1P103 EGFR 細胞内領域の変異による EGF 受容体活性化
Spontaneous activation of EGFR by mutations in its
intracellular region in the absence of bound ligand

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EGFR is a single-path transmembrane protein with a tyrosine kinase in its intracellular domain. Aberrant activation of EGFR causes various cancers. The ‘dimerization model’, in which ligand binding to monomers induces dimers, has been used to explain the activation of EGFR. However, we have shown that EGFR exists as preformed, yet inactive, dimers prior to ligand binding, and have proposed an alternative ‘twist model’. To test our model, we examined which residues are essential for the dimer formation by introducing various mutations into the intracellular domains. Deletion of four charged residues spontaneously activated EGFR without bound ligand, suggesting that consistently with our model, the receptor dimer is stabilized through ionic interaction of the region.

1P106 計算機シミュレーションによる Hv1 プロトンチャネルの荷
電性残基の影響の検討
Evaluating the impact of charged residues in proton channel
Hv1 by computer simulations

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Hv1 is a human voltage-gated proton channel. Since its crystal structure is unknown, the proton permeation mechanism through this channel is unclear. In this study we used homology modeling and molecular dynamics simulation to explore the influence of the charged residues in proton permeation. We observed that Asp 112 and Arg211, which are reportedly critical to proton selectivity, are included in the intra-molecular salt bridge network and interact with water molecules in the narrowest part of the channel. Mutations of these residues to Ala significantly distorted the structure and impaired hydrogen bond network. These results indicate the importance of stable interactions between protein and water molecules in the predicted proton conduction pathway.

1P104 再構成膜におけるバクテリオロドプシンと部分フッ素化ホス
ファチジルコリンの低親和性
Low affinity of bacteriorhodopsin to partially fluorinated
phosphatidylcholine in reconstituted membrane

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Partially fluorinated lipids are expected to be very useful for biophysical and biochemical studies of membrane proteins. The reconstituted bacteriorhodopsin (bR) in diF4H10-PC retained the trimeric structure even after the chain melting phase transition and showed a photocycle similar to native purple membrane, which is in a striking contrast with bR reconstituted in DMPC. In order to investigate the factors for retaining the trimeric structure of bR molecules in diF4H10-PC liposome in the liquid crystalline phase, we have examined the distribution behavior of bR in binary immiscible membrane of diF4H10-PC and DMPC. We found that bR molecules have a tendency to be selectively distributed into DMPC-rich domain, suggesting that bR is essentially immiscible to diF4H10-PC.

1P107 Behavior of potassium ions around the potassium channel in
relation to permeation events

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Voltage-dependent K⁺ channels play a critical role in the movement of K⁺ ions across cell membrane under influence of membrane potential. Transition of K⁺ ions through the pore of the channel has been intensively studied by using molecular dynamics (MD) simulations but how the ions attach to and detach from the pore is not well understood. Here we present the analysis of ion movement around Kv1.2-2.1 chimera channel embedded in lipid bilayer by using MD trajectories. The ions frequently occupied the extracellular side of the pore in comparison with the bulk water and the ion density of this position decreased as the ion concentration or the membrane voltage increased. Our results imply that the conformation outside the pore can influence ion permeation events.

1P105 バクテリオロドプシンの色変異体に関する理論的研究
A theoretical study on color variants of bacteriorhodopsin

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Bacteriorhodopsin(bR) is a transmembrane protein which absorbs light around 570 nm and functions as a light-driven proton pump. We attempted a theoretical design of its color variants, which exhibits a large spectral blue-shift (>50 nm), by changing several residues around the retinal chromophore. We propose several mutations that stabilize conformational deformation of the chromophore and in turn leads to the spectral shifts. Structural models and spectral properties are examined by QM/MM RWFE-SCF method.

1P108 光駆動アニオンポンプハロロドプシンと発光タンパク質から
なる融合タンパク質の特性
Characteristic of fusion protein between light-driven anion
pump halorhodopsin and luminescence protein

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Seven-transmembrane helix protein, halorhodopsin (NpHR), is an inward light-driven anion pump which exists in biomembrane of *N. pharaonis*. To construct the anion pump system utilizing the emission light by bioluminescent protein, we established the *E. coli* expression system for fusion protein between the NpHR and luciferase from click beetle (ELuc). NpHR fused ELuc at the C-terminal was successfully expressed on the biomembrane, and bioluminescence from ELuc by reaction with D-luciferine was observed. Furthermore, separation between the NpHR and ELuc by the poly-glycine linker contributed to the increase of the luminescence intensity. The capability of the luminescence energy transfer from the ELuc to the retinal chromophore in the NpHR is discussed.