Development of Molecular Systems for Gene or Antibody Delivery against Cancer Cells

船本, 大起

（様式３）

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論 文 名　：The Possibility of Gene or Antibody Therapy against Intracellular Oncoproteins

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論　文　内　容　の　要　旨

In this thesis, I focus on the possibility of gene or antibody therapy against intracellular oncogene proteins and the methodology for emphasis the cancer therapies. The potential of synthetic peptides is evident from a variety of different strategies for cancer treatment and diagnosis. Therefore, the effective cancer treatment and diagnosis using synthetic peptides which can directly target cancer cells has been extensively studied as an alternate strategy to conventional chemotherapy with a side effect. Such peptides can be utilized as an effective small biomaterial for specifically targeting cancer cells. Besides, the combination of therapeutic peptide and chemotherapy is an emerging strategy to achieve synergistic effects against cancer cells comparing with a single strategy alone that may not be efficient enough.

Here, I investigate the two strategies of gene delivery system using cationic substrate peptide responding to abnormally activated protein kinase Cα (PKCα) and therapeutic antibody internalization into living cell via the peptide-based crosslinker.

In chapter 2, I reported a preparation of cancer-specific gene carrier by native chemical ligation of a substrate peptide of protein kinase Cα (PKCα), which highly expresses in many types of cancer. This carrier is a tetramer of the substrate peptide connected with adequate spacer to maintain reactivity toward PKCα. The carrier successfully regulated the reporter gene expression responding to the phosphorylation of its serine residues.

In chapter 3, I reported an alternative strategy of antibody internalization by crosslinker-mediated endocytosis. This crosslinker consists of IgG binding peptide and folic acid as cancer targeting ligand toward folate receptor which highly expresses in many cancer cells surface. This crosslinker successfully facilitated antibody internalization into cancer cell by the folate receptor-mediated endocytosis.

In chapter 4, I summarize the contributions of this thesis.