【Grant-in-Aid for Transformative Research Areas（B）】

Sex-chromosome cycle: Dissecting mechanisms of sex-extinction avoidance approaching from sex-chromosome turnover

Head Investigator	Tokyo Metropolitan University, Graduate School of Science, Assoc. Professor NOZAWA Masafumi　Researcher Number:50623534
Research Area Information	Number of Research Area : 22B304　Project Period (FY) : 2022-2024 Keywords : Sex determination, Recombination suppression, Sex-chromosome turnover, Y-chromosome degeneration, Y-chromosome loss

Purpose and Background of the Research

●Outline of the Research

Sex chromosomes are among major systems of sex determination. Y (or W) chromosomes are known to degenerate in general. Indeed, some researchers have predicted that the human Y chromosome will completely disappear within 14 million years, which may result in the loss of sexes and eventually lead to species extinction. How organisms have overcome this crisis during evolution? To tackle this question, five researchers who have studied the organisms with unique sex chromosomes built a research group and elucidate the mechanisms of sex-extinction avoidance under the degeneration of Y/W chromosomes (Fig. 1).

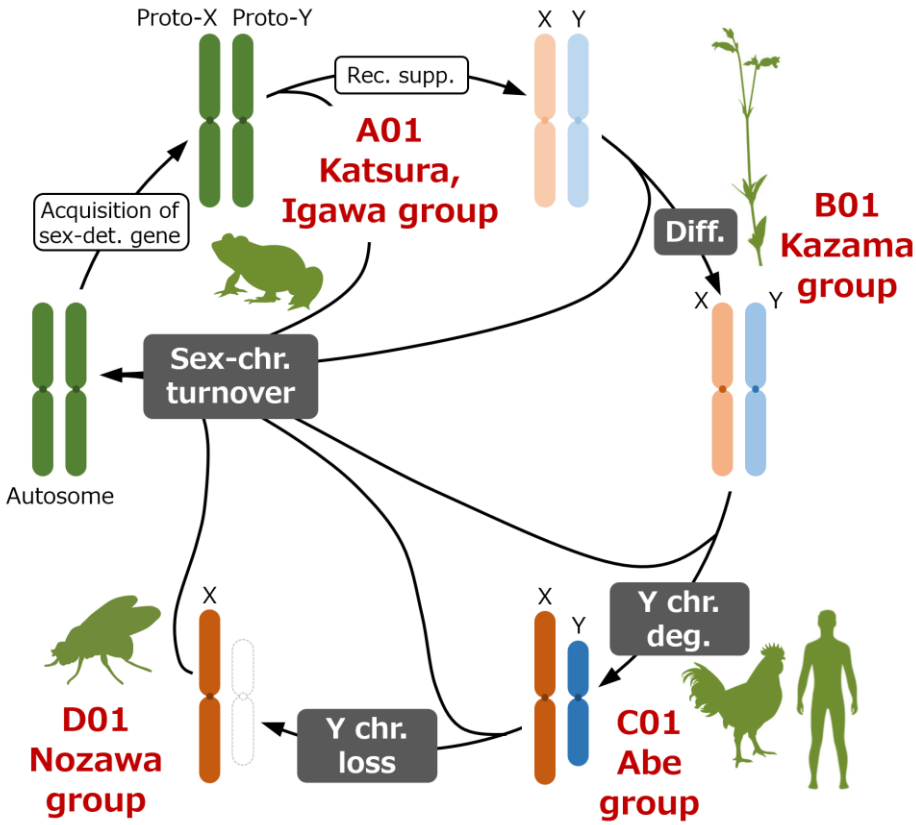

Figure 1. Four target sex-chromosome stages to be tackled in our research area

●Uniqueness of our research area

Five researchers from different areas (i.e., evolutionary genetics, molecular biology, plant morphology, bioinformatics, and conservation ecology) try to elucidate the mechanisms of sex-extinction avoidance with tight collaboration. Extensive comparison of nucleotide sequences will uncover the evolution of sex chromosomes in details. Also, evolution of sex chromosomes will experimentally be mimicked by completely removing sex chromosomes with sophisticated genome editing or partially deleting sex chromosomes with a heavy-ion accelerator.

Expected Research Achievements

●Research contents of each group

【A01 Katsura and Igawa: Turnover】

Identify the sex-determination genes in the two frog species with frequent turnover and clarify the mechanism of sex-extinction avoidance via turnover.

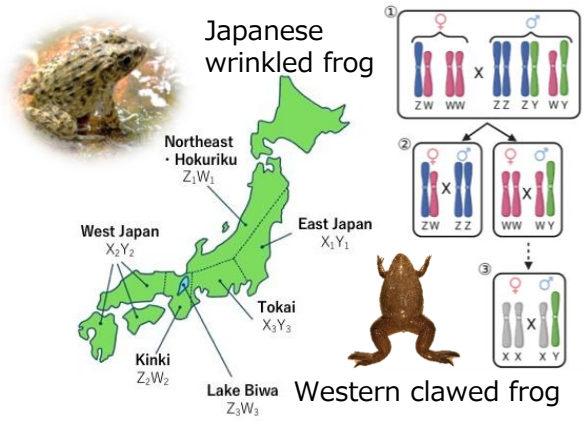

Figure 2 Distribution of karyotypes in Japanese wrinkled frog and the predicted path of karyotype evolution in western clawed frog.

【B01 Kazama: Differentiation】

Clarify how to enhance the mechanism of sex-extinction avoidance using the campion species, *Silene latifolia*, in which X and Y chromosomes have just started to diverge.

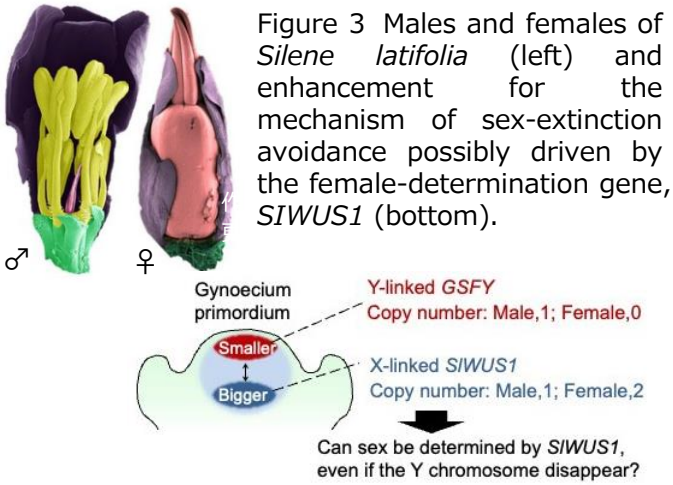

Figure 3 Males and females of *Silene latifolia* (left) and enhancement for the mechanism of sex-extinction avoidance possibly driven by the female-determination gene, *SIWUS1* (bottom).

【C01 Abe: Degeneration】

Uncover the mechanism of sex-extinction avoidance using cultured cells of humans and chickens with the degenerate Y and W chromosomes, respectively.

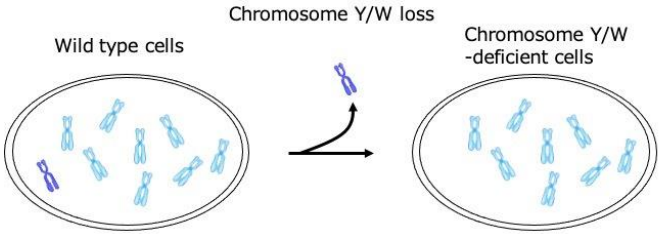

Figure 4 Comparison of Y/W-chromosome absent cells and wildtype cells.

【D01 Nozawa: Loss】

Elucidate genetic basis and evolutionary process that enabled to avoid sex extinction under Y chromosome loss using *Drosophila lacteicornis*.

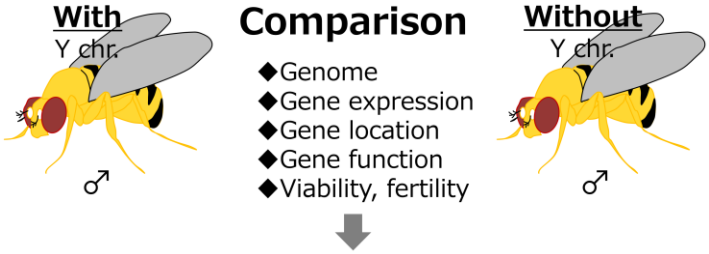

Figure 5 Comparison of males with and without Y chromosome.

Finally, we integrate outcomes from four groups and clarify the evolutionary process of sex chromosomes and the mechanism of sex-extinction avoidance that can be applied to a wide range of organisms.

●Future direction

Sex is determined by a variety of mechanisms, such as haplodiploidy in honeybees and temperature dependency in turtles. Each mechanism is also expected to have a cycle as in the case of sex chromosomes. Moreover, there must be a cycle even among the sex-determination mechanisms (e.g., temperature dependency → sex chromosome). Therefore, we plan to establish a research area focusing on "sexual reproduction cycle" in the future. We also plan to integrate evolution of sex chromosomes and autosomes that have enabled to evolve complex phenotypes such as mimicry through recombination suppression.

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