

**Smith MF, Vearing C, Lackmann M, TREUTLEIN HR, Himanen J, Chen K, Saul A, Nikolov D, W. Boyd A.**

**Dissecting the EphA3/Ephrin-A5 Interactions Using a Novel Functional Mutagenesis Screen.**

<http://www.jbc.org/cgi/content/full/279/10/9522> (Full article)

**J. Biol. Chem., 279, 9522 – 9531, Mar 2004.**

The EphA3 receptor tyrosine kinase preferentially binds ephrin-A5, a member of the corresponding subfamily of membrane-associated ligands. Their interaction regulates critical cell communication functions in normal development and may play a role in neoplasia. Here we describe a random mutagenesis approach, which we employed to study the molecular determinants of the EphA3/ephrin-A5 recognition. Selection and functional characterization of EphA3 point mutants with impaired ephrin-A5 binding from a yeast expression library defined three EphA3 surface areas that are essential for the EphA3/ephrin-A5 interaction. Two of these map to regions identified previously in the crystal structure of the homologous EphB2-ephrin-B2 complex as potential ligand/receptor interfaces. In addition, we identify a third EphA3/ephrin-A5 interface that falls outside the structurally characterized interaction domains. Functional analysis of EphA3 mutants reveals that all three Eph/ephrin contact areas are essential for the assembly of signalling-competent, oligomeric receptor-ligand complexes.

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