Juxtamembrane domain

The juxtamembrane domain is a region of a protein that is located adjacent to the cell membrane, or the lipid bilayer that separates the inside of the cell from the extracellular environment. This region can play important roles in regulating protein function, including signaling, trafficking, and cleavage.

In the case of transmembrane receptors, like the Notch protein, the juxtamembrane domain is important for regulating the cleavage of the protein. Notch receptors undergo a series of proteolytic cleavages when they are activated by ligand binding, resulting in the release of the intracellular domain of the protein, which is responsible for activating downstream gene expression. The juxtamembrane domain of the Notch protein contains a site that is recognized by a protease called ADAM10, which initiates the first step of the cleavage process.

The juxtamembrane domain of transmembrane receptors can also interact with other proteins that are involved in the signaling pathway, including those that regulate the internalization and trafficking of the receptor. For example, the juxtamembrane domain of the epidermal growth factor receptor (EGFR) interacts with proteins that regulate its internalization and degradation, which can affect the strength and duration of signaling.

Mutations in the juxtamembrane domain of transmembrane receptors can also lead to disease. For example, mutations in the juxtamembrane domain of the MET receptor have been associated with hereditary papillary renal carcinoma, a type of kidney cancer.

Overall, the juxtamembrane domain plays a critical role in regulating the function of transmembrane receptors and other proteins that are involved in cellular signaling. Understanding the structure and function of this domain is important for understanding the mechanisms of cellular signaling and developing new therapies for disease.