

Supplementary Table 3. Evolutionary conservation of the CS histidine mutated in A/J mice. NCBI BLAST results showing the alignment of 40 amino acids from the CS sequences of diverse species. All mammals and most other species examined retain the histidine (H, highlighted in yellow) that is mutated to asparagine (N, highlighted in blue) in A/J mice. The few exceptions are highlighted in gray. The high degree of evolutionary constraint on this amino acid indicates that the H55N mutation is likely to impact protein function.

species	Genbank	residues	amino acid sequence
A/J mice			VLSNLIIPKEQARIKTFKQON ^N GKTVVGQITVDMMYGGMRGM
all other mice	NP_080720	36-75	VLSNLIIPKEQARIKTFKQOH ^H GKTVVGQITVDMMYGGMRGM
rat	NP_570111	36-75	ILSNLIIPKEQARVKTFRQOH ^H GKTVVGQITVDMMYGGMRGM
dog	XP_531634	36-75	ILADLIIPKEQARIKTFRQOH ^H GKTVVGQITVDMMYGGMRGM
human	NP_004068	36-75	ILADLIIPKEQARIKTFRQOH ^H GKTVVGQITVDMMYGGMRGM
pig	NP_999441	36-75	ILADLIIPKEQARIKTFRQOH ^H GNTVVGQITVDMMYGGMRGM
horse	NP_001182444	36-75	ILADLIIPKEQARIKTFRQOH ^H GNTVVGQITVDMMYGGMRGM
cow	NP_001038186	36-75	ILADLIIPKEQTRVKAFRQOH ^H GKTVVGQITVDMMYGGMRGM
<i>Danio rerio</i>	NP_955892	38-77	VLSDLVPKEQSRIKNFKQOY ^Y GKTSIGQITVDMVYGGMRGV
<i>Xenopus laevis</i>	NP_001080194	38-77	VLSDLIPKEQTRIKNFKQOH ^H GKTVIGQVTVDMVYGGMRGM
<i>X. tropicalis</i>	NP_001017313	38-77	VLSDLIPKEQTRIKNFRQOY ^Y GKNVIGQITVDMMYGGMRGM
<i>Drosophila</i> - all species	NP_572319	37-76	VLAAKVPQEQERVKNFRKQH ^H GATKMGETTIDMMYGGMRGI
<i>Anopheles</i>	XP_320478	39-78	VLTEKIPKEQERVKNFRKQH ^H GNTKVGEVTVDMMYGGMRGI
<i>Aedes aegypti</i>	XP_001656210	38-77	VLSEKIPKEQERVKNFRKQF ^F GATKVGEVTVDMMYGGMRGI
<i>C. elegans</i>	NP_499264	38-77	VLSKKIPAHNAKVKSFRTEH ^H GSTVVQNVNIDMIYGGMRSM
<i>Arabidopsis</i>	NP_566016	44-82	LQELIPEQQDRLKCLKSEH ^H GKVQLGNITVDMVIGGMRGM
<i>Zea mays</i>	NP_001149070	28-66	LQELIPEQQDRLKCLKSEH ^H GKTQLGNITVDMVLGGMRGM
<i>Oryza sativa</i>	NP_001068031	44-82	LQELIPEQQDRLKCLKSEH ^H GKVQLGNITVDMVLGGMRGM
<i>Neurospora</i>	XP_956898	42-80	FAELLPENIEKIKALRKEH ^H GSKVVDKVTLDQVYGGARGI
<i>Hydra</i>	XP_002163668	40-78	LQEIIPKPKKQVADFRKEH ^H ANTKIGEVTVGMVYGGMRSI