Development of novel therapy in regenerative medicine by application of human laminins produced in yeast

Yasuo Kitagawa

(Nagoya University, Graduate Schhol of Bioagricultural Sciences, Professor**)**

【Outline of survey】

Stem cell studies are in rapid progress in regenerative medicine. However, such studies lack the viewpoint of extracellular matrix (ECM). We should not forget that animal tissues are composed of cells and ECM. Especially for mesemchymal tissues as the target of regenerative medicine, we should bare in mind the image that cells are migrating among the meshwork of ECM. We have shown that migration, proliferation and differentiation of endogenous stem cells can be manipulated only by injecting ECM and have suggested a novel method of tissue regeneration without transplantation of stem cells. In this project, we will develop the technique of industrial production of human laminins in large amount enough for clinical application. Facing to the complicated and huge structure of laminins stabilized by interchain disulfide-bonding between a, b and g chains and added with many N-glycan chains, researches have tried the production only in cultured animal cells despite the high cost and low yield. In such approach, we need to be afraid of contamination of the product by pathogens common to human and animal cells. In this project, we aim the development of novel therapy in regenerative medicine by application of human laminins produced by industrial technique.

【Expected results】

This project is unique in aiming industrial production of human laminis that can activitate endogenous stem cells for the tissue-regeneration. For regeneration of large mesenchymal organs such as bones, cartilages, muscles and adipose tissues, technology of laminin-production with a scale of gram/therapy will be needed. For this, we are developing methods of laminin-production in cultured yeast and by cell-free translation of mRNAs. Once cheep and safe human laminins will became available for the clinical uses, they may change the present situation of regenerative medicine.

【References by the principal researcher】

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• Yamashita H, Beck K, Kitagawa Y. Heparin binds to the laminin alpha4 chain LG4 domain at a site different from that found for other laminins. ***J Mol Biol.*** 2004;335:1145-1149.

【Term of project】 FY2006－2009	【Budget allocation】19,500,000 yen

【Homepage address】 http://www.agr.nagoya-u.ac.jp/~tagen/KitagawaG(Eng).html