【Grant-in-Aid for Scientific Research(S)】
Integrated Science and Innovative Science (New multidisciplinary fields)

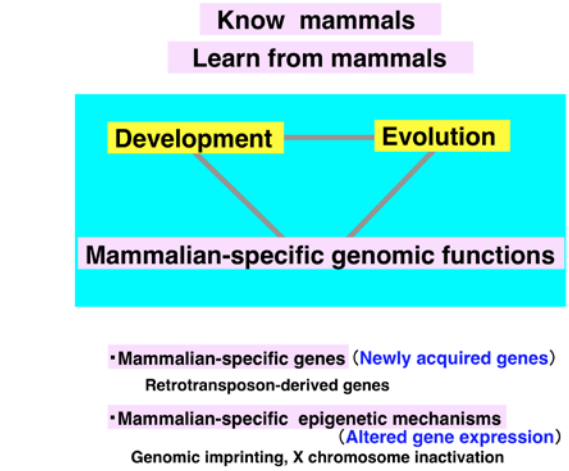
Title of Project：Mammalian-specific genomic functions

Fumitoshi Ishino
（Tokyo Medical and Dental University, Medical Research Institute, Professor）

Research Area：New multidisciplinary
Keyword：Genomic function, Genome evolution

【Purpose and Background of the Research】

Viviparity and placentation are representative characters in mammalian reproduction system. We have recently demonstrated that two retrotransposon-derived genes specific to mammals, *Peg10* and *Peg11/Rtl1,* play essential roles in placenta formation and functions. These are paternally expressed imprinted genes relating early embryonic lethality and late fetal/neonatal lethality, respectively. Genomic imprinting is one of mammalian-specific epigenetic mechanisms and known to be essential for mammalian development. How this mechanism emerged and how these mammalian-specific genes are acquired from retrotransposons? These questions are related to the origin or evolution of the mammals. The aim of this project is to dissolve these questions.



【Research Methods】

Our project comprises four subjects as below:

1. Biological function of *Peg10*: identification of functional domain of Peg10 protein and production of parthenogenons in mice.
2. Role of *antiPeg11/Rtl1*: biological functions of essential miRNAs in *antiPeg11/Rtl1.* Its roles in human pUPD14 and development of new miRNA therapy.
3. Biological function of *Sirh* genes: Analyses on *Sirh3*, *4-6*, *7* and *9* knockout mice.
4. Reprogramming of genomic imprinting memories in germ cells: molecular mechanism of DNA demethylation in PGCs.

【Expected Research Achievements and Scientific Significance】

Elucidation of evolution of mammals, a part of our history as human beings. Elucidation of the meechanism of epigenetic reprogramming for promoting regenerative medicine.

【Publications Relevant to the Project】

1. Kaneko-Ishino T and Ishino F. Retrotransposon silencing by DNA methylation contributed to the evolution of placentation and genomic imprinting in mammals. Develop Growth Differ **52**(6), 533-543 (2010).
2. Sekita Y, Wagatsuma H, Nakamura K, Ono R, Kagami M, Wakisaka-Saito N, Hino T, Suzuki-Migishima R, Kohda T, Ogura A, Ogata T, Yokoyama M, Kaneko-Ishino T and Ishino F. Role of retrotransposon-derived imprinted gene, *Rtl1,* in the feto-maternal interface of mouse placenta. Nat Genet **40**(2), 243-248 (2008).
3. Ono R, Nakamura K, Inoue K, Naruse M, Usami T, Wakisaka-Saito N, Hino T, Suzuki-Migishima R, Ogonuki N, Miki H, Kohda T, Ogura A, Yokoyama M, Kaneko-Ishino T and Ishino F. Deletion of *Peg10,* an imprinted gene acquired from a retrotransposon, causes early embryonic lethality. Nat Genet **38**(1), 101-106 (2006).

【Term of Project】 FY2011-2015

【Budget Allocation】 165, 200 Thousand Yen

【Homepage Address and Other Contact Information】

http:// www.tmd.ac.jp/mri/epgn/index.html
fishino.epgn@mri.tmd.ac.jp