

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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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 (2 nd 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 <i>Harunire</i> (1 st 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 <i>Grandview</i> (16 th 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)

- Aoyama S & Kamiya R
*Department of Biological Sciences, Graduate School of Science,
University of Tokyo*
**High-Speed Inter-Microtubule Sliding Driven by Aligned Axonemal
Outer-Arm Dynein** 21
- Yamada M¹⁾, Kondo K¹⁾, Maeda H¹⁾, Maruta S¹⁾ & Arata T^{2,3)}
*¹⁾Department of Bioinformatics, Soka University; ²⁾Department of
Biological Sciences, Graduate School of Science, Osaka University,
³⁾CREST/JST, Japan*
**Conformational Dynamics of Loop L11 in Kinesin Measured by
Site-Directed Spin Labeling Electron Paramagnetic Resonance** 22
- Aspengren S, Morfini G, Pigino G & Brady S
*Department of Anatomy and Cell Biology, University of Illinois at
Chicago*
**Identification of Regulatory Mechanisms Mediating Retrograde
Axonal Transport of Neurotrophins** 23
- Braun M¹⁾, Cross RA²⁾ & McAinsh AD¹⁾
*¹⁾Chromosome Segregation Laboratory, ²⁾Molecular Motors Laboratory,
Marie Curie Research Institute*
Biochemical Characterisation of the *S. pombe* Kinesin Klp2 24
- Erent M¹⁾, Osei M¹⁾, Amos L²⁾, Cross R¹⁾ & Drummond D¹⁾
*¹⁾Marie Curie Research Institute, ²⁾MRC Laboratory of Molecular
Biology*
**Biochemical Characterisation of *S. pombe* Kinesin-8 Family
Members Klp5 and Klp6 *in vitro*** 25
- Huang CF, Petersen J, Kaech S & Banker G
*Center for Research on Occupational and Environmental Toxicology,
Oregon Health and Science University*
**Motor-Microtubule Interactions and the Selective Translocation of
Kinesins in Cultured Hippocampal Neurons** 26
- Iwane AH, Watanabe TM & Yanagida T
*Department of Physiology, Division of Physiological Sciences,
Graduate School of Medicine, Osaka University, Japan Biomedical and
Engineering Research Organization, Tohoku University*
How Conventional Kinesin Regulates Its Tails During Movement 27
- Kamimura S¹⁾ & Iwamoto H²⁾
*¹⁾Department of Life Sciences, Graduate School of Arts and Sciences,
University of Tokyo, ²⁾Life and Environmental Division, SPring-8, JASRI*
**Dynein Arm Arrangement in Flagellar Axonemes and Its Dynamic
Change Revealed by Small-Angle X-ray Diffraction Analysis** 28

Okada KA, Kobayashi M, Masaike T & Nishizaka T <i>Department of Physics, Gakushuin University</i> Rotation and Conformational Changes of F₁-ATPase	29
Komori T, Nishikawa S, Ariga T, Iwane AH & Yanagida T <i>Graduate School of Frontier Biosciences, Osaka University</i> Simultaneous Observation of ATPase and Displacement by Myosin V	30
Kon T, Imamula K, Ohkura R & Sutoh K <i>Department of Life Sciences, Graduate School of Arts and Sciences, University of Tokyo</i> Dissection of Intra-Molecular Communications Between the Catalytic Head and Microtubule-Binding Site in the Dynein Heavy Chain	31
Leduc C, Ruhnoff F, Howard J & Diez S <i>Max Planck Institute of Molecular Cell Biology and Genetics</i> Detection of Fractional Steps in Cargo Movement by the Collective Operation of Kinesin-1 Motors	32
Mishima M ¹⁾ & Glotzer M ²⁾ <i>^{1)Wellcome/CRUK Gurdon Institute, University of Cambridge} ^{2)Department of Molecular Genetics and Cell Biology, University of Chicago}</i> Self-Assembly of Centralspindlin Kinesin-6/RhoGAP Complex Critical for Cytokinesis	33
Morimatsu M, Nishikawa S, Tsukasaki Y, Okada T, Iwane AH & Yanagida T <i>Graduate School of Frontier Biosciences, University of Osaka</i> The Micro Needle Study of the Relationship Between Myosin and a Single Actin Filament	34
Nakano I & Shingyoji C <i>Department of Biological Sciences, Graduate School of Science, University of Tokyo</i> Effects of Potassium Iodide on the Regulation of Dynein Activity in Sea Urchin Sperm Flagella	35
Nguyen H ¹⁾ , Kaya M ¹⁾ , Kon T ²⁾ , Sutoh K ²⁾ & Higuchi H ¹⁾ <i>^{1)Biomedical Engineering Research Organization, Tohoku University,} ^{2)Department of Life Sciences, Graduate School of Arts and Sciences, University of Tokyo}</i> The Contribution of Individual Dynein Head to the Processive Movement Generated by Two Single Headed Dynein	36
Nishiyama M, Kimura Y & Terazima M. <i>Department of Chemistry, Graduate School of Science, Kyoto University</i> Direct Observation of Pressure-Induced Inhibition of Microtubule-Based Kinesin Motility	37

Nitta R, Okada Y & Hirokawa N

*Department of Cell Biology and Anatomy, Graduate School of
Medicine, University of Tokyo*

**Proposed Mechanism of Regulation of Nucleotide Exchange in
Kinesin/Microtubule System**

38

2:00 pm

PHOTO

2:30 pm – 6:00 pm

SESSION 2 Motility

Chairpersons: Sharyn A. Endow
Robert Cross

2:30 pm

ROBERT CROSS

Alonso M¹, Yajima J², Carter N¹ & Cross R¹

*¹Marie Curie Research Institute, ²Department of Physics, Gakushuin
University*

Mechanics of Kinesin-1

5

3:15 pm

TOSHIO YANAGIDA

Komori Y^{1,2}, Iwane AH^{1,3} & Yanagida T^{1,2,3}

*¹Laboratories for Nanobiology, Graduate School of Frontier
Biosciences, Osaka University, ²Formation of Soft Nano-Machines,
CREST JST, ³Department of Physiology and Biosignaling, Graduate
School of Medicine, Osaka University*

Myosin-V Makes Two Brownian 90° Rotations per 36 nm-Step

6

4:00 pm

COFFEE

4:30 pm

SHARYN A ENDOW

Endow SA¹, Zou J¹, Yankel CD¹, Amos LA² & Hirose K³

*¹Duke University Medical Center, ²MRC Laboratory of Molecular
Biology, ³National Institute of Advanced Industrial Science and
Technology (AIST)*

Kinesin Motor Structural Changes and Function in Meiosis

7

5:15 pm

JONATHON HOWARD

Howard J, Brouhard G, Helenius J, Hyman AA, Stear J & Varga V
Max Planck Institute of Molecular Cell Biology and Genetics

**Regulation of Microtubule Length by Depolymerizing Kinesins
and Polymerases**

8

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, Aneuploidy and Tumorigenesis** 9

9:15 am

CLAIRE E WALCZAK

Walczak CE, Ems-McClung SC, Hertzler 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** 39Toba S¹⁾, Sakakibara H¹⁾, Ishikawa T²⁾, Iwamoto H³⁾ & 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

- Pack-Chung E, Kurshan PT, Dickman DK & Schwarz TL
Department of Neurobiology, Harvard Medical School, and Program in Neurobiology, Children's Hospital
Immaculate Connections, a Drosophila Kinesin, Is Required for Synaptic Bouton Formation and Synaptic Vesicle Transport 41
- Pigino G, Morfini G, Atagi Y, LaDu M & Brady S
Department of Anatomy and Cell Biology, College of Medicine, University of Illinois at Chicago
Intracellular Amyloid Beta Down Regulates Fast Axonal Transport 42
- Kotani N¹⁾, Toba S²⁾, Mellor C³⁾, Sakakibara H²⁾, Kojima H²⁾, Molloy J³⁾ & Oiwa K^{1,2)}
¹⁾Graduate School of Life Science, University of Hyogo, ²⁾Kobe Advanced ICT Research Center, National Institute of Information and Communications Technology, ³⁾National Institute for Medical Research
The Heterodimeric Axonemal Dynein f: Its Mechanical and Enzymatic Properties and Possible Roles in Beating of Flagellar Axonemes 43
- Liu L & Satir BH
Department of Anatomy & Structural Biology, Albert Einstein College of Medicine
Is Parafusin, an Exocytic Scaffold Component, Involved in Exocytic Vesicle Transport? 44
- Yoshimura A, Ishikawa R, Inoue Y, Nakano I & Shingyoji C
Department of Biological Sciences, Graduate School of Science, University of Tokyo
Roles of ATP, ADP and Mechanical Signals in the Regulation of Dynein Activity in Flagellar Motility 45
- Sugawa M, Nishikawa S, Iwane A & Yanagida T
Graduate School of Frontier Bioscience, Osaka University
Single Molecule FRET Imaging of Enzymatic Reactions at High Concentrations of Fluorescently Labeled Ligands 46
- Dong M, Tanaka Y, Niwa S, Takei Y & Hirokawa N
Department of Cell Biology and Anatomy, Graduate School of Medicine, University of Tokyo
Establishment of New Hypomorphic Mouse Model for KIF1A Molecular Motor 47
- Toda H¹⁾, Mochizuki H²⁾, Zhan C¹⁾, Sugiura Y¹⁾, Flores R III¹⁾, Josowitz R³⁾, Krasieva TB⁴⁾, LaMorte VJ⁴⁾, Suzuki E⁵⁾, Gindhart JG³⁾, Furukubo-Tokunaga K²⁾ & Tomoda T¹⁾
¹⁾Division of Neurosciences, Beckman Research Institute of the City of Hope, ²⁾Graduate School of Life and Environmental sciences, University of Tsukuba, ³⁾Department of Biology, University of Richmond, ⁴⁾Beckman Laser Institute, University of California, Irvine, ⁵⁾Gene Network Laboratory, National Institute of Genetics
Regulation of Axonal Transport via a Phosphorylation-Dependent Cargo-Motor Assembly 48

<u>Togashi Y¹⁾, Ueda M¹⁾, Mikhailov AS²⁾ & Yanagida T¹⁾</u> <i>¹⁾Nanobiology Laboratories, Graduate School of Frontier Biosciences, Osaka University, ²⁾Department of Physical Chemistry, Fritz Haber Institute of the Max Planck Society</i>	
Nonlinear Conformational Motion in Elastic Networks and Dynamical Features of Molecular Motors	49
<u>Tominaga M¹⁾, Murayama T²⁾, Kurebayashi N²⁾ & Katayama E¹⁾</u> <i>¹⁾The Institute of Medical Science, The University of Tokyo, ²⁾Department of Pharmacology, School of Medicine, Juntendo University</i>	
Conformational Change of Myosin Vb Is Involved in the Regulation of Peripheral Membrane Traffic	50
<u>Nakayama A¹⁾, Torisawa T¹⁾, Furuta K¹⁾, Edamatsu M¹⁾, Hirotsune S²⁾ & Toyoshima YY¹⁾</u> <i>¹⁾Department of Life Sciences, Graduate School of Arts and Sciences, University of Tokyo, ²⁾Department of Genetic Disease Research, Osaka City University Graduate School of Medicine</i>	
The Regulation of Dynein Motility by LIS1 and NDEL1	51
<u>Ueno H¹⁾, Yasunaga T²⁾, Shingyoji C³⁾ & Hirose K¹⁾</u> <i>¹⁾Research Institute for Cell Engineering, AIST, ²⁾Department of Biochemical Engineering and Science, Kyushu Institute of Technology, ³⁾Department of Biological Sciences, Graduate School of Science, University of Tokyo</i>	
Structural Analysis of Outer Arm Dynein Molecules Bound to Microtubules	52
<u>Varga V, Leduc C, Diez S & Howard J</u> <i>Max Planck Institute of Molecular Cell Biology and Genetics</i>	
The Mechanism of Microtubule Depolymerization by the Yeast Kinesin-8, Kip3p	53
<u>Yajima J^{1,2)}, Nishizaka T²⁾ & Cross RA¹⁾</u> <i>¹⁾Molecular Motors Group, Marie Curie Research Institute, ²⁾Department of Physics, Gakushuin University</i>	
Microtubule Sliding and Rotation Driven by Multiple Single-Headed Rat Kinesins	54
<u>Yamamoto R, Yanagisawa HA, Yagi T & Kamiya R</u> <i>Department of Biological Sciences, Graduate School of Science, University of Tokyo</i>	
Identification of Novel Subunits of Inner Arm Dynein Conserved Among Various Eukaryotes	55

SUNDAY, August 26

8:30 am – Noon

SESSION 4 Transport

Chairpersons: Vladimir I Gelfand

Gary Banker

8:30 am

GARY BANKER

Banker G, Huang CF, Petersen J & Kaech S

*Center for Research on Occupational and Environmental Toxicology,
Oregon Health & Science University*

**The Long-Range Carriers that Transport Polarized Membrane
Proteins to Axons and Dendrites**

13

9:15 am

KRISTEN VERHEY

Cai D¹⁾, Reed N¹⁾, Meyhofer E²⁾ & Verhey K¹⁾

*Departments of <sup>1)Cell and Developmental Biology and <sup>2)Mechanical
Engineering, University of Michigan, USA</sup></sup>*

**Regulation of Kinesin-1 Transport by Microtubule
Post-Translational Modifications**

14

10:00 am

COFFEE

10:30 am

BRUCE J SCHNAPP

Schnapp BJ¹⁾, Sheets L¹⁾, Ransom DG¹⁾, Mellgren EM²⁾ & Johnson SL²⁾

*<sup>1)Department of Cell and Developmental Biology, Oregon Health and
Science University, ^{2)Department of Genetics, Washington University}</sup>*

**Genetic and Live Cell Imaging Studies of Melanosome Transport
in Zebrafish Melanocytes**

15

11:15 am

VLADIMIR I GELFAND

Kim H, Kulic IM, Brown AEX, Kural C, Blehm B, Selvin PR,
Nelson PC & Gelfand VI

*Department of Cell and Molecular Biology, Feinberg School of
Medicine, Northwestern University*

Organelle Transport: Moving on Moving Tracks

16

1:00 pm – 4:00 pm

SESSION 5 Cilia and Dynein

Chairpersons: Joel Rosenbaum

Peter Satir

- 1:00 pm **PETER SATIR**
 Satir P, Bell A, Guerra C & Awan A
Department of Anatomy and Structural Biology, Albert Einstein College of Medicine
The Role of Kin 5 in *Tetrahymena* Ciliary Signaling 17
- 1:45 pm **JOEL ROSENBAUM**
 Rosenbaum J
Dept. Molecular, Cellular and Developmental Biology, Yale University
Intraflagellar Transport Protein, IFT27, a Small G-Protein, Controls Both the IFT-Dependent Assembly of the Cilium, and Cell Division 18
- 2:30 pm **RICHARD VALLEE**
 Tsai JW, Seale GE & Vallee RB
Columbia University, College of Physicians and Surgeons, Dept. of Pathology and Cell Biology
Multiple Roles for Cytoplasmic Dynein and LIS1 in Neuronal Migration and Axonal Pathfinding 19
- 3:15 pm **RITSU KAMIYA**
 Yagi T, Kikushima K & Kamiya R
Department of Biological Sciences, Graduate School of Science, University of Tokyo
Novel Species and Novel Motor Properties of Axonemal Dyneins 20

4:00 pm **COFFEE**

4:30 pm – 6:30 pm

SESSION 6 Dynein (Short Talks)

Chairpersons: Kazuhiro Oiwa

Ritsu Kamiya

- 4:30 pm Kamimura S¹⁾ & Iwamoto H²⁾
¹⁾*Department of Life Sciences, Graduate School of Arts and Sciences, University of Tokyo* & ²⁾*Life and Environmental Division, SPring-8, JASRI*
Dynein Arm Arrangement in Flagellar Axonemes and Its Dynamic Change Revealed by Small-Angle X-ray Diffraction Analysis 28

- 4:50 pm Kon T, Imamula K, Ohkura R, Sutoh K & Sutoh K
*Department of Life Sciences, Graduate School of Arts and Sciences,
University of Tokyo*
**Dissection of Intra-Molecular Communications Between the Catalytic
Head and Microtubule-Binding Site in the Dynein Heavy Chain** 31
- 5:10 pm Nguyen H¹⁾, Kaya M¹⁾, Kon T²⁾, Sutoh K²⁾ & Higuchi H¹⁾
¹⁾*Biomedical Engineering Research Organization, Tohoku University,*
²⁾*Department of Life Sciences, Graduate School of Arts and Sciences,
University of Tokyo*
**The Contribution of Individual Dynein Head to the Processive
Movement Generated by Two Single Headed Dynein** 36
- 5:30 pm Oiwa K
*Kobe Advanced ICT Research Center, National Institute of Information
and Communications Technology; 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,
and in vitro Motility Assays** 40, 43
- 5:50 pm Yoshimura A, Ishikawa R, Inoue Y, Nakano I & Shingyoji C
*Department of Biological Sciences, Graduate School of Science,
University of Tokyo*
**Roles of ATP, ADP and Mechanical Signals in the Regulation of
Dynein Activity in Flagellar Motility** 45
- 6:10 pm Ueno H¹⁾, Yasunaga T²⁾, Shingyoji C³⁾ & Hirose K¹⁾
¹⁾*Research Institute for Cell Engineering, AIST,* ²⁾*Department of
Biochemical Engineering and Science, Kyushu Institute of Technology,*
³⁾*Department of Biological Sciences, Graduate School of Science,
University of Tokyo*
**Structural Analysis of Outer Arm Dynein Molecules Bound to
Microtubules** 52

6:30 pm **Closing Remark**

7:00 pm **BANQUET**

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 rosette 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 multiple 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.

Authors' Index

A	
Allan V	2
Alonso M	5
Amos LA	7, 25
Aoyama S	21
Arata T	22, 30
Aspengren S	3, 23
Atagi Y	42
Awan A	17
B	
Banker G	13, 26
Bell A	17
Blehm B	16
Brady S	3,23, 42
Braun M	24
Brouhard G	8
Brown AEX	16
C	
Cai D	14
Carter N	5
Cleveland DW	9
Cross R	5, 24, 25, 54
D	
Dickman DK	41
Diez S	32, 53
Dong M	47
Drummond D	25
E	
Edamatsu M	51
Ems-McClung SC	10
Endow SA	7
Erent M	25
F	
Ferreira V	11
Flores R III	48

Furukubo-Tokunaga K	48
Furuta K	51

G	
Gelfand VI	16
Gindhart JG	48
Glotzer M	33
Guerra C	17

H	
Helenius J	8
Hertzer KM	10
Higuchi H	36
Hirokawa N	1, 38, 39, 47
Hirose K	7, 52
Hirotsune S	51
Howard J	8, 32, 53
Huang CF	13, 26
Hyman AA	8

I	
Imamula K	31
Inoue Y	45
Ishikawa R	45
Ishikawa T	40
Iwamoto H	28, 40
Iwane AH	6, 27, 30, 34, 46

J	
Johnson SL	15
Josowitz R	48

K	
Kaech S	13, 26
Kamimura S	28
Kamiya R	20, 21, 55
Katayama E	50
Kaya M	36
Kikkawa M	39
Kikushima K	20
Kim H	16
Kim Y	48

Kimura Y	37
Kobayashi M	29
Kojima H	43
Komori T	30
Komori Y	6
Kon T	31, 36
Kondo K	22
Konzack S	4
Kotani N	43
Krasieva TB	48
Kulic IM	16
Kural C	16
Kurebayashi N	50
Kurshan PT	41

L

LaDu M	42
LaMorte VJ	48
Leduc C	32, 53
Liu L	44

M

Maeda H	22
Mandelkow E	4
Mandelkow E-M	4
Maruta S	22
Marx A	4
Masaike T	29
McAinsh AD	24
Mellgren EM	15
Mellor C	43
Meyhofer E	14
Mikhailov AS	49
Mishima M	33
Mochizuki H	48
Molloy J	43
Morfini G	3, 23, 42
Morimatsu M	34
Murayama T	50

N

Nakano I	35, 45
----------------	--------

Nakayama A	51
Nelson PC	16
Nguyen H	36
Nishikawa S	30, 34, 46
Nishiyama M	37
Nishizaka T	29, 54
Nitta R	38
Niwa S	47

O

Oda T	39
Ohkura R	31
Oiwa K	40, 43
Okada KA	29
Okada T	34
Okada Y	38
Osei M	25

P

Pack-Chung E	41
Peset I	11
Petersen J	13, 26
Pigino G	3, 23, 42

R

Ransom DG	15
Reed N	14
Rizk R	10
Rosenbaum J	18
Ruhnow F	32

S

Sakakibara H	40, 43
Sardon T	11
Satir BH	44
Satir P	17
Schnapp BJ	15
Scholey JM	12
Schwarz TL	41
Seale GE	19
Selvin PR	16
Sheets L	15

Shingyoji C	35, 45, 52
Silk A	9
Stear J	8
Sugawa M	46
Sugiura Y	48
Sutoh K	31, 36
Suzuki E	48

T

Takei Y	47
Tanaka Y	47
Terazima M	37
Thies E	4
Toba S	40, 43
Toda H	48
Togashi Y	49
Tominaga M	50
Tomoda T	48
Torisawa T	51
Toyoshima YY	51
Tsai JW	19
Tsukasaki Y	34

U

Ueda M	49
Ueno H	52

V

Vallee RB	19
Vanneste D	11
Varga V	8, 53
Verhey K	14
Vernos I	11

W

Walczak CE	10
Watanabe TM	27
Weaver B	9
Wozniak M	2

Y

Yagi T	20, 55
--------------	--------

Yajima J	5, 54
Yamada M	22
Yamamoto R	55
Yanagida T	6, 27, 30, 34, 46, 49
Yanagisawa HA	55
Yankel CD	7
Yasunaga T	52
Yoshimura A	45

Z

Zhan C	48
Zhang X	10
Zou J	7

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