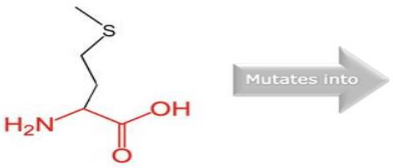
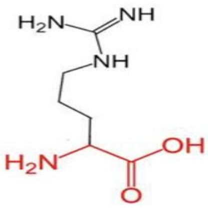
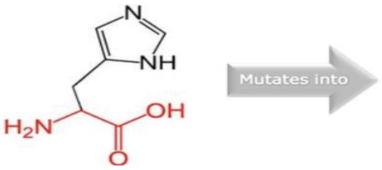
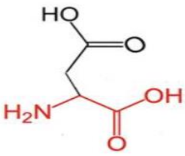
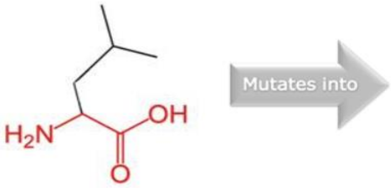
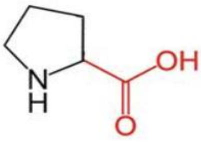
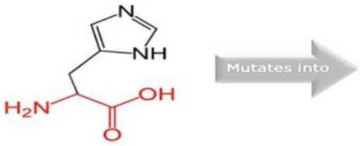
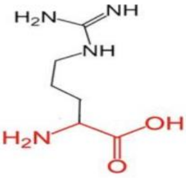
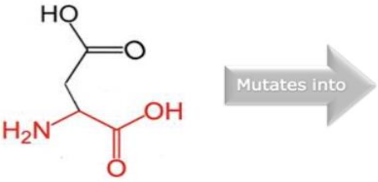
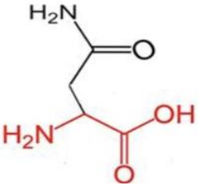
Supplementary Table S1: Property Analysis by Project HOPE.

Variants	Wild type	Mutant type	Biological Effect
M35R	 Neutral	 Positive	The mutant residue introduces a charge in a buried region, potentially leading to protein folding issues and loss of interactions. The wild-type residue is more hydrophobic.
H61D	 Neutral	 Negative	The mutant residue is smaller, which may result in the loss of interactions with other molecules, possibly affecting external interactions.
L70P			The mutation creates a void in the protein core, potentially destabilizing the structure.
H93R	 Neutral	 Positive	The mutant residue is larger, disrupting interactions with other molecules or different regions of the protein.
D107N	 gative	 Ne Neutral	The mutation leads to the loss of charge in the wild-type residue, which may disrupt interactions with other molecules.

L112P				Proline disrupts an α-helix; this mutation may destabilize the helix, severely affecting protein structure.
C124R		Neutral	Positive	The mutation disrupts hydrophobic interactions in the protein core, potentially leading to folding issues. The wild-type residue is more hydrophobic.
G129E		Neutral	Negative	The mutant residue is larger and introduces a charge in a buried region, which may cause protein folding problems. The wild-type residue is more hydrophobic.
R130G		Positive	Neutral	Glycine's flexibility can compromise the necessary rigidity of the protein at this position. The wild-type residue is more hydrophobic.
R130Q		Positive	Neutral	The mutation eliminates the charge of the buried wild-type residue, creating a void in the protein core.
G132V				The glycine mutation forces the local backbone into an incorrect conformation, disrupting the local structure. The wild-type residue is more

				hydrophobic.
I135T				The mutant residue is smaller, potentially leading to a loss of hydrophobic interactions in the protein core. The wild-type residue is more hydrophobic.
R173C		Positive	Neutral	The mutant residue is smaller, which may result in the loss of interactions with other molecules, possibly affecting external interactions. The wild-type residue is more hydrophobic.
R173H		Positive	Neutral	The mutation results in the loss of the wild-type residue's charge, affecting interactions with other molecules or residues.
D252G		Negative	Neutral	Glycine's flexibility can disrupt the required rigidity of the protein at this position. The wild-type residue is more hydrophobic.

Supplementary Table S2: Predicted secondary structure of each amino acid residue in mutants and native.

Wild Type and Variants	No. of Helices	No. of Strands	No. of Coil
PTEN (WT)	9	16	25
M35R	10	15	25
H61D	9	16	25
L70P	9	15	24
H93R	9	17	26
C124R	9	18	27
G129E	9	17	26
R130G	10	17	27
R130Q	10	15	24
G132V	10	16	26
R173C	9	17	26
R173H	9	16	25
D252G	9	16	25