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Introductory Chapter: Invitation for Peripheral Membrane Proteins

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1. Introduction

The peripheral membrane proteins transduce the outer membrane signaling into the cells. The molecules include trimetric G proteins that consist of alpha, beta, and gamma subunits; transporters; and channels. These proteins trigger the intercellular signaling by the stimulations such as ligands including proteins and chemicals. The signaling which is transduced via the peripheral membrane proteins activates several pathways including the G protein signaling, mitogen-activated protein kinase (MAPK) signaling, tumor necrosis factor (TNF) signaling, transforming growth factor (TGF) beta signaling, Wnt signaling, and Hedgehog signaling. Meanwhile, the peripheral membrane proteins, such as cadherins, transduce the signaling from the extracellular ligands into the cells. This book intends to provide the readers with a comprehensive overview of the features and signaling of membrane proteins, which includes the molecular structure and interaction. The insights in membrane proteins associated with diseases and the therapeutics and the effects of the drugs and chemicals are also in the scope of the book.

2. Peripheral membrane proteins

The peripheral membrane proteins exist in the cellular membranes, usually hydrophobic domains are embedded in the lipid membrane and the hydrophilic domains transduce the intercellular signaling. The peripheral membrane proteins include the G protein-coupled receptors (GPCRs), receptor tyrosine kinases (RTKs), channels, and the transporters. The cell-cell communications are mediated with cell adhesion molecules such as cadherins or interactions of antigen and antibody through T cell receptors (TCRs). Transmembrane signaling is mediated via molecular complexes such as dimers, multimers of the receptors, and

colocalized signaling proteins [1–3]. The transmembrane proteins can be classified into receptors, transporters, enzymes, and others [2]. Among receptors, human G-protein-coupled and seven transmembrane receptors include rhodopsin, adhesion, secretin, glutamate, V1R, frizzled, and taste2 [2]. RTKs include epidermal growth factor (EGF) receptors, fibroblast growth factor (FGF) receptors, Ephrin receptors, Ser/Thr kinase receptor family, Axl, neurotrophin receptors, insulin receptors, receptor guanylate cyclases, and platelet-derived growth factor (PDGF) receptors [2]. Furthermore, receptors of the immunoglobulin (Ig) superfamily include TCRs, killer cell Ig-like receptors, leukocyte Ig-like receptors, Fc receptor, netrin receptors, and cytokine receptors [2]. The other receptors include TNF/nerve growth factor (NGF) receptors, integrins, receptor-like protein tyrosine phosphatases, low-density lipoprotein (LDL) receptors, Toll-like receptors, plexins, contactin-associated protein, notch, interleukin (IL) 17 receptors, neurexins, selectin, syndecan, neuropilins, transferrin receptors, adiponectin and progestin, and patched receptors [2]. The transporters contain channels including ion channels and aquaporins, solute carrier superfamily, and active transporters [2]. Ion channels are further classified into chloride channels, voltage-gated-like ion channels, and ligand-gated ion channels [2]. Enzymes include oxidoreductases such as nicotinamide adenine dinucleotide (NADH)/nicotinamide adenine dinucleotide phosphate (NADPH), cytochrome c, and oxygenases; transferases such as acyltransferases transferring other groups than aminoacyl groups, glycosyltransferases, transferring phosphorus-containing groups; and hydrolases such as protein tyrosine phosphatases (non-receptors), O- and S-glycosylases, peptidases, and nucleoside diphosphatases [2]. Miscellaneous class includes ligands such as major histocompatibility complex (MHC), semaphorins, delta, neuroligin, and ephrin B and structural/adhesion proteins such as Ig superfamily, cadherin, and claudin [2].

3. Signaling mediated by peripheral membrane proteins

Membrane proteins mediate signal transduction [4]. EphrinA1 linked to the membrane by glycosylphosphatidylinositol (GPI) anchor or by a single transmembrane segment that triggers Eph signaling which is important for development and cancer via EphA2 RTK [4]. G protein transduces extracellular signaling to inside of the cells via the binding and dissociation of GPCRs [5]. The G protein signaling consists of the cascades from stimulus of the receptor leading to the dissociation of the G protein from the receptor to transduce the downstream pathways to activate various cellular responses. The signaling pathways activated by G protein include MAPK signaling and small G protein signaling [1]. It is very important to elucidate G protein functions and characteristics to know the various cellular activities induced by receptor stimulus. Membrane structure consists of varieties of lipids, which mediates essential functions of gases as substrates or ligands to proteins [6]. Plasma membrane phospholipids are reorganized by membrane potential and induce K-Ras-dependent MAPK signaling [7]. The membrane proteins bind lipids, which leads to the changes in the protein structure and function [8]. The transportomes of eukaryotes which consist of transporters exhibit the energetic evolution [9].

The immune signaling is mediated via transmembrane proteins such as TCRs and B cell receptors [10]. The ligands outside of the cells bind to the extracellular binding domain of the receptor, which leads to the activation of the intracellular signaling via the signaling domain

of the receptor [10]. Multichain immune recognition receptors including TCRs, glycoprotein VI, natural killer (NK) receptors and Fc receptors such as FcεRI, FcαRI, FcγRI, and FcγRIII have a binding subunit and a signaling subunit, both of which are membrane proteins, and assemble together via transmembrane interactions [10]. Upon the ligand binding towards the binding subunit, the signaling subunits form homooligomers to activate downstream signals in signaling chain homooligomerization model [10]. The targeting of the transmembrane interactions between the binding subunit and the signaling subunit has therapeutic potential in which the interference with the transmembrane agent leads to modulate the intracellular signaling [10]. The inhibition of TCRs has the potential in arthritis and skin disease, whereas the inhibition of FcRs targets allergy or asthma [10].

The RTK signaling is induced by the binding of the extracellular ligands leading to oligomerization of the receptors [10]. Among transmembrane RTKs, erb-b2 receptor tyrosine kinase 2 (ErbB2) receptor and epidermal growth factor receptor (EGFR) are targets for cancer treatment, whereas the targeting β-2 adrenergic receptor (β-2AR) has the therapeutic potential for cardiovascular disease or asthma [10].

4. Conclusion

In conclusion, the peripheral membrane proteins regulate and are regulated by several signaling molecules. These proteins transduce signaling triggered by the outside stimulus into the cells, which leads to the regulation of gene and protein expression via transcription of the modulated DNA. The peripheral membrane proteins consist of the several classes and activate the downstream signaling pathways involving in cellular changes and diseases. The new approach to treat diseases might be possible by targeting the peripheral membrane proteins.

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Conflict of interest

The author declares no conflict of interest.

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