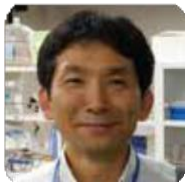
Laboratory of Cellular Life Science

Graduate School of Science



Professor Naotada ISHIHARA
Assistant Professor Emi OGASAWARA
Assistant Professor Keisuke TAKEDA

naotada takaya @bio.sci.osaka-u.ac.jp
eogasawara @bio.sci.osaka-u.ac.jp
takeda.keisuke.sci @osaka-u .ac.jp

URL: https://mitochondria.jp/

Mitochondria are intracellular organelles derived from endosymbiosis of bacteria. Mitochondria are involved in higher biological functions such as disease and aging through their diverse functions, including energy production by oxygen respiration, metabolism, and regulation of cell death. In live cells, long, branched mitochondria are actively moving within the cell and "division" and "fusion" are frequently observed (Figure 1). Mitochondria have their own genes (mtDNA), and they are also dynamic, changing their structure and distribution. However, the molecular details of the dynamic properties of these mitochondrial structures and their roles remain to be elucidated.

Our research group focuses on the shape and movement of mitochondria in mammalian cells, particularly the mitochondrial fission and fusion, and the dynamic features of mtDNA.

Mitochondria fusion reaction in mammalian cells

By labeling mitochondria with fluorescent proteins and observing live cells, we found that mitochondria frequently fuse each other and exchange their contents (Fig. 2). To understand the details of mitochondrial fusion, we established biochemical and biophysical analyses using purified proteins and live cell observations, respectively. We have discovered a mitochondrial quality control mechanism in which mitochondrial fusion activity is regulated by the mitochondrial respiratory activity, to eliminate dysfunctional mitochondria.

Physiological function of mitochondrial fission

Although mitochondria are originated from bacterial symbiosis, bacteria-type cell division machinery was lost and a mitochondrial fission system was acquired after symbiosis. To analyze higher-order biological functions of mitochondrial fission, we constructed mitochondrial fission-deficient mice. We found that mitochondria are required for proper mitochondrial positioning during early development and in neuronal differentiation, and that they are also important for maintaining oocyte function. Further analysis will reveal the involvement in integrated higher-ordered functions of mitochondria in various diseases and aging.

Dynamics of mitochondrial DNA

In humans, each cell contains more than several hundred copies of circular mtDNA (Figure 3). We constructed a live imaging system to visualize mtDNA and showed that mitochondrial membranes and DNA are cooperatively regulated. We also found that the structure and distribution of mtDNA should have an important roles such as in maintenance of respiration and myocardiac functions. Now we are analyzing the molecular mechanism of mtDNA inheritance in cultured cells and in vivo.

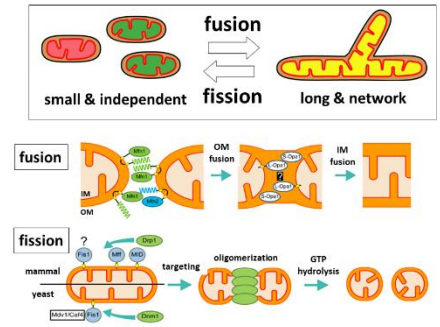


Figure 1. Model of mitochondrial membrane fusion and fission

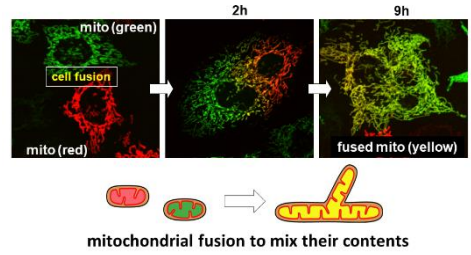


Figure 2. Fluorescence microscopy visualization of mitochondrial fusion in living mammalian cells.

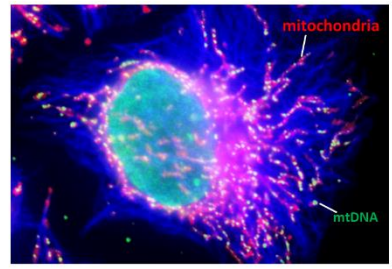


Figure 3. Distribution of mitochondria and their DNA (mtDNA)
Fluorescence microscopy reveals long branched mitochondria (red) and dotted mtDNA nucleoids (green) in mouse embryonic fibroblast. Blue indicates microtubules.

We are enjoying to watch and analyze the dynamic mitochondrial movement, that is interesting for me and useful for life and medical sciences.

Department of Biological Sciences
Graduate School of Science, Osaka University
1-1, Machikaneyama-cho, Toyonaka, Osaka 560-0043, Japan

TEL: +81-6-6850-6706

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