FUNDING PROGRAM FOR NEXT GENERATION WORLD-LEADING RESEARCHERS

Project Title: Research project on the establishment of novel non-invasive therapy for siRNA-induced vasculogenesis by use of nano-size drug delivery system	
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1. Background of research

Over the last four decades, Japanese food customs and culture have dramatically changed to become more westernized. As a result, in a rapidly aging population, lifestyle diseases (such as high blood pressure, heart disease, diabetes, obesity, etc.) are now rampant in Japan and have become serious social problems.

In order to treat peripheral blood flow obstruction, produced for example by arteriosclerosis, a common severe lifestyle disease, medical treatments involving high invasiveness (i.e. surgical load to patients) are mainly carried out. **It would be a great advantage if state-of-the-art medical technology could be employed to develop novel treatments for these conditions with low invasiveness.**

2. Research objectives

The first aim of this research project is to establish a reformative treatment method to improve blood flow obstruction with minimal invasiveness and therefore 'relief' and greater 'safety' to patients. The second aim is to determine the clinical efficacy of such a treatment in early stage clinical trials.

3. Research characteristics (incl. originality and creativity)

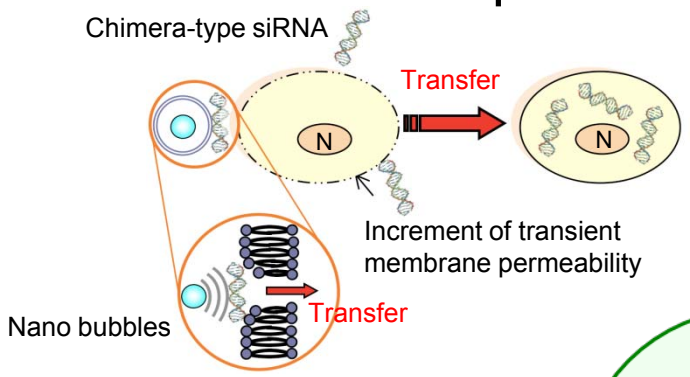
Combining supersonic waves and nano-size bubbles (i.e. small bubbles with diameters of hundreds of nanometers), we will deliver extracellular materials (such as drugs, genes, proteins, etc.) into cells using potent shock waves. This method is generally termed '<u>sonoporation</u>'. Using sonoporation, novel nucleic acid drugs (i.e. architectural components of DNA and RNA), which are specifically coded to produce vasculogenesis, can cross the membrane and alter cellular functions. By modifying vasculogenesis-gene information in the nucleus, through <u>small interference RNA (siRNA) mechanisms</u>, new blood vessels will be produced. In the present project, the improvement of peripheral blood flow through new blood vessels will be studied at both cellular and organ levels using functional and morphological analyses. We will also investigate the effects of siRNA drugs in blood flow obstructed rat models to determine the extent of the improvement in ischemic conditions.

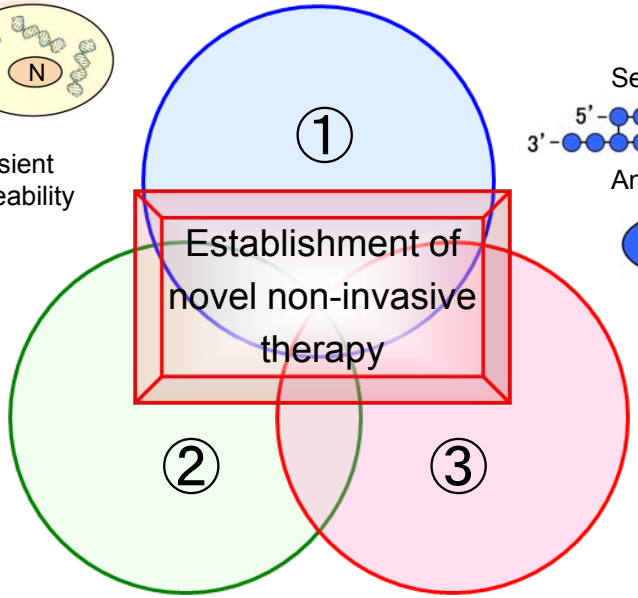
4. Anticipated effects and future applications of research

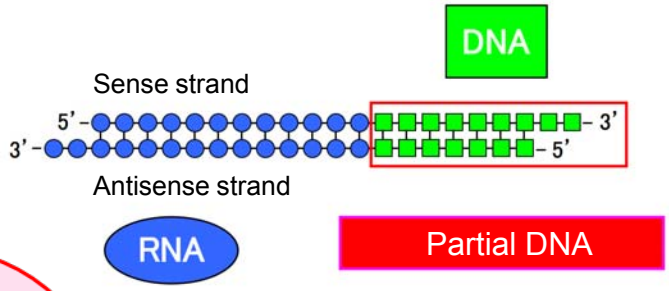
The method developed will provide a significant ancillary therapy in several new fields of modern medical treatments (such as organ transplants, regenerative medicine, etc.). It is probable that the method will greatly shorten the time before improvement of blood flow occurs and also facilitate wound healing. Such an approach with minimum invasiveness can only be of great national benefit to the welfare of the Japanese population.

Novelty and originality of the project

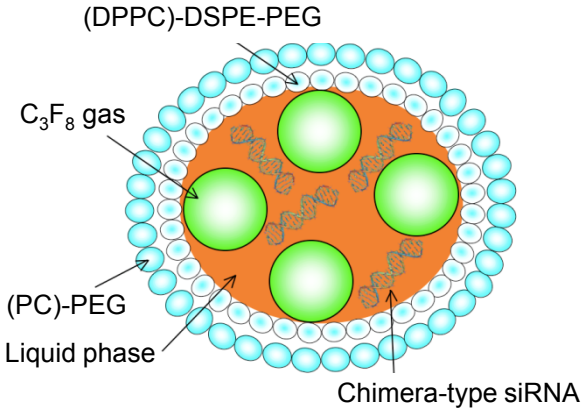
① Chimera-type siRNA introduction by use of sonoporation with minimum invasiveness







② Novel hybrid-type nano-bubbles



③ Vasculogenesis, targeting HIF-2α inhibitory transcript factor, Int6