【Grant-in-Aid for Scientific Research(S)】
Biological Sciences (Medicine, dentistry, and pharmacy Ⅱ)

Title of Project : Integrative approaches toward the development of next-generation therapeutics for myocardial infarction.

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Research Area : Medicine, Dentistry, Pharmacology

Keyword : Molecular Cardiovascular Science

【Purpose and Background of the Research】

Myocardial infarction, commonly known as heart attack, is a leading cause of death for men and women in all industrialized countries in the world. Myocardial infarction is caused by blockage of the coronary artery, one of the major arteries in the heart. This condition leads to the oxygen- and nutrients-deprivation of the heart, which then causes cardiac muscle cell death, and eventually results in cardiac dysfunction.

There are three major therapeutic approaches to treat myocardial infarction. The first is to regenerate cardiac muscle cells. Another way is to induce new blood vessel formation to enhance oxygen and nutrients delivery to the damaged heart (i.e., therapeutic angiogenesis). The last, but not the least, is to partially suppress cardiac fibrosis, the scar tissue formation in the damaged heart. The scar in the heart, not only causes the defects in the cardiac functions, but also interferes with the cardiac muscle regeneration and the new blood vessel formation.

Development of therapeutics based on each of these individual approaches has been extensively pursued. However, very few studies have been successful in integrating these three approaches to develop effective therapies to treat myocardial infarction. To achieve this goal, we propose the following two specific aims.

Aim 1. To uncover mechanisms by which three major pathological processes in myocardial infarction (i.e.. cardiac muscle death, blood vessel formation, and fibrosis) are orchestrated.

Aim 2. To develop a new and effective integrative approaches to treat myocardial infarction by accomplishing three major therapeutic goals (cardiac muscle regeneration, therapeutic angiogenesis and controlling fibrosis).

【Research Methods】

We will use biochemical and cell biological methods in combination with mouse and zebrafish models to accomplish our proposed goals. We also use these methods and animal models to develop gene therapy methods, to screen and identify small chemicals, and to identify molecular targets, which will be useful to accomplish our therapeutic goals to treat myocardial infarction.

【Expected Research Achievements and Scientific Significance】

It is expected that our integrative approaches will lead to the invention of new therapeutics to effectively treat myocardial infarction (Fig.1). Thus, our successful accomplishment of the proposed research goals contributes to improving our health.

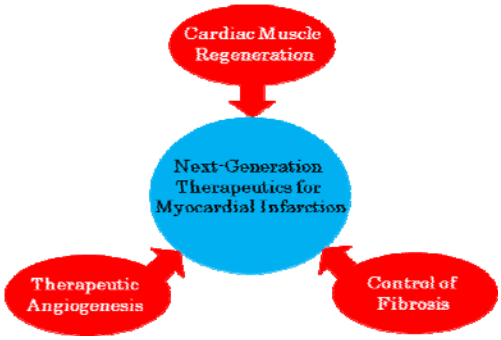

Fig. 1. Integrative approaches toward the development of next-generation therapeutics for myocardial infarction.

【Publications Relevant to the Project】

- K. Kobayashi, et. al., (2009) Secreted Frizzled related protein 2 is a procollagen C-proteinase enhancer with a key role in fibrosis associated with myocardial infarction. Nature Cell Biol. 11:46-55.
- R.P. Visconti, et. al., (2002). Orchestration of angiogenesis and arteriovenous contribution by angiopoietins and vascular endothelial growth factor (VEGF). Proc. Natl. Acad. Sci. USA 99: 8219-8224.

【Term of Project】 FY2010-2014

【Budget Allocation】 127, 400 Thousand Yen

【Homepage Address and Other Contact Information】

http://bsw3.naist.jp/tns/