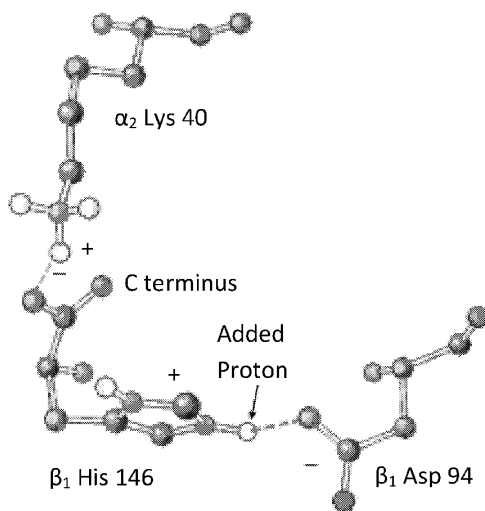


FIG. 1

(57) Abstract: A method of producing a conditionally active polypeptide from a parent polypeptide, which comprises steps of: (i) evolving the parent polypeptide by introducing mutations into the parent polypeptide to produce mutant polypeptides that have a pI the same as or lower than a pI of the parent polypeptide; (ii) subjecting the mutant polypeptides to a first assay under a normal physiological condition to measure the activity of the mutant polypeptides under the normal physiological condition and a second assay under an aberrant condition to measure the activity of the mutant polypeptides under the aberrant condition, wherein the normal physiological condition and the aberrant condition are the same condition but having different values; and (iii) selecting the conditionally active polypeptide from the mutant polypeptides which exhibits an increased activity in the second assay compared to the same activity in the first assay. Conditionally active polypeptides and uses are also provided.

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