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Commentary and Perspective

Japan–US symposium on motor proteins and associated single-molecule biophysics

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Japan is one of the countries where motor protein studies are popular. The characteristic of Japanese motor protein studies lies in the fact that the single-molecule studies, a Japanese specialty, have developed, bridging and merging with other fields such as physics, engineering, and medical studies. Dr. Kumiko Hayashi and Dr. Jakia Jannat Keya thought of once again promoting the exchange of motor protein studies between Japan and USA, which was divided owing to the COVID-19 pandemic. We organize the Japan-US symposium on motor proteins and associated single-molecule biophysics, which is held at the 60th Annual Meeting of the Biophysical Society of Japan in September 2022 (Figure 1). This joint symposium is the second trial following the one organized in November 2021, in which Dr. Zev Bryant, Dr. Erika Holzbaur, and Dr. Kristen Verhey from the USA and Dr. Jakia Jannat Keya, Dr. Shinsuke Niwa, and Dr. Kyoko Chiba from Japan had participated [1].

Dr. Kumiko Hayashi (Tohoku University) [2], one of the organizers of the joint symposium, is an engaged council member of the Biophysical Society [3] and the International Affairs Committee of the Biophysical Society of Japan [4]. Since she joined the committee of the Biophysical Society of Japan after receiving the young scientist award of the society, she has tried contributing to the internationalization of the society. She is highly interested in the exchange as a member of these two societies. In addition, she is a KIF1A.org [5] Mini Grants recipient and personally thinks that the Japanese single-molecule techniques can majorly contribute internationally toward elucidating the mechanisms of disease-associated kinesin mutants to help patients with related neuronal disorders.

Dr. Jakia Jannat Keya (National Institutes of Natural Sciences, University of Michigan), the other organizer of the joint symposium, is a young scientist who has been engaged in motor protein research to promote it in artificial systems [6] with Dr. Akira Kakugo [7] and its single-molecule biophysics in collaboration with Ryota Iino laboratory [8]. She has been serving as a regular member of the Biophysical Society of Japan since her Ph.D. and postdoc research in Japan. She achieved the young scientist award from the society in 2020. Currently, she is pursuing her interest to understand motor protein kinesin's function to drive microtubule damage and lattice repair in cells toward developing a treatment for neural disorders and related diseases at the Medical School, University of Michigan, USA (Kristen Verhey lab [9]).

We have invited three speakers from USA. Dr. Ahmet Yildiz (University of California, Berkeley) [10] will talk about the regulation of motors by microtubule-associated proteins [11]. He describes the work by saying that "the microtubule (MT)-associated protein, MAP7 is a required cofactor for kinesin-1 driven transport of intracellular cargoes. Using cryo-electron microscopy and single-molecule imaging, we investigated how MAP7 binds MTs and facilitates kinesin-1 motility. Unexpectedly, MAP7 partially overlapped with kinesin-1's binding site and inhibited kinesin-1 motility. However, by tethering kinesin-1 to the MT, the projection domain of MAP7 prevented dissociation of the motor and facilitated its binding to available neighboring sites. The inhibitory effect of microtubule binding is dominated as MTs became saturated with MAP7. Our results reveal biphasic regulation of kinesin-1 by MAP7 in the context of their

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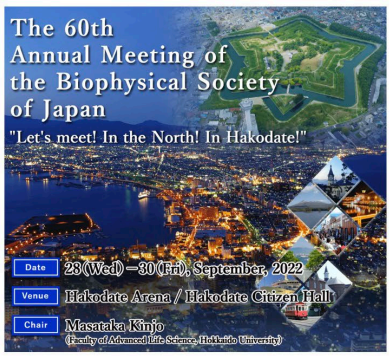
competitive binding of MTs."

Dr. Jing Xu (University of California, Merced) [12] will talk about the inhibitory effect of tau on kinesin-1-based transport amplified by cholesterol in the cargo membrane [13]. She describes the finding by saying that "Intracellular cargos are often membrane-bound and transported by microtubule-based motors (such as kinesin-1) in the presence of microtubule-associated proteins (MAPS). Whereas increasing evidence reveals how MAPs impact the interactions between motors and microtubules, critical questions remain about the impact of the cargo membrane on transport. Here we show that attaching kinesins to a fluid lipid membrane decreases the inhibitory effect of tau in comparison to membrane-free cargos in vitro. Adding cholesterol, which reduces kinesin diffusion in the cargo membrane, amplifies the inhibitory effect of tau on kinesin in a dosage-dependent manner. Our study establishes a direct link between the physical properties of cargo membrane and MAP-based regulation of kinein-1."

Dr. Sam Peng (Massachusetts Institute of Technology, Stanford University) [14] will talk about ultralong-term, real-time tracking of single cargoes in living neurons [15]. He describes the results by saying that "Single-molecule fluorescence microscopy has enabled numerous novel findings in biology. However, its full potential has been limited by the photo-instability of current probes. I will describe our development of rare-earth ion doped upconversion nanoparticles whose non-blinking luminescence is extremely stable, allowing single-particle imaging for several hours. I will demonstrate how the photostable probes enable ultralong-term single-particle tracking in living neurons and allow us to address fundamental questions regarding axonal transport. First, I will describe how we measure the number of active dynein motors driving the transport. Second, I will describe our proposed chemomechanical model for dynein which requires the hydrolysis of two ATP molecules per step."

From the Japanese perspective, Dr. Hiroyuki Noji (University of Tokyo) [16], the current president of the Biophysical Society of Japan, will deliver a talk about the torque generation mechanism of F_1-ATPase [17,18]. He describes the work by saying that "F_1-ATPase is the catalytic domain of ATP synthase, and functions as a rotary motor driven by ATP hydrolysis when isolated. Rotational dynamics as well as chemomechanical coupling scheme have been well characterized by single-molecule studies on the F_1-ATPase from thermophilic *Bacillus* (TF_1). However, the structural studies of TF_1 have been restricted because TF_1 is not suitable for crystallization, which has hampered the elucidation of torque generation mechanism of F_1. Recently, we succeeded in cryo-EM analysis of TF_1 and revealed the structures of almost all catalytic states of F_1 in rotational catalysis. In this presentation, I will discuss the torque generation mechanism of F_1 based on the structural study as well as our previous single-molecule studies."

Two young researchers will also join the joint symposium: Dr. Tomohiro Shima (University of Tokyo), who will talk about SLC26 ion transporters acting as electricity-driven motor proteins; Dr. Huong T Vu (University of Warwick), who will talk about the asymmetrical response of plus and minus ends of microtubules to kinesin binding by a long-range



08:45～11:15 Room F (Hakodate Citizen Hall 1F Main Hall)
2SFA Japan-US symposium on motor proteins and associated single-molecule biophysics

Organizers: Kumiko Hayashi (Tohoku Univ.), Jakia Jannat Keya (NINS)

2SFA-1 Torque Generation Mechanism of F_1-ATPase
Hiroyuki Noji, Hiroshi Ueno (*Grad. Sch. Eng., Univ. Tokyo*)

2SFA-2 Regulation of Motors by Microtubule-Associated Proteins
Ahmet Yildiz (*University of California Berkeley*)

2SFA-3 Cholesterol in the cargo membrane amplifies the inhibitory effects of tau on kinesin-1-based transport
Qiaochu Li[1], James Ferrare[2], Jonathan Silver[2], John Wilson[1], Luis Arteaga-Castaneda[1], Weihong Qiu[3], Michael Vershinin[4], Stephen King[5], Keir Neuman[2], **Jing Xu[1]** ([1]*Physics, University of California, Merced, CA, USA*, [2]*Laboratory of Single Molecule Biophysics, National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, MD, USA*, [3]*Physics, Oregon State University, Corvallis, OR, USA*, [4]*Physics and Astronomy, University of Utah, Salt Lake City, UT, USA*, [5]*Burnett School of Biomedical Sciences, University of Central Florida, Orlando, FL, USA*)

2SFA-4 Ultralong-Term, Real-Time Tracking of Single Cargoes in Living Neurons
Sam Peng (*Stanford University*)

2SFA-5 (1Pos137) Plus and minus ends of microtubules respond asymmetrically to kinesin binding by a long-range directionally driven allosteric mechanism
Huong T Vu[1], Zhechun Zhang[2], Riina Tehver[3], Dave Thirumalai[4] ([1]*University of Warwick*, [2]*Harvard University*, [3]*Denison University*, [4]*University of Texas*)

2SFA-6 (3Pos143) SLC26 ion transporters act as electricity-driven motor proteins
Tomohiro Shima (*Grad. Sch. Sci., Univ. Tokyo*)

Figure 1 Program of the Japan-US symposium on motor proteins and associated single-molecule biophysics. The symposium will be held in 29th September, 2022 (Japan time). It is a hybrid and on-demand symposium.

directionally driven allosteric mechanism. We hope that the joint symposium will promote the exchange of ideas between the research communities of Japan and USA.

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