2P037 cAMP 結合による Catabolite Activator Protein のアロステリック構造変化のダイナミクスに関する Molecular dynamics 研究
Molecular dynamics study on dynamics of allosteric conformational change of Catabolite activator protein induced by cAMP binding

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The Catabolite activator protein (CAP) is a bacterial DNA binding protein. CAP is a homodimer, and each subunit consists of two domains which are a cyclic adenosine monophosphate (cAMP) binding domain (CBD) and a DNA binding domain (DBD). The binding of cAMP to the CBD of CAP induces allosteric conformation change of the DBD into the DNA binding form. We perform a molecular dynamics (MD) study to investigate the dynamics of allosteric conformation change of CAP induced by cAMP binding. Our results for the non-ligand CAP show the flexibility in both of the CBD and the DBD, while cAMP binding to the CAP makes the CBD more rigid compared to the DBD. From our thermodynamics result, the first cAMP binding step is supposed to be the rate-determining step.

2P038 カチオン分布がトロンビン-基質会合に及ぼす影響
Influence of Cation Distribution on the Thrombin-substrate Association

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Thrombin is activated by Na⁺, and the mechanism has been explained by site-directed interaction of Na⁺. However, the recent challenge of redesigning K⁺-activated thrombin suggested that site-directed interaction does not simply result in the enzymatic activation. To explain this inconsistency, we performed molecular dynamics (MD) simulations of thrombin in three aqueous solutions of NaCl, LiCl and CsCl. We analyzed cation's distributions around thrombin, and found that the number of cations changes in inverse proportion to their ionic radius. Both surplus and deficit of cations around thrombin should prevent substrates from binding to thrombin. This observation suggests that thrombin-substrate association is optimized under moderate distribution of Na⁺.

2P039 Ectopic A-lattice seams destabilize microtubules

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Microtubules (MTs) typically include one A-lattice seam within a B-lattice tube. It is currently unclear how A-lattice seams influence MT dynamics. Here we find that including extra A-lattice in GMPCPP MTs destabilizes them, enhancing their shrinkage rate. Dynamic MTs nucleated by seeds containing extra A-lattice seams have growth rates similar to MTs nucleated by B-lattice seeds, yet have increased catastrophe frequencies at both ends. Furthermore, binding B-lattice GDP MTs to a rigor kinesin surface stabilizes them against shrinkage, whereas MTs with extra A-lattice seams are stabilized only slightly. On this basis, we propose that the single A-lattice seam of natural B-lattice MTs may act as a trigger point, and potentially a regulation point, for catastrophe.

2P040 cDNA ディスプレイ法による固相上のアミノ基認識ペプチドの探索とその分子認識機構の解析
Exploring the peptide aptamer against amino group on a solid-phase by cDNA display and analysis of its molecular recognition mechanism

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Disulphide-rich peptides are an attractive non-antibody affinity reagent because of their extreme specificity and affinity towards a target protein. However, molecular recognition ability of disulphide-rich peptides against non-protein target molecules including small molecules has not been investigated yet. We have screened peptide aptamers that specifically bind to the amino group on a solid-phase by in vitro selection using the cDNA display method [1]. We revealed the identified peptides have a unique structure containing two cyclic loops with disulphide bonds and a linkage region, which were indispensable for molecular recognition.

[1] Y. Mochizuki, K. Nishigaki, and N. Nemoto, *Chem. Commun.*, **50**, 5608-5610 (2014).

2P041 ミトコンドリア呼吸鎖のシトクロム c-シトクロム c 酸化酵素複合体における 電子伝達反応の構造制御機構
Conformational Gating for Electron Transfer Reaction from Cytochrome c to Cytochrome c Oxidase in Mitochondrial Respiratory Chain

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Cytochrome c (Cyt c) mediates single electron transfer (ET) from cytochrome bc₁ complex to cytochrome c oxidase (Cyt c) in the mitochondrial respiratory chain, which promotes reduction of molecular oxygen to two water molecules. Based on the NMR measurements, we proposed the "gating ET mechanism", where the disruption of hydrogen bond between Lys13 and Glu90 in Cyt c regulates the ET reaction with CcO. Here, we mutated Lys13 to disrupt the hydrogen bond and measured the NMR spectra in the presence and absence of CcO. The NMR spectra revealed that the area of the interaction site with CcO in the mutant is reduced and the interactions with CcO are perturbed, showing that the disruption of the hydrogen bond would play the primary role in the ET reaction from Cyt c to CcO.

2P042 MD シミュレーションを用いたマウス・線虫 ABCB1 トランスポーターの構造・ダイナミクスの解析
Analysis of dynamics and structure of ABCB1 transporters from mouse and *C. elegans* using molecule dynamics simulations

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P-glycoprotein (P-gp) is a multidrug transporter that catalyzes the transport of several substrates. In order to reveal the underlying mechanism of this type of substrate transport, we performed molecular dynamics (MD) simulations using the X-ray crystal structures of mouse and *C. elegans* P-gps, which have inward-facing conformations. Our simulations showed that the dimerization of the NBDs is driven by the binding of ATP to the NBDs and/or the binding of the substrate (verapamil) to a cavity in the TMDs, and that the so-called tetrahelix bundle might mediate communication between the NBDs and TMDs. In contrast, only partial contacts between the NBDs were observed in the ATP-free (Apo) state during the 100 ns MD simulations.