

# Gene network for sex differentiation

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## **【 Outline of survey 】**

Organisms, which reproduce with a sexual process, have developed a system to transfer their genomic information through two highly specialized germ cells, the sperm and egg. This is the fundamental strategy for reproduction for propagation of a variety of species, and thus the mechanisms underlying sex differentiation is one of quite important and interesting subjects. We have investigated molecular mechanisms of the gonad (the testis and ovary) sex differentiation by focusing on functions of transcription factors, and succeeded to identify novel factors and their functions.

Moreover, based on an aspect that elucidation of a gene cascade developed by these genes is the next target, we have produced and collected gene disrupted and transgenic mice displaying gonadal abnormality, and have adjusted their genetic backgrounds. In this study, we will systematize relation of these genes by genetic analyses with these mice, and identify the substantial relationship with biochemical analyses. These studies will finally lead us to comprehensive understanding of the genetic bases for regulation of sex differentiation.

## **【 Expected results 】**

In the present study, we will investigate genetic relation between the genes essential for gonadal sex differentiation with a variety of gene disrupted and transgenic mice. However, it is quite difficult to clarify substantially the genetic relation only with the genetic analyses. Based on this notion, we have started to purify complexes containing transcription factors involved in gonadal development, which will allow us to understand the results obtained with the genetic studies at protein level. Through the two distinct studies, we believe that the genetic bases for regulation of sex differentiation will be elucidated.

## **【 References by the principal researcher 】**

Mutations of *Arx/ARX* cause abnormal migration and differentiation of GABAergic interneurons and abnormal development of testes in mice, and X-linked lissencephaly with abnormal genitalia in humans. Kunio Kitamura, Ken-ichirou Morohashi et al. *Nature Genet.* **32**, 359-369, 2002

**【 Term of project 】** FY 2004 - 2008

**【 Budget allocation 】** 90,000,000 yen

**【 Homepage address 】** <http://www.nibb.ac.jp/%7Eceldif/>