

Study Sessions for Administrative Staff FY2023

#1 Activities of Researchers

September 13th, 2023 Mizuki Shimanuki



OIST



C-HUB

Center for
Professional Development
& Inclusive Excellence

OKINAWA INSTITUTE OF SCIENCE AND TECHNOLOGY GRADUATE UNIVERSITY

沖縄科学技術大学院大学



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OIST's Mission, Central Concepts, and Core Values

- **Mission Statement:** The University shall conduct internationally outstanding education and research in science and technology, and thus contribute to the sustainable development of Okinawa, and promote and sustain the advancement of science and technology in Japan and throughout the world. (PRP 1.2)

- **Central Concepts :** Best in the World, International, Flexible, Global Networking, Collaboration with Industry

- **Core values:** Integrity, honesty, fairness, respect for others, and dedication to the OIST mission
 - Openness in research, Respectful workplace, Commitment to students
 - ✓ **University Code of Conduct:** Equality of opportunity. No undermining of fundamental principles of human dignity. No discrimination on the basis of gender, gender identity, gender expression, age, sexual orientation, mental or physical disability, medical condition, race, ethnicity, ancestry, culture, national origin, religion, or marital status.



1 Research organizations, positions, roles, and activities

Main features of a university

Faculty (Professor, Associate Professor, Assistant Professor)

= PI, Teacher, Mentor, and Manager

Assistant Professor = on the Tenure-track system

PI: Principal Investigator

preside over an independent laboratory.
in charge of budget of the laboratory and research project.
in charge of instructing subordinate and graduate students
corresponding author of published papers

Laboratory

“Research Unit” at OIST

Researcher (Staff scientist, Post doctoral fellow) = conduct research and produce results

Graduate Student (Subject/customer of education, and Researcher at the same time)
= obtain a doctorate while receiving training = by conducting research, while studying

Technician = provide technical support for research, from house keeping routine to specific technologies.

Core Facility = Common facility equipped with cutting-edge research instruments (and standard ones) & expert support staff

Technical Specialist = provide expert support on experimental design and protocols, equipment operation, data acquisition, data analysis and interpretation, etc.

“Research Support Division” at OIST

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2 Research results – Scientific Papers

Publication of a research paper is official announcement of the research results to the world. (on a peer-reviewed journal) There are a lot of scientific journals.

Research Paper = a logical statement of new discoveries of scientific significance
--> Competition

Letter (Short report), Article (Full size paper)

Supplementary data may be available on-line.

Review (Review Article) = an overview of the current state of research on a topic

Book = a collective description and explanation of established knowledge

Thesis = a written statement submitted to the university to apply for a degree, which is based on their research achievement published on a peer-reviewed journal.
The applicant needs to pass an oral examination (Thesis defense session) as well.

Patent = a monopoly in exchange for the disclosure of an invention. must be obtained before publication in a paper

Scientific papers are structured so that anyone can understand!

Title = a short sentence that expresses the contents

Authors = people who has contributed to this work, and their affiliations

Summary = brief description what was newly discovered and proved in this research

Introduction = prerequisite facts, hypotheses, and background for this study

Materials and Methods = detailed materials and procedures for the experiments

Results = description of experiments, results and findings, with data (figures and tables)

Discussion = interpretation of the findings, new hypotheses, next questions, etc.

Acknowledgements = appreciation for people who have helped (except authors)

Author Contributions = who of the authors did what specifically

References = list of cited papers (indicated for descriptions based on past research)

The basis and responsibilities of the description are fully specified.

Science is the common property of humankind, developed from the work of one's predecessors

An example of a life science paper

Kif1, a C2H2 Zinc Finger-Transcription Factor for Cell Wall Maintenance during Long-Term Quiescence in Differentiated G0 Phase

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Abstract

Fission yeast, *Schizosaccharomyces pombe*, is a model for studying cellular quiescence. Shifting to a medium that lacks a nitrogen source induces proliferative cells to enter long-term G0 quiescence. Kif1 is a Kif1-like transcription factor with a 7-amino acid Cys2His2-type zinc finger motif. The deletion mutant, *kif1*⁻, normally divides in vegetative medium, but proliferation is not restored after long-term G0 quiescence. Cell biology, transcriptomic, and metabolomic analyses revealed a unique phenotype of the *kif1*⁻ mutant in quiescence. Mutant cells had diminished transcripts related to signaling molecules for switching to differentiation, lowered proliferative metabolism for cell-wall assembly and antioxidants had significantly increased. Further, the size of *kif1*⁻ cells increased markedly during quiescence due to the absent accumulation of Calcofluor-positive, 1,2,6-tri-O-methyl-beta-D-glucosylated cell wall. After 4 weeks of quiescence, reversible proliferation ability was lost, but metabolism was maintained. Kif1 thus plays a role in G0 phase longevity by enhancing the differentiation signal and suppressing metabolism for growth. If Kif1 is lost, *S. pombe* fails to maintain a constant cell size and normal cell morphology during quiescence.

Introduction

All cells exist in one of two states, proliferative and quiescent. In the proliferative state, the cell number increases by division, while in the quiescent state, cell life is sustained without division [1,2,3,4,5,6,7]. In multicellular organisms, the majority of cells in tissues and organs are non-dividing, so quiescence is a common cell state. For microbes, quiescence is induced by different environmental conditions, such as nutritional starvation. In the study of a complex organism, some cell types continuously transition between proliferative and quiescent. For example, hematopoietic stem cells give rise to all blood cells during an individual's lifetime, thus their proliferation and quiescence are carefully regulated [8,9]. The cellular mechanism for the transition between proliferative and quiescence is intriguing.

The fission yeast, *Schizosaccharomyces pombe*, is an excellent model organism for cell and molecular biology studies. This eukaryotic microbe contains a genome of 12 Megabase pairs (Mbp), containing ~5000 protein-coding genes [10,11]. *S. pombe* cells grow rapidly and divide in a defined synthetic medium, EMM2, which contains glucose as the sole carbon source and NH₄Cl as the sole nitrogen source. Upon removal of NH₄Cl, *S. pombe* cells cannot combine glucose and amino acids for growth, and undergo two rounds of cell division in the absence of cell growth, so that cells become small and round and contain pre-replicative DNA. Genome-wide studies of transcriptome indicate that a large-scale change in the cell type continuously transition between proliferative and quiescent occurs after nitrogen starvation [12,13,14]. Cells enter either a transient G1 phase prior to committing their entry into the normal phases of mitosis and meiosis (M/G1) or the bacterioid G0 phase, in the absence of cells with the bacterioid G0 phase, which is a long-term quiescent state. Kif1 is a branch point of cell differentiation after nitrogen source deprivation. They either must build metabolic, which requires meiotic cell divisions to produce spores, or toward the

Materials and Methods

Strains, media, culture, and light microscopy

Basic experimental procedures and media were described previously [13,17]. The *S. pombe* heterothallic haploid 972 *his4*-type cell strain was used. Nitrogen-starved G0 cells were prepared by procedures described previously. Briefly, cells were exponentially grown in EMM2 to a density of 2 x 10⁷ cells/ml at 28°C, harvested by vacuum filtration using a microfiltration membrane (0.45 µm pore size), washed in EMM2-N (EMM2 lacking NH₄Cl) once on the membrane, and then re-suspended in EMM2-N at a concentration of 2 x 10⁷ cells/ml. Because two rounds of cell division rapidly occurred, the resulting concentration reached ~8 x 10⁷ cells/ml. The culture was maintained for 48 h in EMM2-N and used as the

Immunoblotting and immunoprecipitation

Immunoblotting procedures were described previously [13]. Anti-GFP antibody (Sigma Chemical Co., St. Louis, MO), anti-FLAG antibody (Sigma) and anti-tubulin (a gift from K. Ochi) were used as primary antibodies. Horseradish peroxidase-conjugated secondary antibodies and an ECL detection/development system (Amersham Pharmacia Biotech) were used to amplify signal expression. Cell extracts were prepared as described in Hayashi et al. [21]. Briefly, exponentially growing cells (1 x 10⁷) carrying chromosomally integrated *kif1*⁻ GFP or *kif1*⁻ FLAG expressed under the native promoter were lysed in extraction buffer (25 mM HEPES-KOH pH 7.5, 200 mM NaCl, 10% glycerol, 0.1% NP-40, 1 mM phenylmethylsulfonyl fluoride) supplemented with a protease inhibitor cocktail (Sigma). Extracts were centrifuged twice (20 min at 7000 rpm and 30 min at 20,000 rpm), and incubated with anti-FLAG M2 affinity gel (Sigma) for 2 h. Beads were then washed with extraction buffer. Eluates were obtained by incubating with 100 µg/ml 3x FLAG-peptide (Sigma).

Electron microscopy

Transmission electron microscopy procedures were described previously [16]. Cells were fixed with 2% glutaraldehyde in 100 mM phosphate buffer pH 7.2 for 2 h at 28°C, post-fixed with 2% potassium permanganate overnight at 4°C, and embedded in Epon812 (EMBED 812, Electron Microscopy Sciences). Ultrathin sections were stained in 2% uranyl acetate and Reynolds' lead citrate, and viewed with a TEM EM10B30P (ECL) operating at 100 kV.

Transcriptomic analysis

Transcriptomic data were acquired by DNA microarray hybridization using the Yeast Genome 2.0 GeneChip (Affymetrix). Procedures used for DNA microarray hybridization were described previously [16]. Data were analyzed using MAS 5.0. Procedures for clustering gene expression profiles were basically the same as described previously [13,16]. SPICED software version 0.7 [22] [22] was used to discover sequence motifs in the 500-bp upstream regions of the genes. Gene Ontology data and genome sequence data used in this



2 Research results – Scientific Papers, “Kagaku Ronbun” in Japanese

Journey to publishing a paper

Writing → Submission to a journal → Screening by the editor → Peer review (typically by 3 reviewers)
→ Revision (after additional experiments) and answers to the reviewers’ questions and comments
→ Second peer review → (could be 2nd Revision) -- → Acceptance! → Subedit/proof → **Publication!!**

The review process improves quality of the research.

--- In case the submitted manuscript is rejected initially or after reviews, the manuscript should be reformed and submitted to another journal that is ranked lower. Then, go through the same process.

--- Multiple submission is strictly forbidden.---

Researchers are always under the pressure: “**Publish or Perish**”

Authors’ status (with the case of life science papers)

First Author = a person who has the most contributed to the work. Cited like “Shimanuki *et al.* (2013)”

Second Author, Third Author, ,, = follow the order of contribution

Corresponding Author = a person who is responsible for the publication procedures, usually the PI of the group (typically the last author of the paper).



2 Research results – Scientific Conferences, "Gakkai" in Japanese

There are various **academic societies** in each field, as various types of corporations. They sometimes publish academic journals.

Annual conference = place for research presentation for the member of the society. Usually, the venue and organizer take turns every year.

Oral presentation:

Plenary Lectures = Lectures by notably distinguished and renowned researchers

Symposium = Presentation of several major research topics. Be chosen for its content.

Workshop = Presenting and exploring related research topics on relatively specific themes.

Poster presentation = Posters summarizing research content are presented in a wide hall.

The audience drop by a poster and discuss with the author.

Special sessions on other topics: research ethics, gender equality, career paths, etc.

Unofficial information exchange: Collaborative research can also result from social gatherings.



2 Research results – Evaluation

Researchers are primarily evaluated on the number of published papers,

and those quality, citation index, including the Impact Factor

(of the journal)

also by

the number of patents

the amount of grants

awards

educational contribution

reviews by the peers

Reviews at OIST on faculty: Tenure Review, Promotion Review, Research Unit Review



3 Restrictions on research activities – Safety and Ethics

Before carrying out a research activity, a review of the research plan for checking safety and ethical issues shall be conducted by the relevant committee including external experts.

(research subjects, scale, duration, location, equipment, methods and procedures, practitioners, etc.)

Safety of People Engaged in Research and Those around Them

Safety committees (radiation, laser, biosafety, chemicals, field activities, etc.)

The low is never ahead of the cutting-edge challenges.

Welfare and Ethics for Research Subjects and the Environment

Ethics committees (human subject research, animal experiments,

environmental conservation and biodiversity protection, etc.)



3 Restrictions on research activities – Research misconduct

Violations in safety, welfare, ethics and rights

Publication:

When irregularities are found, the violated paper will be retracted and deleted.
And the responsible researchers will be expelled from Academia.

Plagiarism = to steal other people's data, ideas, texts and use them as their own.

Falsification = to manipulate data to induce incorrect conclusions.

Fabrication = to create non-existent data

Unintentional errors = reported in a correction paper

Publication on unscrupulous journals (Predatory journals): cannot be canceled.

Abuse of research funding: use without following the rules of the funding agency.

Conflict of interest: Bribery, profiteering, information leaks

Gift authorship: authorship on a paper without contribution

Harassment: Abuse of authority, academic harassment



4 Funds and resources to support research activities

OIST's financial resources = **Subsidy for operations** = Provided from taxes for school corporations
OIST is a specially well supported school corporation under supervision of the Cabinet Office, based on the special law for OIST. (Other school corporations are supervised by the MEXT.)

Ministry of Finance → Cabinet Office → OIST → Research Units

Competitive research funding = The fund distributor recruits research projects and allocates research funds to researchers who conduct research that is selected based on the evaluation of the research plan.

The most popular research fund in Japan = **Kakenhi** = Grants-in-Aid for Scientific Research

Major funding agencies in Japan: **MEXT** (Ministry of Education, Culture, Sports, Science and Technology)

JSPS (Japan Society for the Promotion of Science)

JST (Japan Science and Technology Agency)

AMED (Japan Agency for Medical Research and Development), etc.



4 Funds and resources to support research activities – PI's difficulties

PIs are forced to make the following efforts in order to obtain research funding continuously.

In order to obtain competitive research grants

- A PI must write an easy-to-understand research proposal with attractive theme and concrete plan that can be implemented.
- Past research track records (list of papers) are also important persuasive factors, so it is important to accumulate publications.
- A PI must make a research plan after thorough discussion with collaborators, in the case of large research funds for joint research.

After getting funds

- The research must be advanced within the period.
- The PI have to write and submit a progress report every year.
- Oral reports must be presented every year at research group meetings.
- A good research progress report is necessary to pass mid-term review to get continuous fund till the end of the period.
- Completion report of the research must be written and submitted at the end of the period.



4 Funds and resources to support research activities

– to a project, or to a person

OIST takes this approach, which is effective in supporting young people's independence

Funding for research projects/proposals

- Researchers apply for grants based on preliminary research results
- funded based on the project's potential for success
- to be disadvantageous to high-risk, high-return projects and to impede innovation
- short-term funding creates instability

Funding for researchers (High Trust Funding)

- funded based on an individual's past performance
- It is not a grant for a project, so it is free and flexible.
- promote creative research with stable funding
- long-term funding provides stability



4 Funds and resources to support research activities

– Facilities and technical support

(Research) Core Facility



Expensive shared research equipment that enables advanced research technologies and methods, and support from experts in the technology

Without those,

- Researchers need to purchase the equipment with a big research budget.
- Researchers must master the operation technique of the equipment and use it well by themselves.
- Alternatively, joint research must be conducted with experts who have both equipment and technology.

At OIST, we have a stable research budget and a substantial shared equipment facility (including technical experts). The best research and educational environment is provided to teachers (PIs), researchers, and students.

In addition to a rich lineup of cutting-edge equipment for common use, organizations like OIST's RSD (Research Support Division) with research experience, advanced technology, and dedicated support staff are common overseas, but are still limited in Japan.