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

Title of Project : Creation of Binding Growth Factors by Molecular Evolutionary Engineering and their Medical Applications

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Research Area : Biomaterials

Keyword : Regenerative Medicine, Tissue Engineering

【Purpose and Background of the Research】

To achieve regenerative medicine, it is necessary to create bioactive materials. We found that chemically immobilized growth factor proteins could control the growth and differentiation of cells on material surfaces. In the present study we will create new binding growth factors for development of new medical materials.

We will develop and establish peptide evolutionary engineering method for creation of new proteins binding to organic, metallic, ceramic, and biological materials. The proteins will be employed for modifications of medical materials or drugs.

In addition, extended molecular evolutionary engineering will be accomplished by using non-canonical amino acids. By utilizing this technology, we will obtain more specific and highly binding growth factors.

【Research Methods】

First we will establish peptide evolutionary engineering and will prepare new binding growth factor proteins by the developed methodology. Subsequently the biological activity will be investigated using cell lines culture and animal experiments.

Preparation of new binding growth factors

Random sequence peptide library will be produced by transcription and translation using cell-free system from random sequence DNA library.

From this library some specific sequences will be determined by in vitro selection for target substrata including synthetic polymer, natural polymer, ceramic, metal, cell, and tissue.

Extended molecular evolutionary engineering

Extended peptide evolutionary engineering using non-coding amino acids will be established for selection of highly and selectively binding affinity.

Biological evaluation of novel proteins

The binding affinity of prepared proteins to organic, ceramic, metallic, and biological materials will be precisely investigated by physico-chemical methods.

The biological activities such as growth enhancement and differentiations control of prepared growth factors will be investigated using several cell lines. In addition, the biding domains and growth factor domains will be variously combined for optimal effect. Finally the binding growth factors will be investigated by animal experiments and considered for medical applications.

【Expected Research Achievements and Scientific Significance】

For regenerative medicine it is important to precisely control of stem cells and construct matrices for tissue formation. In this study a new peptide evolutionary engineering and its extension will be achieved by incorporation of artificial amino acids. By the new methodology we will stabilize growth factors for a long time and allow the materials bio-active for new medical applications.

【Publications Relevant to the Project】

T. Kitajima, H. Hasuda, M. Sakuragi, T. Ozu, and Y. Ito, “A chimeric epidermal growth factor with fibrin-affinity promotes repair injured keratinocyte sheets,” ***Acta Biomater.***, **5**, 2623-2632 (2009)

Y.Ito, “Covalently immobilized biosignal molecule materials for tissue engineering,” ***Soft Matter***, **4**, 46-56 (2008)

【Term of Project】 FY2010-2014

【Budget Allocation】 167,600 Thousand Yen

【 Homepage Address and Other Contact Information】

http://www.riken.jp/engn/r-world/research/lab/wako/medical/index.html