Freely changing Females and males

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[About my research]

There are females and males in many creatures. They look different. They also behave differently. Although they are the same species, they are different as if they were different species. If we talk "female" and "male" in an animal's context, it may sound like nothing to do with us. But, if we think of human males and females, we may realize how different they are.

How are two different gender species born, as if they are different species? It has been a great mystery for all ages and countries. And today. The issue of social gender (sex difference between men and women) is also a popular one. There are theories based on social structures and ideals that summarize the desires of individuals. But, we are human beings. Above all, we are living beings beforehand. Even if regenerative medicine and reproductive medicine are realized with iPS, and even if it brings added value (?) that humans do not have today, human beings cannot be more than living creatures. What, then, are the characteristics of sexuality as a living being? In considering gender, it is necessary to understand the unique aspects of females and males as living creatures.

Let's start with the origins of females (women) and males (men).

Most people know that if you have the Y chromosome, you become a male, and if you do not have the Y chromosome, you become a female. Many people also vaguely believe that a fertilized egg will produce a male if it has a Y chromosome. However, in many animals, the embryo (fetus) remains neither female nor male for some time after fertilization. Only at the late stage of the body-building process are formed the gonads, which will become either the future ovaries or the testes. In the cells of these gonads, sex is determined for the first time. Sex hormones are then secreted from the gonads, and other cells and tissues of the body differentiate into female or male. The brain also undergoes sex differentiation. In other words, each cell has sex and is made to respond and behave to sex. This process is the same in many animals. The same is true for Medaka (killifish), which we use in our research.

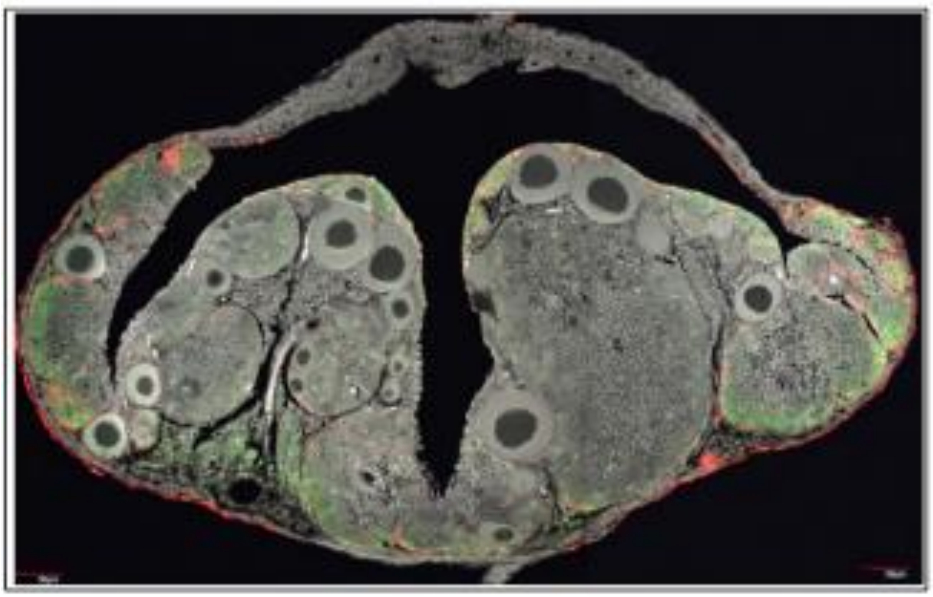
Like humans, Killifish become male if they have the Y chromosome and female if they do not. Killifish has a long history of sex research. It was first shown using Killifish that the Y chromosome has a functional gene that makes it a male. Killifish was the second species, after humans, of sex-determining genes identified. Although there is no difference in the primary

function of reproduction between females and males of killifish and that of men and women in humans, identifying the sex-determining gene in killifish has revealed that the sex-determining gene is entirely different from that of humans. The sex-determination gene is a switch on the Y chromosome that allows individuals to become males, and the switch can differ from animal to animal.

It has also been understood that even before this sex-determining gene is activated, the creature is already on standby to become either a female or a male. Males are not created from scratch after the switch is turned on. Moreover, even after the switch is turned on, the cells are still on standby to become the other sex. In other words, the embryo (fetus) does not end up once it becomes either a female (female) or a male (male), but it continues to maintain being a female (female) or a male (male) afterward. Moreover, if the body cannot remain comfortably in one sex, it has an internal mechanism to change to the other sex.

It is also revealed that the body has another sex-determining gene other than the sex-determining gene on the Y chromosome. The original cells that produce eggs and sperm (germ cells) have their own sex-switch genes. Usually, this gene works in conjunction with the sex-determining gene on the Y chromosome, so its presence is hidden. However, when the switch is intentionally manipulated, the germ cells become producing sperm in the ovary (Figure 1). The germ cells become male even when the body is female, and sadly for the man, the testes are not required if only we want to produce sperm.

Figure 1 Sperm cells produced in the ovary (tiny Petites are sperm cells. The germ cell sex switch was activated accordingly; Nishimura et al. 2015 Science).



It is also gradually revealed that these germ cells have tremendous power over just producing eggs and sperms. In killifish, it becomes clear that germ cells can turn the entire body into a female, even when the body with the Y chromosome turns the switch into a male (Figure 2).

Figure 2: Killifishes with a Y chromosome but became female due to germ cell power. The abdomen is swollen due to a large number of germ cells. (Morinaga et al. 2007 PNAS).

Apparently, cells have ability to freely change their sex according to the environment in which they are placed. This is probably why animals that change sex under nature were born in the process of evolution. Even animals that do not seem to change sex throughout their lives, including humans, seem to have this sex-generating characteristic working in various ways at the cellular level. Cells come together to form tissues and organs. These tissues and organs also collectively display sex characteristics, and their coordination is what establishes sex as an individual. Basic science is beginning to tell us that, even if we see one sex as either female or male, there are various degrees of sex.

Japanese Review etc.

Nishimura T., Tanaka M. Discovery of a Mechanism for Determining "Whether to be a Sperm or an Egg.
Clinical Immunology and Allergy, 2016, 65, 164-168.

Tanaka Minoru. Ability to change sex.
Iwanami Science Special Issue on “Science of Love and Sexuality,” July 2014

Tanaka M., Morohashi K. (eds.). Cellular Engineering February 2013. Special Issue on "New Developments in Sex Determination and Sex Differentiation that Bring the Dawn of Sex Difference Medicine.

Please refer to our laboratory's website for more specific information and original papers.
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