



Title of Project : Molecular Mechanisms for Establishment of Sex Differences

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【Purpose of the Research Project】

Many organisms develop into male and female sexes, and there are clear differences between them. These differences become more prominent over time and their development often spans from fetal stages into adulthood. The process of the sex differentiation can be divided into two steps. The first step involves gonadal development in the fetus, with differentiation of particular types of cells that synthesize sex steroids. At the following second step, sex differences are induced in a whole body by the functions of the sex steroids.

These two steps progress with spatio-temporal and hierarchical gene expression. Generally speaking, the first step occurs under the influence of 'genetic regulation' while the second step occurs mainly via 'endocrine regulation' with sex hormones. It is quite important to understand that a complex interaction between 'endocrine regulation' and 'genetic regulation' exists during the second step. We think that the mechanism of sex reversal would not be clarified without this viewpoint. Based on this, we aim to demonstrate molecular mechanisms for the establishment of sex differences to better understand the biological significance of the sexes.

【Content of the Research Project】

'Genetic regulation' and 'endocrine regulation' develop primarily molecular bases in establishing sex differences. As such, understanding both forms of regulation at the molecular level is critical in the context of our group research project. Moreover, given the considerable cross-talk between these two forms of regulation, it is important that the mechanisms by which they interact in sexual differentiation are understood.

The study of 'genetic regulation' will focus on the development of steroidogenic cells in the testis and ovary. The molecular basis for 'genetic regulation' will be elucidated by studying novel aspects, such as sex specific enhancers, sex specific structural changes in

chromatin, sex differences established after XY or ZW sex determination, and its molecular evolution.

The study of 'endocrine regulation' will focus on sex differentiation of the reproduction-related tissues after the sex steroids started to be secreted. Considering the integration of various stimuli in sex steroid stimuli, the general molecular basis of 'endocrine regulation' will be elucidated by examining components of nuclear receptor complexes. Collateral data from our study of 'genetic regulation' will demonstrate the epigenetic regulation for sex differentiation.

【Expected Research Achievements】

'Sex differences' are the nature of sexes, and the two sexes are matured with establishment of 'sex differences'. As the consequence, we acquired sexual reproduction, which has been discussed to result in evolution of variety of organisms. Accordingly, we think that an understanding of these differences will allow a deeper insight into the biological significance of the sexes as well as the diversity of organisms.

Neither domestic nor international collaborative group studies have yet been conducted in this field. Therefore, our group studies for sex differences based on the novel views will potentially lead to significant new insight in the scientific community, both domestically and abroad.

【Key Words】

Sex difference, Sex hormone, Sex specific gene expression

【Homepage Address】

<http://www.seisa.med.kyushu-u.ac.jp/>