Collective movement and morphogenesis of epithelial cells

Hisashi Haga (Division of Biological Sciences, Graduate School of Science, Hokkaido University)

Collective cell movement is essential for many physiological events, such as embryonic development, wound healing and tumor invasion. We have shown that epithelial cells (MDCK cells) migrate collectively along one direction on a collagen gel, whereas the cells move randomly on a rigid collagen-coated-glass. A particular cell named a leader appears at the edge of an epithelial colony and leads the neighboring cells named followers. We found that this role assignment between a leader and followers is essential for the collective migration.Moreover, morphogenesis of cells such as cyst and tubule formation in 3D environment is essential events in diverse physiological processes, including tissue generation and angiogenesis. However, the dynamical behavior of epithelial cells during lumen formation and the underlying mechanism are less well understood. Our studies demonstrated that collective cell movement occurred during the lumen formation when an epithelial sheet on a collagen gel was overlaid with another collagen gel. A turnup of the periphery of the epithelial sheet appeared within several hours after the gel overlay, and then the collective cell movement continued until the cells completed the lumen formation.In this symposium, these dynamical behaviors of the collective cell movement in 2D and 3D environments are discussed in terms of cellular contractile force.

Reference

H. Haga, C. Irahara, R. Kobayashi, T. Nakagaki, K. Kawabata, Biophys. J., **88**, 2250 (2005).

1S8-3　アメーバ運動の数理モデル

A Mathematical Model of Amoeboid Locomotion

Ryo Kobayashi (Dept. Mathematical and Life Sciences, Graduate School of Science, Hiroshima Univ.)

Amoeboid motion is widely observed in the single cell movement of eucaryote, from the corpuscles of higher organisms to the single cell creature. in this paper, we concentrate on the locomotion of the naked amoebae which are crawling around on the substrate. An amoeba extends the part of its body to the direction of movement, which is called pseudopod. Cytoplasm of the amoeba is composed of the gel layer under the cell membrane and the cytosol exhibiting a strong flow. During the locomotion, contraction of the actomyosin fibers produce a power, a part of the cell is extended, and also sol-gel transformation is taking place. To guarantee the normal amoeboid motion, lots of processes are going simultaneously in the coordinated manner. In order to understand such a motion as a whole, we construct a mathematical model. In our model, we adopt the combination of the two models of different type, the one is a phase field model and the other is a smoothed particle hydrodynamics (SPH). We uses a phase field as an expression of cell membrane since the phase filed model is quite tough to the large deformation of interfaces. Also, SPH particles are used for the expression of gel phase and sol phase, which are considered to be two type of fluids with different mobility. We will demonstrate simulations of our model which reproduce realistic amoeboid locomotion.

1S8-4　細胞間接着装置における力を用いたコミュニケーションの分子機構

Molecular mechanism for communications between cells using forces through cell-cell junctions

Shigenobu Yonemura (Electron Microscope Laboratory, Riken Center for Developmental Biology)

α-catenin is an essential protein for cadherin-based cell-cell adhesion. It binds to cadherin through β-catenin, forming a cadherin/catenin complex. α-catenin can bind also to vinculin, a major component of adherens junctions (AJ) and vinculin is known to be recruited to AJ through this binding. Recently we have shown that myosin II activity is required for vinculin recruitment to AJ. Then we examined the molecular mechanism underlying this force-dependent recruitment. We introduced a number of α-catenin mutants into α-catenin-deficient cells to identify regions responsible for the force-dependent vinculin recruitment and identified an inhibitory region for vinculin-binding and the importance of the C-terminal actin-binding region for the release of the inhibition. We concluded that actin filament-binding and myosin II contractile force are required for α-catenin/vinculin binding within cells and imagined conformational change of α-catenin according to the tension applied on the molecule through actomyosin contraction. Fluorescence recovery after photobleaching analysis showed that α-catenin in AJ is more stable than that in other regions of lateral membranes. Inhibition of force generation by myosin II also caused instability of α-catenin at AJ region. Our study explains how mechanical information leads to assembly of AJ and formation of epithelial sheets through use of α-catenin as a tension transducer.

1S8-5　膜タンパク質引き抜き曲線で探る細胞骨格の力学特性

Cytoskeletal Mechanics as Probed by Membrane Protein Pulling by AFM

Atsushi Ikai (1), Rehana Afrin (2), Masato Nakaji (3) and Tomoro Hakari (3). (1. Innovation Laboratory, 2, Biofrontier Center, 3) Graduate School of Bioscience and Biotechnology, Tokyo Institute of Technology)

The linkage between certain membrane proteins and the cytoskeletal structure is regarded as an important route of information transfer of extracellular signals into intracellular biochemical systems. We applied a tensile force to membrane proteins to probe for their status of their cytoskeletal linkage. On red blood cell membrane, glycophorin A and Band 3 protein showed different tensile profiles that reflected the presence or absence of their linkage to the spectrin based membrane skeleton. We then applied a non-ionic detergent or phospholipase to expose membrane skeleton and pulled the spectrin network through two different anchor points for the AFM probe, i.e., 1) Band 3-ankyrin-spectrin, or 2) anti-actin antibody-actin-spectrin pathway. Interestingly the tensile profiles of spectrin network pulling were different for different anchor points. In either case, there was a significant level of network extension under a tensile force of up to 150 pN signifying a low tensile stiffness for the spectrin network. When pulled with covalent links to the AFM probe, the maximum tensile strength of the membrane skeleton was found to be in the range of ~ 150 pN at a pulling speed of ~2 micron/s. The flexibility of membrane cytoskeleton of red blood cell was in a clear contrast with the actin based network of fibroblasts. References1. Rehana Afrin and Atsushi Ikai (2006) Biochemical and Biophysical Research Communications 348, 238?244.2. Masato Nakaji (2008) MS thesis. Tokyo Institute of Technology.

2S1-1　統合データベースプロジェクトは何の役に立つのか？

What is the integrated database project for?

Toshihisa Takagi (1) (1: Database Center for Life Science)

Database Center for Life Science (DBCLS) was founded in April 2007 as an institute of Research Organization of Information and Systems (ROIS). The Integrated Database Project was launched by Ministry of Education, Culture, Sports, Science and Technology (MEXT) from 2006 as a five year project, and our center was appointed as a core institute of the project. Here we describe the objective, policy and strategy of the project and introduce a variety of services recently released from the project website (http://lifesciencedb.jp/)

2S1-2　統合データベースプロジェクトの提供サービスについて

The services provided by the Integrated Database Projects

Shoko Kawamoto(1) (1:Database Center for Life Science)

Integrated Database Project was started from 2006 as 5 year project funded by MEXT (Ministry of Education, Culture, Sports, Science and Technology-Japan). One of the missions of this project is to develop integrated user services for non bioinformatics experts and promote Japanese life science. As a first step, we have developed the portal site to find easily the databases. And next, we have developed a full text database search service which is able to search multiple databases simultaneously, containing Japanese patents and review articles written in Japanese. For the user who wants to know the detail about international nucleotide sequence database, we have provided INSD (DDBJ/EMBL/GenBank) browser and GEO (Gene Expression Omnibus) browser. And also, we have developed several useful tools and services which use natural language processing techniques and so on. In addition, we have provided a hundred of tutorial videos named TogoTV to help using the databases and the bioinformatics tools for the laboratory researcher. To support these services, we are making efforts to develop the various fundamental technologies. Before this project has been started, there had been no specialized institutions which provided the services covered the databases from molecules to literatures. Although this project has just started and the services have not integrated, we try to make more useful services and to facilitate data sharing in life science field in Japan.

2S1-3　統合 DB の運営と利用にむけた教育活動

Education for life science database users and operators.

Jun Sese (Ochanomizu University)

For sustainable operation of life science database, various people having special skills for the handling data or database are required. In this project, we have education courses: database constructor (at Univ. of Tokyo), advanced database user (at Ochanomizu Univ.), and curator and annotator (at Nagahama Bio Univ.). We introduce the basic skill for the operation of life science database, and present the education of the detail of these courses.

2S1-4　熱力学データと構造データの統合化

Integration of Thermodynamic and Structural Data

Akinori Sarai (Department of Bioscience and Bioinformatics, Kyushu Institute of Technology)

Genome analyses of many organisms have produced enormous amount of information about sequence, structure and interactions of biomolecules. In order to understand the function of biomolecules, these pieces of information are essential. However, biomolecules are microscopic entities and their behavior is determined by the thermodynamic law. In order to understand the mechanism of biomolecular function, it would be critical to have quantitative thermodynamic data for their stability and interactions with other molecules, in addition to sequence and structural data. In particular, the relationship between structure and thermodynamics of biomolecules provides insight into the detailed mechanism of molecular function. Compared to sequence and structural information, there are a few thermodynamic databases. Thus, we have developed thermodynamic databases of proteins and their interactions with DNA and ligands. These databases include several thermodynamic parameters along with sequence and structural information, experimental methods and conditions and literature information. We are trying to integrate our thermodynamic databases with the structural database in PDBj. For efficient data integration, we are developing XML and ontology for the thermodynamic data. We are also applying text mining