

**Supplementary Table 6. Overview of the interactions at the interface between AXIN1 and APC for the mutated amino acids and their predicted effects.**

Amino acid change in AXIN1	Number in structure (37 aa register shift)	Located at interface	Original interaction of side chain	Predicted effect of amino acid change	Expected effect on AXIN stability and complex formation
S88P	S125	No	Surface exposed polar serine in loop	Proline may be properly accommodated in loop	none
H90Y	H127	No	Surface exposed polar histidine in $\alpha$ -helix	Polar tyrosine side chain can be easily accommodated,	none
S91F	S128	No	Surface exposed polar serine in $\alpha$ -helix	Polar serine gets replaced by non-polar phenylalanine, space enough	Maybe little lower solubility of AXIN due to hydrophobic side chain at surface. No direct effect on complex
D94N	D131	No, very close, but no interaction	Surface exposed aspartate on helix, but makes no interactions with any other residue within AXIN or with APC	Conservative mutation to asparagine, same shape, still polar	none
G98R G98E	G135	No, not the glycine, but residues on the other side of the helix are at the interface	Densely packed hydrophobic core with Trp122 and Leu129	Serious steric clashes with Trp122 and Leu129, will not fit, both for Arg and Glu mutations	Yes, local restructuring of AXIN1 to accommodate new sidechain, destabilization and reduced complex formation because close to interface
S100N	S137	no	Surface exposed polar serine on helix, no interactions with other residues	Mutation to polar residue at surface	None
L101P	L138	No, not the leucine, but residues on the other side of the helix are at the interface	Partially exposed leucine side chain makes favorable vdWaals contacts with Trp122, Tyr247 and Phe238.	Mutation to proline will locally distort the geometry of the $\alpha$ -helix	Yes, local structural changes will destabilize AXIN1
R103M	R140	No, but right next to it	Surface-exposed bidentate salt-bridge with Asp153	Loss of salt-bridge	Possible slight destabilization of AXIN1, no direct effect on complex
T104N	T141	No	Surface exposed threonine on helix, no interactions	None, asparagine still polar and can be accommodated on surface	None
L106R	L143	No	Completely buried in hydrophobic core of AXIN1	Arg will not fit (different shape and size) and positive charge is energetically unfavorable at this location	Large destabilization incorrect folding of AXIN1 protein, interface will probably not form, so large effect on complex formation