Cell Proliferation and Gene Editing Unit

Assistant Professor Franz Meitinger

(Back) Franz Meitinger, Junho Lee, Sharon Babar, Anna Pavlovska, Midori Ota, Esther Feng Ying Ng, Carmen Sparr, (Front) Hazrat Belal, Hitomi Ohtaki, Orie Arakawa.

Abstract

Every day, millions of cells in our body divide to maintain essential tissue functions. Errors in cell division can lead to developmental disorders or cancer. The unit's research focuses on molecular mechanisms of cell division and quality control in normal and cancer cells to understand tumor-suppressive mechanisms and identify biomarkers that confer a cancer-specific vulnerability to chemical drugs. The unit combines high-throughput imaging, gene editing and genome-wide screens to open new avenues for therapeutic development.

1. Staff

- Dr. Esther Feng Ying Ng, Postdoc
- Dr. Md Hazrat Belal, Postdoc
- Orie Arakawa, Technician
- Carmen Sparr, Technician

- Anna Pavlovska, Research Intern (February 3 – August31, 2023)
- Zoran Gavrilov, Research Intern (April 6 – July 6, 2023)
- Hamzah Muhammad, Ph.D. Rotation Student (May 1 – August 31, 2023)
- Sharon Babar, Ph.D. Rotation Student (Jan 1 – April 30, 2024)
- Hitomi Ohtaki, Research Unit Administrator (from November 1, 2022)

2. Activities and Findings

Quality Control of Mitosis

During mitosis, the cells distribute their chromosomes evenly between the two daughter cells. This process is strictly controlled and takes around 30 minutes. Defects in mitosis lead to a maldistribution of chromosomes and consequently to genome instability, which is a hallmark of cancer. Prolonged mitosis is characteristic of cells with defects that cause chromosome maldistribution. We have identified a mechanism by which mitotic defects can be detected by measuring mitotic length. We call this mechanism the mitotic stopwatch, which depends on the increasing formation of complexes between 53BP1, USP28 and p53 during prolonged mitosis (see **Fig. 1**). The mitotic kinase PLK1 is required for the formation of the complex. We have found that the mitotic stopwatch is often inactivated in cancer due to mutations in p53, USP28 and other pathways that repress p53 activity. Cancers with an inactive mitotic stopwatch are less sensitive to antimitotic agents, which is an important consideration for cancer treatment. This work was published in Science.

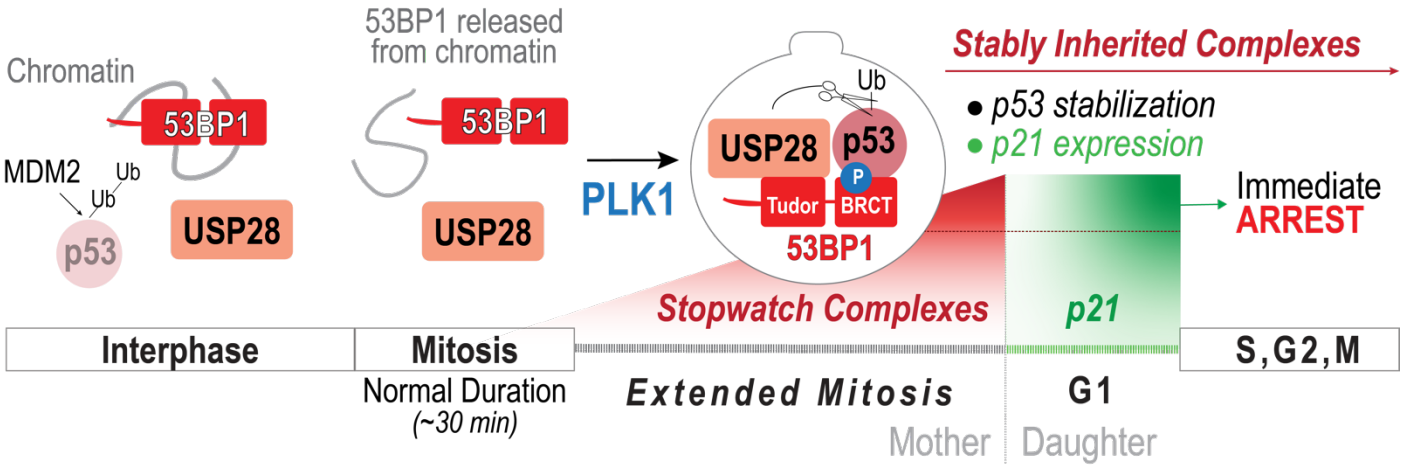

Figure 1: A mitotic stopwatch forms during prolonged mitosis to protect from the pathogenic consequences of mitotic defects.

3. Publications

3.1 Journals

1. Meitinger, F.[#], Belal, H., Davis, R.L., Martinez, M.B., Shiau, A.K., Oegema, K.[#], Desai, A[#]. (2024). Control of cell proliferation by memories of mitosis. Science 383 (6690):1441-1448.

3.2 Oral Presentations

1. Meitinger, F. OIST-Kyushu University, Onna, Japan (February 28, 2024)
2. Meitinger, F. OIST-JST/PRESTO Workshop, Onna, Japan (January 22, 2024)
3. Meitinger, F. MBSJ Meeting, Kobe, Japan (December 7, 2023)
4. Meitinger, F. NTU, Taipei, Taiwan (November 8, 2023)
5. Meitinger, F. Academia Sinica, Taipei, Taiwan (November 7, 2023)
6. Meitinger, F. OIST-RIKEN Workshop, Onna, Japan (November 17, 2023)
7. Meitinger, F. OIST-Keio University Symposium, Onna, Japan (November 16, 2023)
8. Meitinger, F. EMBO Workshop, Centrosomes in development, disease and evolution, Istanbul, Turkey (September 28, 2023)

3.3 Poster Presentations

1. Meitinger, F., Belal, H., Davis, R.L., Martinez, M.B., Shiau, A.K., Oegema, K., Desai, A. Control of cell proliferation by memories of mitosis. MBSJ Meeting, Kobe, Japan (December 8, 2023).

4. Outreach

4.1 Summer Camp

Medical students from Keio University visited OIST (August 2-9, 2023). We had the pleasure to host Kotone for one week in our lab. Esther and Belal explored together with Kotone the effects of anti-mitotic drugs on cell division by live imaging (left image). Kotone learned how to passage a human cell culture (right image).