

Non-ET residues are not as functionally important

Bottom 20% of trace residues

- Only **51/114 (45%)** mutations affect function compared to **88%** of top 20% ET residues.
- χ^2 test significance of difference: P-value of **0.0005** or better

Effect	Top 20%	Bot. 20%
No effect	0	14
CA/ Expression	16	1
G-Coupling	7	2
Ligand Binding	14	19
No data	2	3

ET residue mutations affect function in multiple receptors

Positions with effective mutations in 3 or more receptors

Effect Type	Top 20%	Bottom 20%
Ligand Binding	13/14 (98%)	6/19 (32%)
CA/Expression	9/16 (56%)	1/1 (100%)
G-Coupling	5/7 (71%)	0/2 (0%)
Total	27/37 (73%)	7/36 (19%)

Average # mutations per ET residue position

	Top 20%	Bottom 20%	Ratio
Ligand Binding	6.5	2.4	2.7
CA/Expression	5.3	1	5.3
G-Coupling	5	1.5	3.3
No effect	0	1.7	0