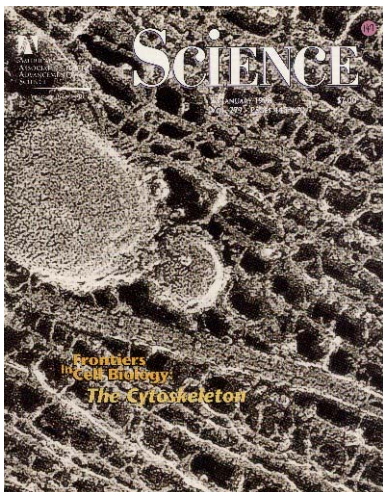
Molecular Cell Biology

Cell Biology and Anatomy

http://cb.m.u-tokyo.ac.jp/

Cells transport various kinds of proteins, lipids and mRNAs after synthesis to their specific destinations such as several types of membranous organelles, protein complexes and the mRNA complex. Thus, intracellular transport is fundamental to cellular functions, survival and morphogenesis. Our laboratory is studying the mechanisms of intracellular transport and cellular morphogenesis, especially focusing on molecular motors, Kinesin superfamily proteins (KIFs) and microtubule associated proteins (MAPs) using molecular cell biology, biophysics, structural biology, and molecular genetics.

- Molecular cell biological study of KIFs
- Studies of the mechanism for recognition of and binding to cargoes by KIFs and the regulation of this mechanism
- Studies of the mechanisms of differential directional transports and sorting
- Studies of the dynamics and mechanism of motility of KIFs using molecular biophysics and structural biology
- Molecular genetics of KIFs
- Studies of KIFs and related diseases
- Molecular cell biology and molecular genetics of MAPs



Quick freeze-deep etch electron micrograph of a mouse nerve axon showing a microtubule (25 nm diameter, linear tube-like structure) and a cross-bridge linking the microtubule and a membranous organelle. Microtubules are a major component of the cytoskeleton and serve as a type of rail along which motor proteins transport organelles inside cells. (Reproduced from the cover of Science vol. 279, Jan 23 1998.)

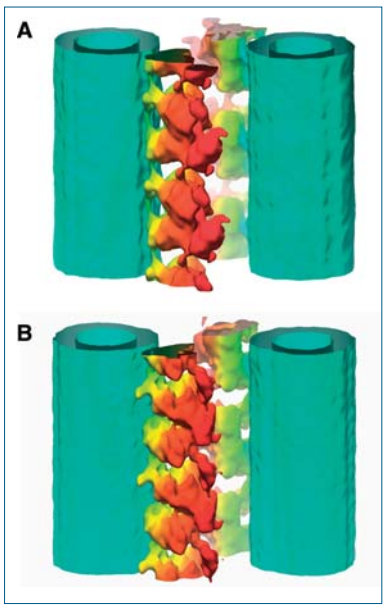
Structural Biology

http://structure.m.u-tokyo.ac.jp/

Kikkawa lab is interested in flagella/cilia, which works as an actuator as well as a sensor of cells. We are studying the mechanism of formation and function of flagella/cilia using cryo-electron microscopy, optical microscopy, and genetics. We are also developing new technologies to analyze images taken by microscopes.

Our focuses are:

- Molecular formation of flagella and axonemal dyneins.
- Mechanism of force generation by dyneins.
- Structures of microtubule-associated proteins
- Development of new image analysis methods for cryo-electron microscope

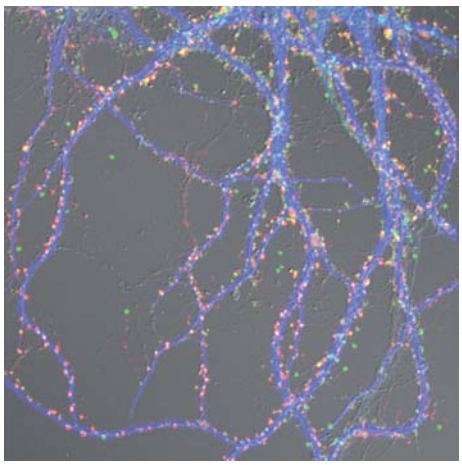


Three dimensional reconstruction of the outer dynein arm-microtubule complex from wild type. A: rigor state and B: relaxed state.

Cellular Neurobiology

The Laboratory of Cellular Neurobiology is interested in understanding the molecular mechanisms regulating synapse formation and maintenance, which are essential in proper function of neural circuits in the brain. The laboratory is using optical imaging of synaptic molecules in live neurons, in combination with molecular biological approaches to modify neuronal functions.

- Molecular architecture of the postsynaptic density
- Molecular mechanisms of activity-dependent synapse remodeling
- Regulation of synapse functions by glial cells
- Regulation of synapse formation and maintenance in vivo



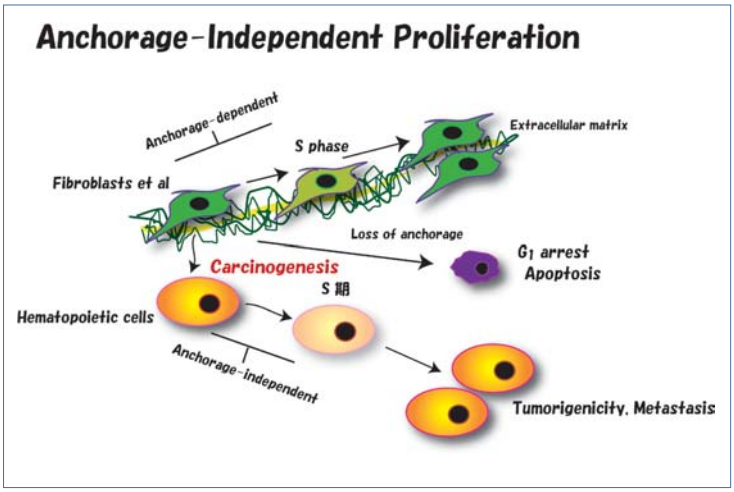
Quantitative fluorescence imaging of cultured hippocampal neurons (green: postsynaptic protein and calibrated fluorescent microspheres, red: presynaptic protein, blue: microtubule-associated protein)

Molecular Biology

http://www.cellcycle.m.u-tokyo.ac.jp

We have been studying the molecular mechanism enabling anchorage–independent S phase onset that is the key for malignant transformation.

- Understanding the anchorage signal cascades that control cell cycling
- Understanding the mechanism by which anchorage signals control the G1-S transition

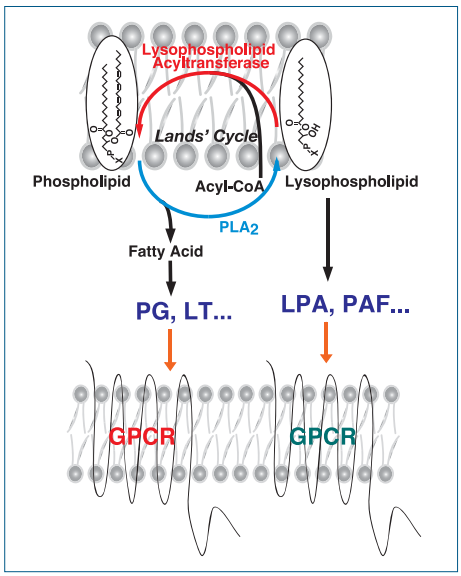


Cellular Signaling

http://biochem2.umin.jp/index_j.html

Our laboratory specializes in biochemistry, molecular and cellular biology, and genetic engineering to elucidate the roles of lipid mediators in vivo. We further study the molecular mechanism and biological significance of diversity and asymmetry of cellular membrane lipids. In collaboration with the Department of Metabolome, we analyze stimulus induced dynamic changes in the lipid composition of the cellular membrane.

- Discovery and structural determination of novel lipid mediators
- Cloning, functional characterization and K/O studies of enzymes involved in the metabolism of lipid mediators and receptors for lipid mediators
- Structure, function and dynamics of GPCR
- Lipidomics and enzyme characterization of membrance organization



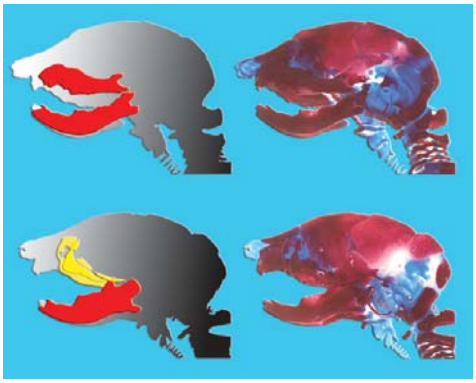
Production of lipid mediators during Lands' Cycle and activation of GPCRs
(Shimizu,T., Ann. Rev. Pharmacol. Toxicol. 49, 123-150, 2009)

Physiological Chemistry and Metabolism

http://bio.m.u-tokyo.ac.jp/

We are investigating signaling mechanisms underlying cell fate determination, morphogenesis and organogenesis in embryonic development.

- Molecular mechanisms of neural crest fate determination and craniofacial morphogenesis
- Molecular mechanisms of cardiovascular development
- Epigenetic control of embryonic development
- Roles of microRNA in embryonic development



Transformation of the upper jaw into a lower jaw in endothelin-1 knock-in (misexpressing) mouse (upper). The lower is the wild-type control.