Elucidation of Structural Models of Formyl Peptide Receptors, FPR & FPR2, and Identification of Features, Responsible for their Differential Ligand-Binding Affinities

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Formyl peptide receptors are glycoproteins and belong to a broad category of G-Protein Coupled Receptors (GPCR) of Rhodopsin family. Invading pathogenic microorganisms and mitochondria on metabolism release fMLP and other formyl peptides. These peptides, upon binding to a neutrophil formyl peptide receptor (FPR), form a ligand-receptor-G-protein complex, which triggers several intracellular signals through G-coupled protein pathway and a series of biological actions such as chemotaxis, superoxide anion productions and enzyme secretion [1]. Although the inflammatory response inducing ligand, fMLP bind to FPR with high affinity, it interacts with a homologous chemotactic receptor, FPR2 with 400-fold less efficiency. Knowledge of structural details about formyl peptide receptors is crucial to understand the mechanism of chemoattractant receptors and design of anti-inflammatory drugs. In the present work, structural models of FPR and FPR2 have been developed with the application of homology modeling technique. An attempt has been made to identify structural features in FPR & FPR2, which are responsible for their significantly different ligand-binding affinities.

[1] Rathore R.S., *Biopolymers (Peptide Sci.)*, 2005, 1-14, *in press (early view)*.

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