

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

Biological Sciences (Medicine, Dentistry, and Pharmacy)



Title of Project : Development of Innovative Treatment Targeting the Sphere Formation Mechanism Involving Cancer Stem Cells

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Research Project Number : 15H05792 Researcher Number : 80165662

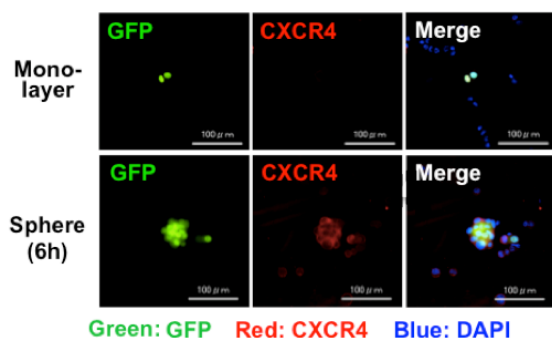
Research Area : Medicine, Dentistry and Pharmaceutical Sciences

Keyword : Cancer, Surgery, Cell/Tissue, Drug Responsiveness, Translational Research

【Purpose and Background of the Research】

Recurrence of cancer is explainable if we assume the existence of cancer stem cells (CSCs) that are resistant to various therapies. One of the typical CSC research methods is the sphere formation assay, however, the specific molecular mechanism of cancer cell transformation resulting from sphere formation is unknown. In this research project, we will advance and accelerate sphere biology to elucidate the mechanism of sphere formation that makes cancer an intractable disease, with the aim of its therapeutic application (Figure 1).

Figure 1 Sphere formation and expression of CXCR4



CXCR4 was detected by immunohistochemistry.

【Research Methods】

- 1) The molecular biological mechanism of sphere formation will be elucidated. A molecule essential for sphere formation will be identified using a comprehensive method based on transcriptome, proteome, and metabolome analyses. A comprehensive search for inhibitors of sphere formation will be carried out using chemical libraries.
- 2) The relationship between changes after sphere formation and cancer stem cells will be elucidated. Downstream signals, genetic and epigenetic changes, and gene expression following sphere formation will also be analyzed.
- 3) Analysis will be performed using clinical samples. At our department and the institutions of co-collaborators, malignant tumor samples from

tumor organs are systematically stored. Using these samples, expression analysis of the target molecule(s) identified through the above-mentioned research will be performed.

4) An innovative treatment modality for the inhibition of sphere formation will be developed.

【Expected Research Achievements and Scientific Significance】

This research is unique in that its achievements can be applied both directly and indirectly to the fields of cancer stem cell research and regenerative medicine through an understanding of the new concept of “sphere biology” from a molecular biological perspective. In this research project, clarification of the relationship between sphere formation and cancer stem cells, identification of cancer stem cell niches, and analysis of these molecular biological characteristics will allow for the identification of therapeutic target molecule(s) to zero in on cancer stem cells and destroy them. In addition, the combination of such molecule(s) with existing treatments can be a potential breakthrough in cancer treatment.

【Publications Relevant to the Project】

- Taniguchi K, Maehara Y, et al. A gp130-Src-YAP module links inflammation to epithelial regeneration. *Nature*. 2016; 519:57–62.
- Morodomi Y, Maehara Y, et al. BioKnife, a uPA activity-dependent oncolytic Sendai virus, eliminates pleural spread of malignant mesothelioma via simultaneous stimulation of uPA expression. *Molecular Therapy*. 2012; 20:769–77.

【Term of Project】 FY2015-2019

【Budget Allocation】

144,000 Thousand Yen

【Homepage Address and Other Contact Information】

<http://www.kyudai2geka.com>