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Crystal Structure of an Eph Receptor-Ephrin Complex

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The Eph family of receptor tyrosine kinases and their ephrin ligands play important roles in regulating cell-cell interactions by initiating a unique bidirectional signal transduction cascade whereby information is communicated into both the Eph-expressing and ephrin-expressing cells. Initially described as important regulators of axon pathfinding and neuronal cell migration, Ephs and ephrins are now known to have roles in a diverse array of other cell-cell interactions, including those of vascular endothelial cells and specialized epithelia. We have determined the crystal structure of the complex between EphB2 and ephrin-B2 at 2.7 Å resolution. Each Eph receptor binds an ephrin ligand via an expansive dimerization interface dominated by the insertion of an extended ephrin loop into a channel at the surface of the receptor. Two Eph/Ephrin dimers are then joined to form a tetramer in which each ligand interacts with two receptors and each receptor with two ligands. The Eph and ephrin molecules become precisely positioned and oriented in these complexes, promoting higher-order clustering and the initiation of bidirectional signaling.