Abstracts of papers presented
at the 56th Fujihara Seminar as

International Conference on Molecular Mechanism of Intracellular Transport: The Roles of Kinesin and Dynein Superfamily Proteins

The Molecular Motor Conference 2007

August 23–26, 2007

At **Grand Hotel New Oji in Tomakomai,** Hokkaido, Japan

Organizer **Nobutaka Hirokawa**

The Fujihara Foundation of Science

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This meeting is sponsored by

The Fujihara Foundation of Science

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56th Fujihara Seminar

The Molecular Motor Conference 2007

Thursday, August 23 - Sunday, August 26, 2007

Thursday, 23rd	7:00 pm	Registration, Poster hanging
	7:30 pm	WELCOME PARTY in Foyer (2nd Floor)
Friday, 24th	8:00 am	Opening Remarks
	8:30 am	**1** Intracellular transport (1-4)
	1:00 pm	POSTER SESSION I (A-N; 21-38)
	2:00 pm	PHOTO
	2:30 pm	**2** Motility (5-8)
	6:30 pm	RECEPTION at *Harunire* (1st Floor)
Saturday, 25th	8:30 am	**3** Mitosis (9-12)
	1:00 pm	POSTER SESSION II (O-Y; 39-55)
	2:00 pm	EXCURSION
Sunday, 26th	8:30 am	**4** Transport (13-16)
	1:00 pm	**5** Cilia and Dynein (17-20)
	4:30 pm	**6** Dynein (Short Talks)
	6:30 pm	Closing Remark
	7:00 pm	BANQUET at *Grandview* (16th Floor)

All sessions are located at Fuyou Hall (2nd Floor).

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FRIDAY, August 24

8:00 am – 8:30 am **Opening Remarks**

8:00 am Greeting
Soji Ban, *Executive Director, The Fujihara Foundation of Science*

8:10 am Introductory Remark
Susumu Nishimura, *Visiting Professor, Center for TARA, Univ. of Tsukuba*

8:20 am Introductory Remark
Nobutaka Hirokawa, *Graduate School of Medicine, University of Tokyo*

8:30 am – Noon **SESSION 1 Intracellular transport**

Chairpersons: Eckhard Mandelkow
Nobutaka Hirokawa

8:30 am Nobutaka Hirokawa
Hirokawa N
Department of Cell Biology and Anatomy, Graduate School of Medicine, University of Tokyo
Integrative Biology of Kinesin Superfamily Molecular Motors, KIF 1A, KIF 3 and KIF 4: Structure, Dynamics and Functions 1

9:15 am Viki Allan
Allan V & Wozniak M
Faculty of Life Sciences, University of Manchester
Kinesin-1 and Endoplasmic Reticulum Motility 2

10:00 am **COFFEE**

10:30 am Scott Brady
Brady S, Morfini G, Pigino G & Aspengren S
Dept of Anatomy and Cell Biology, Univ. of Illinois at Chicago
Pathogenesis in Adult-Onset Neurodegenerative Diseases and Regulation of Fast Axonal Transport 3

11:15 am Eckhard Mandelkow
Mandelkow E, Thies E, Konzack S, Marx A & Mandelkow E-M
Max-Planck-Unit for Structural Molecular Biology
Interplay Between Motors, Microtubules, and MAPs in Neuronal Traffic 4

1:00 pm – 2:00 pm

POSTER SESSION I (A-N)

2:00 pm **PHOTO**

2:30 pm – 6:00 pm **SESSION 2 Motility**

Chairpersons: Sharyn A. Endow
Robert Cross

4:00 pm **COFFEE**

SATURDAY, August 25

8:30 am – Noon **SESSION 3 Mitosis**

Chairpersons: Isabelle Vernos
Don W Cleveland

8:30 am DON W CLEVELAND
Weaver B, Silk A, Kim Y & Cleveland DW
Ludwig Institute for Cancer Research, University of California at San Diego
Guarding the Genome: Centromeres, Aneupoidy and Tumorigenesis 9

9:15 am CLAIRE E WALCZAK
Walczak CE, Ems-McClung SC, Hertzer KM, Rizk R & Zhang X
Medical Sciences, Indiana University
Control of Mitotic Spindle Assembly by the Mitotic Kinesin MCAK 10

10:00 am **COFFEE**

10:30 am ISABELLE VERNOS
Ferreira V, Peset I, Sardon T, Vanneste D & Vernos I
Cell and Developmental Biology Program, Centre of Genomic Regulation, CRG
Phosphorylation Dependent Regulation of Spindle Assembly and Chromosome Movements during Mitosis and Meiosis 11

11:15 am JONATHAN M SCHOLEY
Scholey JM
Department of Molecular and Cell Biology, University of California at Davis
Functional Coordination of Kinesins Involved in Mitosis and Ciliogenesis 12

1:00 pm – 2:00 pm **POSTER SESSION II (O-Y)**

Oda T, Hirokawa N & Kikkawa M
Department of Biophysics, Graduate School of Science, Kyoto University
Three-Dimensional Structures of Flagellar Dynein-Microtubule Complex by Cryo-electron Microscopy 39

Toba S[1)], Sakakibara H[1)], Ishikawa T[2)], Iwamoto H[3)] & Oiwa K[1,4)]
[1)]Kobe Advanced ICT Research Center, National Institute of Information and Communications Technology, [2)]Department of Biology, Swiss Federal Institute of Technology (ETH Zürich) [3)]SPring-8, Japan Synchrotron Radiation Research Institute, [4)]Graduate School of Life Science, University of Hyogo
Force-Generating Mechanism of Axonemal Dynein Arms Studied by Cryoelectron Tomography and X-Ray Fiber Diffraction Analysis 40

2:00 pm – 6:30 pm **EXCURSION**

SUNDAY, August 26

8:30 am – Noon **SESSION 4 Transport**

Chairpersons: Vladimir I Gelfand
Gary Banker

1:00 pm – 4:00 pm **SESSION 5 Cilia and Dynein**

Chairpersons: Joel Rosenbaum
Peter Satir

4:00 pm **COFFEE**

4:30 pm – 6:30 pm **SESSION 6 Dynein (Short Talks)**

Chairpersons: Kazuhiro Oiwa
Ritsu Kamiya

Nobutaka Hirokawa

Integrative Biology of Kinesin Superfamily Molecular Motors, KIF 1A, KIF 3 and KIF 4: Structure, Dynamics and Functions

Hirokawa N

Department of Cell Biology and Anatomy, Graduate School of Medicine, University of Tokyo, Hongo 7-3-1, Bunkyo-ku, Tokyo, 113-0033 Japan

The intracellular transport is essential for cell morphogenesis, functioning and survival. To elucidate this mechanism we have identified and been characterizing kinesin superfamily proteins, KIFs, using multidisciplinary and integrative approaches combining molecular cell biology, molecular genetics, biophysics, X-ray crystallography and cryoelectron microscopy. In this seminar I will focus on KIF 3, KIF 4 and KIF 1A.

To know the in vivo function of KIF3 in brain we conditionally knocked out KAP3, an associated protein of KIF3 to suppress function of KIF3 in brain. In mutant brain progenitor cells proliferate and invade upper layers to cause tumor like rossete formation. In the KAP 3 knock out cells transport of N-cadherin and beta-catenin from Golgi to plasma membrane was affected. We found that the cargoes of KIF 3 contain N-cadherin and beta catenin and that KIF 3 controls a balance between beta catenin in the cytoplasm and it in the plasma membrane working as cell-cell adhesion molecule. Beta catenin in the cytoplasm tends to get in the nucleus to work as a transcriptional factor together with T cell factor and enhances cell proliferation. Thus this study suggests a potential tumor-suppressing activity of KIF 3.

In brain development, apoptosis is a physiological process that controls the final numbers of neurons. We found that the activity dependent prevention of apoptosis in juvenile neurons is regulated by KIF 4. The C-terminal domain of KIF 4 is a module that suppresses the activity of poly(ADP-ribose)polymerase-1(PARP-1), a nuclear enzyme. When neurons are stimulated by membrane depolarization, calcium signaling mediated by CaMKII induces dissociation of KIF 4 from PARP-1, resulting in upregulation of PARP-1 activity, which supports neuron survival. After dissociation from PARP-1, KIF 4 enters into the cytoplasm from the nucleus and moves to the distal part of neuritis in a microtubule-dependent manner. We suggest that KIF 4 controls the activity-dependent survival of postmitotic neurons by regulating PARP-1 activity in brain development.

In terms of the mechanism of motility the slow rate-limiting ADP release from free kinesin is accelerated by more than 10^4-fold following interaction with MT. This MT-dependent regulation serves as a chemical checkpoint to suppress futile consumption of ATP by free kinesin. Thus, ADP release is a key fundamental regulatory step for kinesin. We propose an atomic mechanism for this regulation based on five new crystal structures of ADP-releasing intermediates of the monomeric kinesin KIF1A and supporting kinetic measurements of mutant KIF1As.

VIKI ALLAN

Kinesin-1 and Endoplasmic Reticulum Motility

Allan V & Wozniak M

Faculty of Life Sciences, University of Manchester,
The Michael Smith Building, Oxford Road, Manchester, M13 9PT, United Kingdom

Kinesin-1 is thought to drive the movement of many different cargoes, including membrane-bound organelles such as the endoplasmic reticulum (ER). Kinesin-1-driven movement towards microtubule plus ends would transport the ER tubules towards the cell periphery in most cells, and this movement, together with the fusion of ER tubules with each other, is proposed to generate the typical reticular-tubular membrane network. Since kinesin-1 transports multiple cargoes, an important question is how the motor associates with these different structures. One possibility is that identical motor molecules bind to distinct cargo-specific receptors, such as kinesin heavy chain (KHC) binding to kinectin in the ER. However, kinesin light chains (KLCs) also bind to certain cargo molecules, and KLC1 exists in at least 8 splice isoforms, which differ only at their C-termini. We have tested whether distinct KLC1 isoforms play a role in targeting kinesin-1 to different organelles. Using a combination of in vitro motility assays and biochemical approaches, we have found that KLC1B is involved in targeting and function of kinesin-1 on the ER, whereas KLC1D is required for the movement of vesicles in a Golgi membrane fraction. We have confirmed these results using a new assay for ER motility that uses semi-intact cells. However, when transient transfection is used to express KHC or KLC fragments in cells, or when KHC expression is knocked down using RNAi, only subtle effects are seen on ER morphology and motility. This may be because ER tubules can extend in mutliple ways—via kinesin or dynein, or by attaching to growing microtubules. Moreover, it is clear that other motile organelles such as endosomes, lysosomes, mitochondria and peroxisomes, may form transient interactions with the ER, and therefore extend ER tubules indirectly using motors other than kinesin-1.

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