

Molecular Basis during iPS Cell Generation and Its Application

Shinya Yamanaka

2010 Balzan Prize for Stem Cells: Biology and Potential Applications

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Shinya Yamanaka is Director of the Center for iPS Cell Research and Application (CiRA) and Scientific Advisor at the Institute for Integrated Cell-Material Sciences (iCeMS) at Kyoto University, Senior Investigator at the Gladstone Institute of Cardiovascular Disease in San Francisco, and Professor of Anatomy at the University of California, San Francisco. Yamanaka has planned a five- to six-year research project on molecular mechanisms and application of induced pluripotent stem (iPS) cells at the Center for iPS Cell Research and Application (CiRA) at Kyoto University. CiRA hired one young faculty member, Dr. Saito to promote the research to control cell fate using synthetic RNA-based gene manipulation technologies. His laboratory developed unique synthetic RNA molecules in order to detect and purify target cells derived from iPS cells and control the fate of target cells depending on intracellular environment. He was responsible for the following research projects: developing new methods to control mammalian cell fate with high safety and purity using artificial RNA switches and circuits. These RNA systems detect specific protein and/or RNA expressed in target cells and then control gene expression.

Advances made in fiscal year 2015 included the successful development of synthetic “microRNA switches” that points to next-generation technology for control of gene expression and stem cell engineering. In their latest work, the Saito group developed a method that makes it possible to detect and purify target live cell populations derived from human iPS cells. In addition, the Saito group succeeded in constructing synthetic gene circuits that selectively control the cell fate by RNA-only delivery. Because these

circuits are entirely RNA-based, they would be safer to use in cells than their DNA-based counterparts and therefore available for a number of biomedical applications.

In early 2013, Shinya Yamanaka decided to use his prize to spread iPS cell research over institutes other than CiRA with Dr. Aoi at Kobe University to study recapitulation of several intractable diseases, including cancer by iPS cell technology. In 2013, a new laboratory for the Aoi Group was built at the Kobe University graduate school of medicine. The basic arrangement of the study environment and the measures for regulations with which the iPS cell establishment or induction to various cell differentiation can be conducted have already reached completion. Until fiscal year 2015, various projects in collaboration with more than 10 clinical departments have been launched to cure intractable diseases.

Aoi group also focuses on cancer stem cells, which have been suggested to be the potential for self-renewal and tumorigenesis in certain cancers. To start off, inspired by iPS cell technology, Aoi's group successfully established a novel technology to induce cancer stem cell (CSC) properties in intestinal cancer cells by introducing defined factors and collecting the cells with CSC properties, which leads to a further understanding of cancer disease mechanisms and medical applications. Currently, in addition to working on generation and analyses of induced cancer stem cells from various types of human cancer cells, they are also constructing various carcinogenesis models using several types of human iPS cell-derived cells.

Publications

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