3P043 Mechanism of glycan receptor recognition for influenza virus Hemagglutinins: Comparative molecular dynamis studies

Katsumi Omagari (*Department of Virology, Medical School, Nagoya City University*)

The heamagglutinins (HAs) of influenza viruses mediate receptor binding, the initial event in virus infection. The differences in receptor-binding specificity of human and avian viruses are determined by the amino acid residues in the HA receptor-binding pocket. Asp at position 190 and 225 of H1 HAs confer binding to human-type receptors, whereas E190 and G225 confer binding to avian-type receptors. However some isolated viruses have E190 or G225, and D190E/D225G substituted virus does not prefer avian-receptor always. To clarify the detail effects of changes on binding for different HAs, molecular dynamics simulations were performed for the H1HA-glycan receptor complexes which comprise wild type and one point amino acid substituted HAs at positions 190 or 225.

3P044 Free energy landscape of substrate passing inside proteasome - activator complex

Hisashi Ishida (*Japan Atomic Energy Agency*)

Proteasome is involved in the degradation of the majority of cellular proteins. Proteasome activators bind to 20S proteasome core particle (CP) and facilitate opening a gate on the end of the CP. Then, the CP allows protein substrates to move into its interior through a channel between the gate and the α -annulus in order to hydrolyze the substrates to small fragments, and releases the products outside. To understand the gating mechanism of the CP, molecular dynamics simulations of the CP complexed with a PAN (analog of ATP-dependent 19S activator)-like activator, and of the CP complexed with an ATP-independent PA26 activator. The free-energies of the translocation of a poly-peptide substrate through the channel of these complexes were estimated.

3P045 MD シミュレーションを用いた CD44 のヒアルロン酸結合による構造変化に関する研究

Molecular dynamics simulation study on hyaluronan induced structural change of CD44

Saki Hongo¹, Yoshifumi Fukunishi², Masami Lintuluoto¹ (¹*Grad. Sch. of Life and Environ. Sci., Kyoto Pref. Univ.*, ²*Natl. Instit. of Adv. Indust. Sci. and Technol.*)

CD44 contains hyaluronan binding domain (HABD) in the extracellular region. The 3D structures of the HABD in HA-bound and -free states were revealed by NMR and X-ray studies. The structures found by both studies in the HA-free state were similar, and two modes of the HA binding to the HABD were suggested. Moreover, the NMR structure in the HA-bound state revealed that the C-terminal segment of the HABD enhanced the flexibility compared to the HA-free state. Our molecular dynamics study showed that the NMR structure in the HA-free state is different from that of the X-ray on the HA binding surface and has lower free energy compared to its crystal structure. We will report the difference and the dynamics between the structures of the HA-bound and -free states.

3P046 代謝型グルタミン酸受容体の活性化過程の動的モデルの構築 Dynamical modeling of the activation process of metabotropic glutamate receptor

Kaita Fujihara, Tatsuki Negami, Tohru Terada, Kentaro Shimizu (*Dept. of Biotech., Grad Sch. of Agri. Life Sci., Univ. of Tokyo*)

The metabotropic glutamate receptor (mGluR) is one of the G-protein coupled receptors. It has a large, ligand-binding extracellular (EC) region. It exists as homo dimer where two mGluRs interact with each other at the EC region. Based on the comparison of the crystal structures of the ligand-free and the ligand-bound forms of the EC region, it is proposed that the relative orientation between the two EC regions changes upon ligand binding, which brings the two transmembrane (TM) regions close to each other and leads to the activation of the receptor. To construct a dynamical model of this activation process, we performed coarse-grained MD simulations with MARTINI. We will discuss how the conformational change in the EC regions causes the change in the TM regions.

3P047 Mutation studies on the mammalian and the bacterial XORs with inhibitors

Hiroto Kikuchi¹, Hiroshi Fujisaki¹, Tadaomi Furuta², Ken Okamoto³, Takeshi Nishino⁴ (¹*Dept. of Phys., Nippon Med. Sch.*, ²*Center for Biol. Resources and Info., Tokyo Inst. Tech.*, ³*Dept. of Biochem. and Mol. Biol., Nippon Med. Sch.*, ⁴*Grad. Sch. Agri. and Life Sci.*)

Xanthine oxidoreductase (XOR), which is distributed widely in various species, is a target of drug for gout. Febuxostat is a commercially available drug that inhibits strongly the mammalian XORs but not the bacterial XOR although the substrate-binding pockets of mammalian and bacterial XOR are well-conserved. We have been experimentally and computationally studying the detailed mechanism of this difference. In this study, we further investigate this problem, comparing new experimental and computational results, including MD simulations with several mutations, binding free energy calculations via MM-PBSA(PBGA) method, and the interaction between XOR and different inhibitors.

3P048 Computational studies of mutational effects on nylon degrading enzyme

Takeshi Baba¹, Katsumasa Kamiya², Toru Matsui³, Masayoshi Nakano¹, Seiji Negoro⁴, Boero Mauro⁵, Yasuteru Shigeta^{1,6} (¹*Grad. Sch. of Eng. Sci., Osaka Univ.*, ²*Grad. Sch. of Pure and Applied Sci., Univ. of Tsukuba*, ³*Adv. Ins. for Comp. Sci., RIKEN*, ⁴*Grad. Sch. of Eng., Univ. Hyogo*, ⁵*Univ. Strasbourg*, ⁶*CREST*)

Nylon-6 degrading enzyme (NylB) breaks the amide bond of the unnatural compound. On the basis of the several mutants, important residues at the catalytic site are unraveled as Ser112, Lys115, Tyr170, and Tyr 215. However, reaction mechanisms are still unknown. A major difference between NylB and other proteases is existence of Tyr170, which belongs to a loop region and binds to the substrate. In order to clarify the role of Tyr170, we inspected mutational effects (Tyr170 to Phe170) on the reaction mechanism of hydrolysis undergoing in this enzyme by using first-principles molecular dynamics with metadynamics approach for free energy analyses. We proposed detailed reaction mechanisms and identified two possible reasons for deactivation due to the mutation.