The collaboration research for the Dual Graduate School between VNU and JAIST

[Title of collaboration research]: Identifying the key genes and elucidating the cellular mechanism during the cardiac commitment.

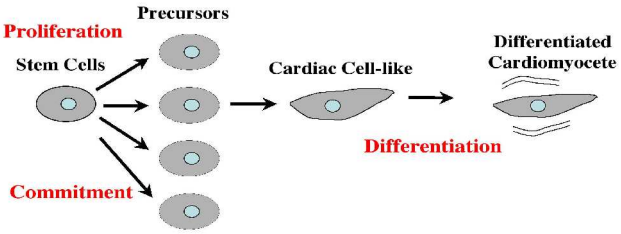
[The members of collaboration research]: Toshifumi Tsukahara

[Reference home-page address]: http://www.jaist.ac.jp/nmcenter/labs/tsukahara-www/

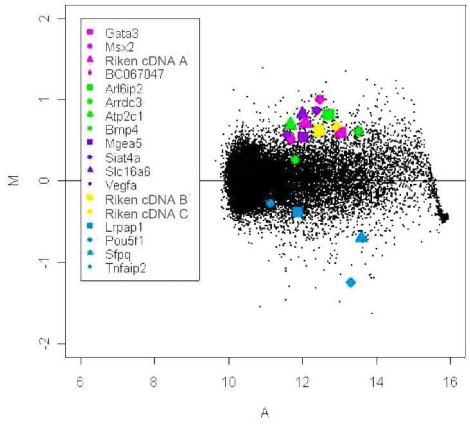
[Other references]: M. Taniguchi, H. Kurahashi, S. Noguchi, T. Fukudome, T. Okinaga, T. Tsukahara, Y. Tajima, K. Ozono, I. Nishino, I. Nonaka, T. Toda: Aberrant neuromuscular junctions and delayed terminal muscle fiber maturation in a-dystroglycanopathies. Hum.Mol.Genet (2006) in press

A. Shinozaki, K. Arahata, T. Tsukahara: Changes in expressions of splicing factors during the neuronal differentiation of P19 embryonal carcinoma cells. *Int.J.Biochem.Cell Biol.* (1999) **31**, 1279-1287.

[Contents] The embryonic stem (ES) cells give rise to cells of different fates including those of cardiomyocytes. Through their differentiation process, various genetic events occur to direct the fate of the undifferentiated ES cells into specific cell types. This fate determination process, called "cardiac commitment," is regulated by various genes and signaling molecules that interact in a complex manner to alter the morphologies of the undifferentiated cells. However, how these genes and signaling molecules are connection and the way they direct the fate of undifferentiated cells into cardiomyocytes is not completely known. Currently, under the *in vitro* conditions, the rate in which the undifferentiated ES cells differentiate into cardiac cells is very low, and the resulting population is heterogeneous to include a variety of cell types. Due to the inclusion of cells that are not cardiac, it is problematic when this kind of cells is used for therapeutic purposes, such as cell transplantation for cardiovascular diseases. In order to avoid this problem, the mechanism in which the undifferentiated cells become cardiac cells must be understood to facilitate the efficient differentiation process. To elucidate this mechanism, it is important to profile the expression changes that occur before and after the cardiac commitment and to identify the genes, which expressions changed significantly during the critical time point of the differentiation.



P19CL6 is a subline of pluripotent P19 embryonal carcinoma cells. Under the adherent conditions and upon the induction by dimethyl sulfoxide, spontaneous beating starts after ten days, and the differentiated cells exhibit the characteristics of cardiomyocytes, including a striated structure. Unlike the parental cell line, P19, and ES cells, P19CL6 cells efficiently differentiate into cardiomyocytes. Because of this reason, this cell line is used in this study to identify the key genes and elucidate the mechanism of the cardiac commitment.



Gene expression analysis during cardiac differentiation.