論文 / 著書情報
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論 文 要 旨

THESIS SUMMARY

専攻： Department of	生物プロセス　専攻	申請学位（専攻分野）： Academic Degree Requested	博士 Doctor of　（　工学　）
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要旨（英文 800 語程度）
Thesis Summary（approx.800 English Words ）

A cell selective drug delivery system is essential for the development of cancer therapy technologies. The construction of effective intracellular drug delivery systems has been studied using various vectors such as viral vectors and non-viral vectors, such as liposome, cationic polymers and cell penetrating peptides (CPPs). Among them, CPP-based delivery systems, which can enter inside cell through the cell membrane, have been focused and could be useful in the research fields of drug delivery, gene therapy, and cancer therapy. They have, however, the problems such as low cell selectivity, low CP activity, and cell toxicity. In this study, to solve these disadvantages, peptides were selected from a 16-amino acid peptide library developed in Mihara group, which showed different CP activities against four cell lines, although these peptides had only one or two amino acid differences among 16 amino acids. A fluorescent dye conjugated with CPPs in the previous research in Mihara group was changed to GNS for designing the nanoprobes. The GNS would function as an imaging agent with multi-peptide conjugation for cell interactions. In this thesis, a cell-selective intracellular delivery system was constructed using α-helical CPPs and gold nanophere (GNS) and evaluated their applicability.

In the chapter 2, four kinds of α-helix peptide nanoprobes were constructed with two different peptides (EF and EA peptides) from an α-helix peptide library conjugating at N-terminus or C-terminus to GNSs. Their peptide binding ability according to GNS size (10, 16, 25, and 41 nm) was also evaluated. Among them, GNS41 conjugated the largest amount of peptide per particle and peptide-conjugated GNS41 (P-GNS41) showed the low cytotoxicity against HeLa cell, indicating high biocompatibility.

In the chapter 3, CP activity and cell death induction were evaluated using four P-GNSs41 constructed in the chapter 2. Peptides EF and EA have only one amino acid difference, Phe vs. Ala in the center of the sequence, however, they showed characteristic CP selectivity with three types of cells. In addition, selective cell death activity was induced using an anti-cancer drug, doxorubicin (DOX), conjugated to the P-GNSs41. P-DOX-GNSs41 showed enhanced cell-selective death induction compared with free DOX in solution and DOX-GNS41 without peptides, which was attributed to the cell-selective penetrating activity of peptides EF and EA.

In the chapter 4, five nanoprobes by conjugating either the TAT peptide or one of four α-helical peptides, RF, RA, EF, and EA, to a 25 nm GNS were constructed. The four α-helical peptide-conjugated nanoprobes showed similar CP and cell death activities compared with the TAT peptide in three cell lines, with high cell selectivity according to cell type and peptide sequence. Moreover, P-DOX-PEG-GNS25, which contained a pH-sensitive DOX linkage, showed levels of cell death induction by DOX (20%-40%) that were approximately two times higher than those (10%-20%) constructed in the chapter 3, P-DOX-GNS41.

In the chapter 5, conclusions and future prospects of this thesis were described.
These data indicate that constructed P-GNS systems have high cell selectivity, high efficiency, and low cytotoxicity. Drugs immobilized P-GNS could be applied to the development of disease diagnosis and therapy, molecular imaging probe, and cell-selective drug delivery system in vivo.

備考 ： 論文要旨は、和文 2000 字と英文 300 語を 1 部ずつ提出するか、もしくは英文 800 語を 1 部提出してください。
Note : Thesis Summary should be submitted in either a copy of 2000 Japanese Characters and 300 Words (English) or 1copy of 800 Words (English).