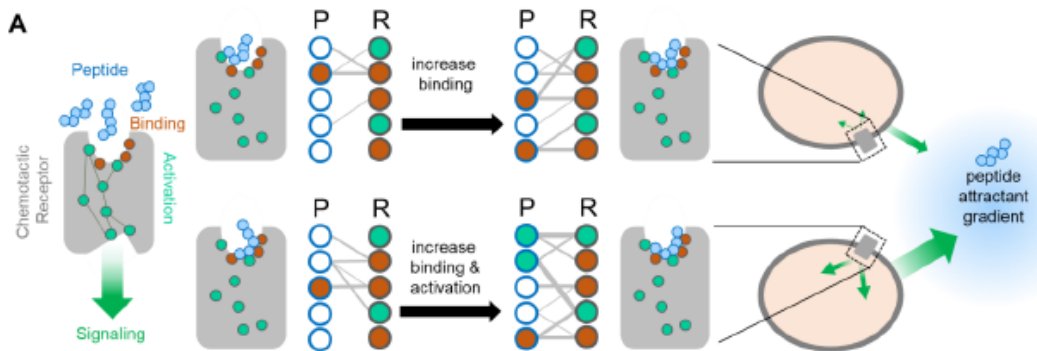


Method for engineering peptide-receptor signaling complexes for enhanced chemotaxis



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Schematic of targeting binding and activation residues for design of chemotactic receptors with enhanced responses towards peptide attractants. The peptide ligand (blue) makes specific contacts with receptor pocket residues that are classified as drivers of binding (orange) or activation (green). Through design, receptor:peptide connectivity can be rewired to promote binding (top), activation, or both (bottom) to ultimately reprogram the cell migratory response.

Description

Protein-peptide interactions play an important role in major cellular processes and are associated with several human diseases. The knowledge of the molecular details of these interactions helps to understand these processes and design drugs regulating disease-associated dysfunctions. Here, we propose a computer-implemented protein design approach for engineering signaling receptors binding flexible peptides that have the ability to trigger potent cell chemotaxis when expressed in human immune cells.

Advantages

Our method allows to engineer very sensitive and potent receptor biosensors that sense either native or designed chemokines.

This method is applicable to any peptide-receptor complexes.

Applications

- Drug discovery
- Engineering of GPCRs
- Synthetic cell biology
- Cell based therapies