Science and Technology Group
Annual Report FY2023

Midori Ota
Science and Technology Associate

Mechanisms of Centrosome Assembly and Activation in cell division

1. Introduction

My work focuses on centrosomes, which are small organelles serving as the major microtubule organizing centers in animal cells (**Fig. 1**). During cell division, centrosomes catalyze the formation of the mitotic spindle, which segregates replicated chromosomes into daughter cells. Centrosomes consist of a centriolar core that organizes a proteinaceous matrix known as the pericentriolar material (PCM). The PCM docks γ-tubulin containing complexes (γTuCs) to nucleate microtubules. Centrosome amplification can cause aneuploidy and drive tumor formation, while defects in centrosome assembly can lead to neurodevelopmental disorders such as microcephaly. Understanding the molecular mechanisms of centrosome assembly and activation is crucial for identifying potential targets and disease-specific therapeutic approaches.

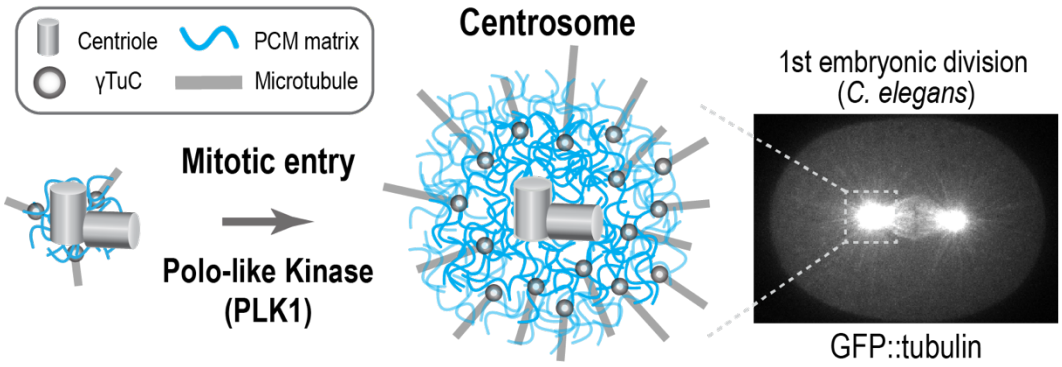

Figure 1. Centrosomes catalyze mitotic spindle assembly for chromosome segregation.

2.Activities and Findings

During mitotic entry, the PCM matrix expands and increases its nucleating capacity to catalyze spindle assembly, a process known as centrosome maturation (**Fig.1**). This maturation is controlled by Polo-Like Kinase (PLK1), which phosphorylates PCM matrix molecules such as SPD-5 in *C. elegans*, Cnn in *Drosophila* and CDK5RPA2 in humans. The N-termini of these PCM matrix molecules contain a conserved motif (CM1 for centrosomin motif 1) that can interact with γTuCs in the absence of PLK1 phosphorylation, but this motif is thought to be masked in the full-length PCM matrix protein (**Fig. 2**).

In FY2023, our work delineated how PLK1 phosphorylation converts the *C. elegans* matrix molecule SPD-5 into a mitotically active γTuC docking site. Our results suggest that phosphorylation by PLK1 triggers the reorganization of the SPD-5 N-terminus, generating an extended interaction surface consisting of two distinct γTuC-binding sites (**Fig. 2**). Selective activation of γTuC docking on PCM matrix molecules by PLK1 phosphorylation likely couples PCM expansion to the increased centrosomal microtubule nucleation that drives spindle formation.

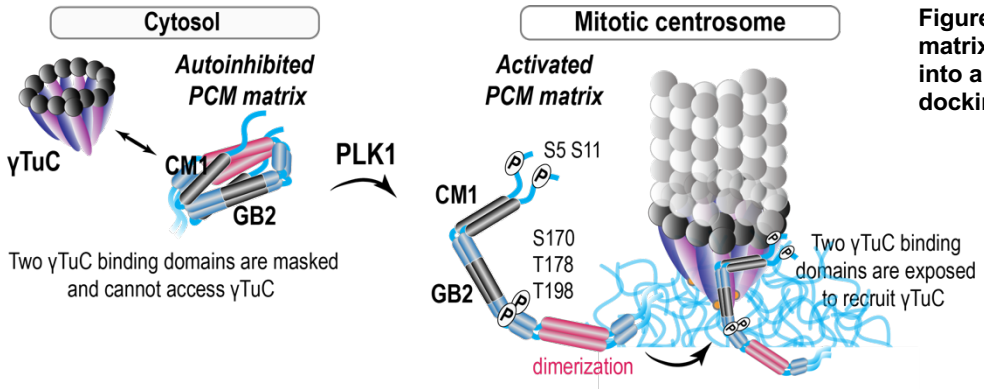

Figure 2. PLK1 phosphorylates the matrix molecule SPD-5, converting it into a mitotically active γTuC docking site at centrosomes.

Science and Technology Group
Annual Report FY2023

Midori Ota
Science and Technology Associate

3. Collaborations

External collaborations:

1. Karen Oegema and Arshad Desai (University of California, San Diego)
2. Yajie Gu and Kevin Corbett (University of California, San Diego)
3. Jeffrey Woodruff (UT Southwestern Medical Center)
4. Nami Haruta (Tohoku University)

Internal collaborations:

1. Orie Arakawa and Franz Meitinger (OIST, Cell Proliferation and Gene Editing Unit)
2. Matthias Wolf (OIST)

4. Publications and other output

Publication:

Houston J, **Ohta M***, Gómez-Cavazos JS*, Deep A, Corbett KD, Oegema K, Lara-Gonzalez P, Kim T, Desai A. BUB-1-bound PLK-1 directs CDC-20 kinetochore recruitment to ensure timely embryonic mitoses. **Current Biology**, **2023**. Apr 28;S0960-9822(23)00469-4, doi:10.1016/j.cub.2023.04.021

Invited talks:

[External Talks]

2023 Molecular Biology Society of Japanese annual meeting, Kobe, Japan
2023 GSB Seminar at Genome and Systems Biology Degree Program, National Taiwan University
2023 Seminar at the Institute of Molecular Biology, Academia Sinica in Taiwan
2023 Advances in Centrosome Biology Satellite meeting at Koc University in Turkey
2023 EMBO Workshop Centrosome in development, disease and evolution in Turkey (flash talk)
2023 Cell Division Workshop at the National Institute of Genetics in Japan, Mishima

[OIST Seminar/Workshop Talks]

2023 OIST-RIKEN RNA translation, proteomics meeting (Nov 16-17)
2023 OIST-Osaka University Joint Workshop, A Recipe for Scientific Synergy Series 4 (May 29)
2023 OIST Internal Seminar (April 14)

5. Awards and Honors:

[External]

2023 Best poster prize at EMBO Workshop Centrosome in development, disease and evolution in Turkey

[OIST Internal]

2023 Travel Award for Joint Symposium with Osaka University

6. Outreach and Services

2023 Judge for flash talks at the Molecular Biology Society of Japanese annual meeting, Kobe, Japan
2023 Organizer for the symposium- Right time, right scale: cell division regulation- at the Molecular Biology Society of Japanese annual meeting, Kobe, Japan
2023 Member of the Peer Mentoring Circle in OIST-Women's Leadership-

Science and Technology Group
Annual Report FY2023

Midori Ota
Science and Technology Associate

7. Service to the University

2023 Organizer of the OIST Cellular and Molecular Biology Internal Seminars (Every month with Wolf, Kono, Terenzio, Kiyomitsu, Meitinger Units and STAs)
2023 Lecture for Keio student at International Research Summer Camp at OIST

8. Grant Support

[External]
2023 Travel Grant for EMBO Workshop Centrosome in development, disease and evolution in Turkey

[OIST Internal]
2023 SHINKA Grant, FY 2023 (Collaboration with Tohoku University)