【Grant-in-Aid for Scientific Research(S)】

Integrated Science and Innovative Science (Comprehensive fields)

Title of Project : Regulation of functions and differentiation of ES/iPS cells by designing cell-recognizable chimera matrices

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Research Area : Biomedical engineering/ Biological material science

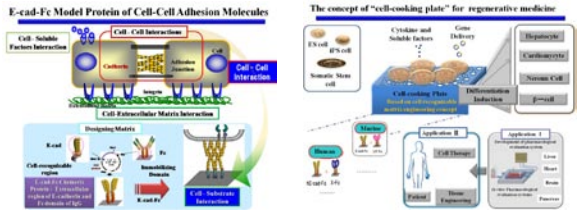
Keyword : Materials for regenerative medicine and engineering, Cell-cooking plate, E-cadherin-Fc, ES/iPS cells, Matrix engineering

【Purpose and Background of the Research】

Pluripotent stem cells (ES/iPS cells) are considered to hold great promise in regenerative medicine. However, most of the studies reported that proliferation of undifferentiated state and induced differentiation of somatic cells from ES and iPS cells have been based on cell-cell aggregated colony culture system. In which, stimulating factors fail to interact with all cells homogeneously and directly in the same time, leading to generate heterogeneous cell population system.

To overcome these problems, we purposed in this project to establish a novel uniform single cell level culture system for controlling ES/iPS cells functions and differentiation process based on E-cad-Fc chimeric protein which was developed as a new type of extracellular matrix for modeling cell-cell adhesion molecules of E-cadherin in our labratory. Previously, we reported the possibility of highly efficient and homogenous differentiation induction of hepatocytes and cardiomyocytes from ES cells at single cell level, less stress and *Xeno*-free conditions. Recently, based on 30 years experience of designing cell recognizable matrix for tissue engineering and artificial organs, we proposed a new concept which was named “cell-cooking plate” and expected to be widely applicable in the fields of regenerative medicine and bio-artificial organs. Utilizing the concept of “cell-cooking palate”, we aimed to develop novel cell culturing system for regulating pluripotent ES/iPS cells functions and the differentiation process to somatic cells.

【Research Methods】



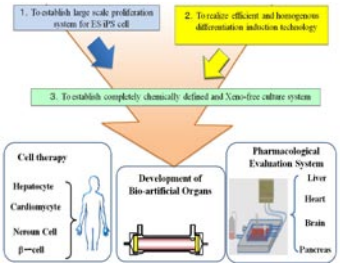
First of all, we will establish large scale culture system for undifferentiated ES/iPS cells based on E-cad-Fc protein. Subsequently, we will complete chemically defined culture system for human ES/iPS cells in the first year. In the second year, we will realize high efficient homogeneous differentiation induction system to hepatocytes and cardiomyocytes from human ES/iPS cells through delivering specific gene and co-immobilizing certain bioactive stimulating factor with E-cad-Fc matrix. Moreover, we will establish purification system of objected somatic cells through combining E-cad-Fc and other cell recognizable matrix to provide clinically applicable culture system and objected cells.

【Expected Research Achievements and Scientific Significance】

The following research achievements are expected in this project.

To generalize single cell level culture system of ES/iPS cells based on E-cad-Fc protein

To establish large scale proliferation culture system for undifferentiated ES/iPS cells.



To realize efficient homogenous induction system at single cell level for ES/iPS cells.

To complete chemically-defined and *Xeno*-free culture system.

【Publications Relevant to the Project】.

- Nagaoka M, Koshimizu U, Akaike T et al: E-Cadherin-Coated Plates Maintain Pluripotent ES Cells without Colony Formation. PLoS ONE., **1**: e15, 2006.
- Haque, A. Hexig, B. Akaike, T. et al: The effect of recombinant E-cadherin substratum on the differentiation of endoderm-derived hepatocyte-like cells from embryonic stem cells. Biomaterials., 32 2032-2042, 2011.

【Term of Project】 FY2011-2014

【Budget Allocation】 157,300 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.akaike-lab.bio.titech.ac.jp/akaike/english/index.html