

Proteomic analysis of reciprocal cell signaling

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Signaling proteins are typically constructed in a modular fashion, from domains that mediate either molecular interactions or catalytic events, and corresponding interaction or substrate motifs. The joining of domains in new combinations can provide novel functions in evolution, both by creating new intermolecular connections, and by forming new and varied modes of allosteric regulation. This notion will be discussed in the context of cytoplasmic tyrosine kinases such as Fes and Abl.

Intercellular signaling is typically investigated experimentally in the context of a signal, such as a growth factor, impinging on a receptor on a target cell. In vivo, however, neighboring cells often signal back-and-forth in a reciprocal fashion. We have used a combination of proteomic and functional screens to investigate the means by which cells exchange and respond to such two-way signals, using phosphotyrosine-based intracellular networks.