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

Integrated Disciplines (Complex systems)

Title of Project : Design of Novel Biomaterials which Scavenge Reactive Oxygen Species and Their Applications

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Research Area : Biomedical engineering/ Biological material science
Keyword : Biomaterials, Nanobiomaterials, Drug Delivery System

【Purpose and Background of the Research】

When materials are applied to living body as biomaterials, medical devices or artificial organs, they cause versatile responses. One of the most significant phenomena between material and living body interaction is generation of reactive oxygen species (ROS). ROS are known to play versatile roles on the occasion of many important events in vivo. However excessive production of ROS causes significant adverse effects to living body. In this project, we are focusing on design of new polymeric materials, which scavenge ROS. For this objective, nitroxide radical is employed as a catalytic center. Several types of nitroxide radical polymers (redox polymers, Fig. 1) will be designed and investigated their functionality in vitro and in vivo.

【Research Methods】

We have so far prepared amphiphilic block copolymers possessing nitroxide radicals as a side chain of its hydrophobic segment, which spontaneously form core-shell type polymeric micelle under physiological conditions. The redox nanoparticle (RNP) thus obtained have confirmed to work as in vivo ROS scavenger for several types of diseases such as cerebral and renal ischemia reperfusion injuries and ulcerative colitis. In this project, we will further study these redox polymers not only as nanomedicines for other oxidative stress-related diseases but also as other biomaterials. Redox polymer micelle mentioned above will be applied for several chronic diseases such as arteriosclerosis, non-alcoholic steatohepatitis, rheumatism and Alzheimer's diseases. We will design new redox injectable gel for periodontal disease and joint inflammation. The gel formation properties improve local retention of these materials and long-term scavenge of ROS. Silica-installed RNP (siRNP) will be prepared for peritoneal dialysis and bioadsorbents. Silica increases absorption capacity of low molecualar wright wastes in addition to the ROS scavenging ability. Surface modification by redox polymers will be investigated for non-biofouling and cell culture surfaces.

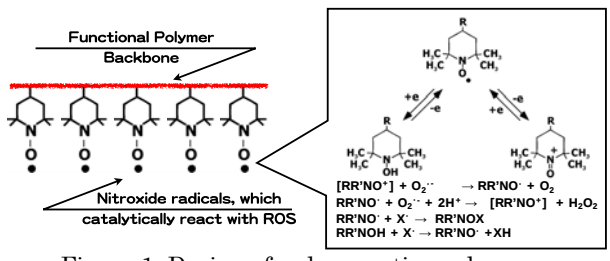

Figure 1. Design of redox reactive polymers

【Expected Research Achievements and Scientific Significance】

Important point of this work is to explore how nitroxide radical containing polymer works as nanomedicines and also as biomaterilas. Because it is not low molecular weight drugs, distribution of these materials in vivo is significantly different. Since they are not internalized in mitochondria in cell, for example, they do not interfere the normal mitochondrial electron transport chain, which is important energy production process in vivo. Since activation of bio-components such as proteins, cells and tissues often occurs when contact with materials, the ROS scavenging polymers are also promising as biomaterials including surface modification agents. Several types of novel biomaterials including nanomedicines will be anticipated in this project.

【Publications Relevant to the Project】

・Long Binh Vong, et al., An Orally Administered Redox Nanoparticle that Accumlates in the Colonic Mucosa and Reduces Colitis in Mice, ***Gastroenterology***, Vol.143, No.4, 1027-1036(2012).
・Yukio Nagasaki, Nitroxide radicals and nanoparticles: A partnership for nanomedicine radical delivery, ***Therapeutic Delivery***, 3(2) 1-15(2012)

【Term of Project】 FY2013-2017

【Budget Allocation】 167,600 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.ims.tsukuba.ac.jp/~nagasaki_lab/index.htm