The extracellular domain of a protein is the portion of the protein that is located outside of the cell membrane. In the case of the Notch receptor, the extracellular domain contains multiple epidermal growth factor (EGF)-like repeats that are involved in ligand binding.

The EGF-like repeats are structural motifs that are characterized by a conserved arrangement of six cysteine residues that form three disulfide bonds. These motifs are found in many proteins that are involved in cell signaling and extracellular matrix organization, and they are involved in protein-protein interactions, such as ligand-receptor binding.

In the case of the Notch receptor, the extracellular domain contains 29-36 EGF-like repeats, depending on the Notch receptor isoform. The EGF-like repeats are involved in binding to the Notch ligands, which are also transmembrane proteins. Binding of the ligand to the Notch receptor triggers a series of proteolytic cleavages that release the intracellular domain of the receptor, which then translocates to the nucleus and activates transcription of target genes.

The extracellular domain of the Notch receptor is a target for therapeutic interventions aimed at modulating Notch signaling. For example, antibodies that target the extracellular domain of the Notch receptor have been developed as potential cancer therapeutics.

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