Division of Organogenesis
Germline Development

Germ cells: the unique cells responsible for producing the next generation
Investigating the mechanisms of germline development as a window to unknown processes of life science

Unlike the somatic cells that make up our organ and tissue,
germ cells have the different yet quite vital role in producing the next generation.
In his research, Dr. Akira Nakamura examines the characteristics of germ cells to shed light on the fundamental processes for controlling life and to further our understanding of the mechanisms of genetic disease.

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Profile

Graduated with a Bachelor' s degree from the College of Biological Science, University of Tsukuba, before completing a Ph.D. degree at the same university.
In 1993, he became a research fellow of the Japan Society for the Promotion of Science (JSPS), at The University of Tsukuba.
In 1995, he was awarded a JSPS Postdoctoral Fellowship for Research Abroad.
In 1997, he took up a researcher position supported by the Medical Research Council in Canada.
In 1998, he became a research associate at the University of Tsukuba. (JSPS Future Research Program)
From 2000 to 2002, he worked as Assistant Professor at the Gene Research Center, Institute of Biological Sciences, University of Tsukuba.
From 2002 to 2012, he was appointed to a team leader at the RIKEN Center for Development Biology.
In December 2012, he joined the Institute of Molecular Embryology and Genetics at Kumamoto University as a professor.

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Germ cells: the ultimate stem cells

Very broadly, our bodies are made up of two types of cells: somatic and germ cells. Somatic cells are essential to the survival of individuals, turning into skin, muscle, and neurons. By contrast, germ cells become eggs and sperm, tasked with producing the next generation. "While somatic cells live and die with the individual, germs cells are passed onto the next generation," explains Dr. Nakamura. "We could even say that our bodies are just a vehicle for germ cells. All of the cells that make up the body are produced from just a single fertilized egg. In this sense, germ cells can be regarded as the ultimate stem cells." What is more, meiosis followed by the fertilization that fuses sperm and the egg causes genetic information to be scrambled, thereby ensuring genetic variety in the next generation. Their role in transmitting mutations into descendants further means that germ cells are intimately associated with the evolution of species. "I hope that by conducting research to enhance our understanding of the characteristics of germ cells, we will further understand the fundamental control processes for vital phenomena as well as the mechanisms by which genetic disease occurs."

Germ plasm formation mechanism as a fundamental principle of life

One of the core projects Dr. Nakamura examines in his research is to clarify the processes by which the germ plasm is formed during oogenesis. Germ plasm is a specific cytoplasmic region found in the eggs of many animal species. Within it are localized mRNAs and proteins required for the formation and differentiation of germ cells.

In *Drosophila*, cells originating from germ line stem cells and located at the tip of the ovary will divide, forming a group comprising the oocyte and nurse cells, which provide the oocyte with nutrition.

These cell clusters communicate with each other, enabling the nurse cells to produce and transfer to the oocyte many factors including those that support the formation of the germ plasm (see Fig. 1). Simply saying, by the time egg is laid, the germ plasm has already been produced, and the germ plasm is inherited by cells referred to as pole cells. These are the only cells that will maintain germ cell characteristics in the new generation. "It is not just proteins that are localized in the germ cells; we know that many mRNAs are localized too," says Dr. Nakamura.

"Research in Japan and overseas has shown how *oskar*, a germ plasm factor, is localized within the oocyte to the posterior pole, where it is translated locally into protein. This Oskar protein, by recruiting many other proteins and RNA, thereby leads to the formation of the germ plasm—this much we know (see Fig. 2). Research focusing on the elucidation of the mechanisms by which RNA is transported and localized within the germ plasm, as well as those by which the translation of mRNA is repressed during its transport and only kicks in after localization at the posterior, really is a fascinating field of science."

Dr. Nakamura's research team is also looking at the localization and the translational control of *oskar* mRNA, trying to identify and isolate previously undiscovered factors involved, and analyzing their molecular functions. "The mechanism by which protein is translated locally through intracellular localization of RNA, is by no means specific to eggs and germ cells only; it has been observed elsewhere, for example, in single-cell organisms such as budding yeast. In particular, in recent years, we have started to understand how RNA transportation and localization-coupled translation are involved in the regulation of axonal growth and synaptic plasticity. In this way, our research holds considerable potential in terms of generating new and significant insight in yet-to-be elucidated fields such as learning and memory."

Mechanisms for germ cell survival

Another topic of Dr. Nakamura's research is the formation and differentiation of germ cells during embryogenesis. "Germ cells produce the next generation, and they must maintain their ability to do so. In *Drosophila*, the pole cells, which are the first cell to be formed during embryogenesis, go on to become the future germ cells. Having said that, when these pole cells are formed, many signals that instruct somatic cell development are being released in the embryo, and pole cells are also capable of receiving these instructions. For this reason, pole cells have the ability to maintain their germ cell characteristics by actively inhibiting the expression of genes that promote cells to be differentiated into the somatic cells" (see Fig. 3). In this way, Dr. Nakamura has discovered that Pgc, a maternal factor localized in germ plasm, is essential for the maintenance of the characteristics of pole cells. He is also conducting molecular analysis of this process.

The regulation of somatic cell gene expression within germ cells has, in addition to Drosophila, been demonstrated in *Xenopus*, ascidian, and *C. elegans*, and even in mice, which do not have the germ plasm; it therefore appears to be a universal phenomenon. "This shows that research undertaken from this sort of approach has the capacity not just to make discoveries about common principles of biological phenomena, but to help us to understand diversity," says Dr. Nakamura.

Drosophila has a genome size around 5% of that of humans, and yet they have a similar number of genes. A fly and a human may look very different, but on a genetic level they are not so far apart. "Things that we discover in flies can have huge ramifications for the health sciences. I certainly want to carry out further research trying to find out principle of life."

Germ cell development in *Drosophila melanogaster*

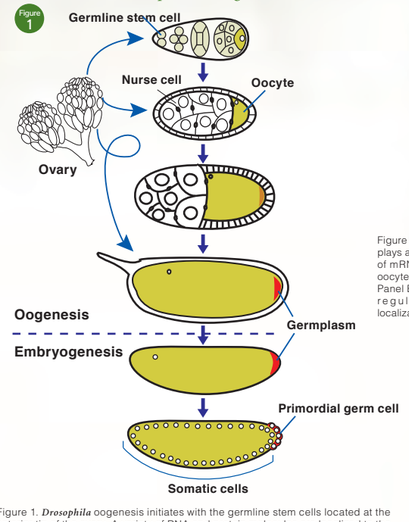

Figure 1. ***Drosophila*** oogenesis initiates with the germline stem cells located at the anterior tip of the ovary. A variety of RNA and protein molecules are localized to the posterior pole of the oocyte to form the germ plasm, a specialized cytoplasm. Only the cells preserving the germ plasm components can differentiate into primordial germ cells.

Localization of maternal mRNAs and the spatio-temporal regulation of their translation in germ plasm assembly

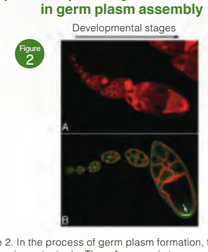

Figure 2. In the process of germ plasm formation, the ***oskar*** gene plays an important role. The ***oskar*** gene is transported in the form of mRNA (colored red in Panel A) to the posterior pole of the oocyte, where it is translated into Oskar protein (colored green in Panel B). Therefore, the functions of ***oskar*** are spatio-temporally regulated by subcellular mRNA localization and localization-coupled translational control.

Genome-wide repression of gene expression in germ cells during early embryogenesis

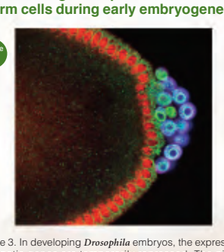

Figure 3. In developing ***Drosophila*** embryos, the expressions of zygotic genes are temporarily repressed. The picture represents a microscopic enlargement of the posterior side of an embryo at the blastoderm stage, with blue and green colors showing germ cells and nuclear membranes, respectively. At this stage of development, RNA polymerase II is activated only in somatic cell nuclei (red).

Teaching Staff

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Tsubasa Tanaka

Our bodies have a limited life span, and one day they will die, but life does not end with the death of the individual body; life will continue to survive. Germs cells—eggs and sperm—are the only type of cells that are able to support the transfer of life. In my work, I seek to further clarify the formative mechanisms of life, and I look forward to welcoming new researchers who wish to take up this challenge with us.