

Supplement 6: Conservation of the p.F220S variant

The actin-binding domain (or calponin-homology domains) of SYNE1 is highly conserved, even in non-metazoan species (paralogues in ichthyospora, fungi and slime mold, E-values in the range of 5×10^{-40} to 10^{-50}) while the spectrin domains of SYNE1 provide no significant alignment with paralogues of the same non-metazoan species (E-values above 10). The p.F220S (chr6:152826476A>G; c.659T>C) mutation affects one of the 6 invariant amino-acid positions of the second calponin-homology domain in nesprin, spectrin and alpha-actinin homologues (see figure below). It was observed in *trans* with a non-sense mutation in family #20.

SYNE1-p.F220S¶

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SYNE1.....Homo.sapiens...AKKALLKWQYTAGKQ--TGIEVKDFGKSWRSGVAFHSVIHAIRPELVLDLETVKGRSNREN¶
SYNE1.....Strongylo.pur..AKEALMNWAQRNVKDY--PGVQIKDFGRSWRDGLAFNAIIHKNRPDLYNESLKPSEHRAN¶
SYNE1.....Apis.mellifera..ARKTLLQWVTNALPKD---IKVRDFGESWRDGNAF LAIIDAIKANLVNIAAMREATNRTR¶
SYNE1.....Drosophila.m...ARKTLLNWVTNALPKD--SGVEVKDFGASWRDGVAF LALIDAIIKANLVNLAELKKTNSNRQR¶
SYNE1.....Nematostella.v..TRKFMLEWAKKATSKASGSNEAIKDFSTSWRTGQAF LQIIHSFRPDLVNIATIAERDNITN¶
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Spectrin.beta.4.Homo.sapiens...AKDALLLWCQMKTAGY--PEVNIQNFETT SWRDGLAFNALIHRHRPDLVDFSKLTKSNANYN¶
Spectrin.beta.2.Strongylo.pur..AKDALLLWCQMKTAGY--ANVDIRNFETT SWRDGLAFNALVHKHRPDLIDYNKLTQVQPVQN¶
Spectrin.beta..Apis.mellifera..AKDALLLWCQKRTNGY--PGVNIQDFTGSWRSGLCFNALIHAHRPDLVNWSELQQNKIDN¶
Spectrin.beta..Drosophila.m...AKDALLLWCQMKTAGY--HNVNVRNFETT SWRDGLAFNAIIHKHRPDLVQFEKLSKTNAIHN¶
Sepctrin.beta..Nematostella.v..AKEALLLWCQRMTRGY--PGVDIQNFSTSWRNGLAFNALLHKHRPDLIDYATLRPSQHEAN¶
Spectrin.beta..Capsaspora.ow..AKEALLLWCQKRTAGY--PGVNVQDFSKSWSNGLAFNALIHKHRPDLIDFNALSSGDPVAN¶
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Alpha-actinin...Homo.sapiens...AKEGLLLWCQKRTAPY--KNVNIQNFHISWKDGLCF CALIHRHRPELIDYGKLRKDDPLTN¶
Alpha-actinin...Strongylo.pur..AKEGLLLWCQKRTAPY--RNVNIQNFHNSWKDGLCF CALIHRHRPDLIDYSKLKKDDPATN¶
Alpha-actinin...Apis.florea...AKEGLLLWCQKRTAPY--KNVNVQNFHLSFKDGLAF CALIHRHRPDLIDYNKLSKDNPLEN¶
Alpha-actinin...Droso.melan...AKEGLLLWCQKRTAPY--KNVNVQNFHLSFKDGLAF CALIHRHRPDLIDYAKLSKDNPLEN¶
Alpha-actinin...Nematostella...AKDGLLLWCQKRTAPY--KNVSVKNFETT SFKDGLAF CALIHRHRPDLIDYDSLKEDPLYN¶
Alpha-actinin...Schizos.pombe..AKEGLLLWCQKRTANY--HPEVDVQDFTRSWTNGLAF CALIHQHRPDLIDYNKLDKKNHRAN¶
Alpha-actinin...Neurosp.crassa..AKEGLLLWCQKRTACY--DEVVDVDFSGSWNDGLAF CALLDIHRPDLIDYDALDKSDHRGN¶
Alpha-actinin...Dictyo.disc...AKEALLLWCQKRTEGY--DRVKVGNEHT SFQDGLAF CALIHKHRPDLINFDLSLNKDDKAGN¶
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