Comprehensive study on molecular basis of action of CCN family proteins as novel signal conductors and its translational application

Masaharu Takigawa
(Okayama University, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Department of Biochemistry and Molecular Dentistry, Professor)

【Outline of survey】

CCN (**C**yr61: cysteine-rich protein 61, **C**TGF: connective tissue growth factor, **N**ov: nephroblastoma over-expressed) family proteins are expected to be useful in promoting harmonized tissue regeneration without adverse effects, because one of the family proteins, CCN2, is capable of inducing tissue regeneration in a quite natural fashion. To understand the molecular mechanism of its action, we wish to test our novel concept that CCN family proteins should be considered a relatively newly classified signaling molecules that comprehensively regulate extracellular signals, and thus may be entitled "Signal Conductors." Thereafter, on the basis of the initial research outcome, we will perform translational research on optimized regenerative medicine and pathobiology of and new therapeutics against intractable diseases such as fibrotic disorders that are thought to result from the over-expression of CCN proteins.

【Expected results】

1) Our new concept of signaling network that webs from gene expression to biological outcome will be validated.
2) The role of CCN family proteins as signal conductors in the regulation of tissue development and body growth will be clarified for further application toward regenerative therapeutics.
3) CCN-targeted therapeutics to combat the dysfunctional CCN protein production involved in fibrotic disorders, atherosclerosis, and certain malignancies will be engineered.

【References by the principal investigator】

1) Perbal, B. and Takigawa, M. (eds): CCN Proteins : A New Family of Cell Growth and Differentiation Regulators. pp. 1-311, Imperial College Press (London), 2005.
2) Kondo, S., Kubota, S., Mukudai, Y., Moritani, N., Nishida, T., Matsushita, H., Matsumoto, S., Sugahara, T. and Takigawa, M.: Hypoxic regulation of stability of connective tissue growth factor/CCN2 mRNA by 3'-untranslated region interacting with a cellular protein in human chondrosarcoma cells. Oncogene, 25(7): 1099-1110, 2006.

【Term of project】 FY2007 − 2011

【Budget allocation】 26,100,000 yen
(2007 direct cost)

【Homepage address】 http://www.dent.okayama-u.ac.jp/seika/index_sc_j.html