

**Table 2. Structural analysis of selected IL-6R mutational data**

	<b>Loop</b>	<b>IL-6 Binding</b>	<b>Signaling</b>	<b>Comment</b>	<b>R</b>
<b><u>Cluster 1</u></b>	<b><u>IL-6 / IL-6R binding interface</u></b>				
P162	L3	<10%	N.T.	PE-LQ double mutant. Glu may interact with IL-6, Pro unlikely to	Y
E163	L3				
S228	L5	100%	<25%	A range of mutants. Possible minor IL-6 cluster 1 residue	K
F229	L5	<5%	0%	Major IL-6 binding site residue	K
Y230	L5	<5%	0%	A range of mutants. IL-6 binding site residue	K
R231	L5	0%	N.T.	RL-SI double mutant. R231 is likely to be an IL-6 binding site residue.	Y
L232	L5			L232 is a buried hydrophobic residue	
E278	L7	0%	N.T.	EF-AI double mutant. IL-6 binding site residues	Y
F279	L7				
<b><u>Cluster 2</u></b>	<b><u>IL-6R dimer interface</u></b>				
F134	L2	>100%	70%	F-L mutation, one of two Phe's in IL-6R dimer interface	Y
S167	L3	50-100%	5-25%	A range of mutants. Buried in loop & forms H bonds.	K
F168	L3	100-130%	50%-110%	A range of mutants. Central aromatic residue in IL-6R dimer interface. F-Y mutant signals at 50%	K
Y169		30-70%	0-15%	A range of mutants – buried /structurally important residue	K
<b><u>Cluster 3</u></b>	<b><u>D3 signaling cluster</u></b>				
N211		75%	N.T	N-D mutant, <10 % (binding to gp130)	S
W214		70%	>150%	W-Q mutant – solvent exposed.	Y
V259		40%	140%	Exposed V-N mutant.	Y
I260		0%	N.T.	I-D mutation. Buried hydrophobic residue	Y
H261		115%	10%	H-I mutation.	Y
D262		30%	<10%	D-G mutant. H-bonds to stabilise binding loop and maybe interacts with gp130 to form part of cluster 3	Y

N.T = not tested; R = Reference

K=(30), Y=(17) &amp; S=(31)