Department of Drug Delivery Research

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Research Projects:

A drug administered systemically is distributed nonspecifically all over the body. It is necessary to optimize the drug's pharmacokinetics in order to enhance the therapeutic effect and reduce side effects. The concept of controlling drug disposition to optimize therapeutic effect is called drug delivery system (DDS). Recently, in addition to low molecular weight compounds, proteins, nucleic acids, and cells have been a new modality for treatment. DDS should be rationally designed based on the physicochemical and biological properties of the drug, as well as based on the structure and function of the target organ. Furthermore, new analytical techniques must be established to evaluate the pharmacokinetics and therapeutic effects of drugs and DDSs according to their features. We are working on the following research topics.

1) Development of novel nano-DDSs for better therapeutic outcomes

We are developing nanoparticles-based DDSs (nano-DDSs) comprising of lipids, synthetic polymers, or biopolymers for targeted drug delivery. We optimize the formulation and manufacturing of nano-DDSs according to the structural and physicochemical properties of the encapsulated drug, in order to improve the encapsulation efficiency and control the retention and release. We also introduce targeting ligands to the nanocarriers to deliver the drug to the target tissue or cells specifically. The specialized systems of interest include glycan-lectin recognition and antigen-antibody interaction. We are also challenging targeted subcellular delivery of mid- and large-size drugs such as peptide and proteins.

2) Association analysis of pharmacokinetics and toxicokinetics of nano-DDSs with their physicochemical properties

Rational design of DDS is inevitable to reduce the side effect of drugs and carriers. We have been evaluating the toxicity of nano-DDSs, but only focusing on the change in well-established specific toxicity markers. In recent years, LS/MS/MS has been enabling for highly sensitive and comprehensive detection of protein expression variation in tissue and cells. Therefore, we are searching for new toxicity markers for nano-DDSs using this method. Particularly, we are interested in the hepatotoxicity of nano-DDSs because the liver is a major organ for the nano-DDSs to accumulate. We evaluate the variation of protein expression and phosphorylation in cultured hepatocytes or mouse liver following nano-DDS treatment, and identify hepatotoxicity-associated maker molecules through pathway analysis. Furthermore, we compare fluctuations in protein expression level in single and multiple doses and analyze the mechanism of long-term chronic toxicity that occurs in multiple doses.

3) Research on DDS technology for cell-based medicine

Mesenchymal stem cell-based medicine is now available for clinical therapy. Similar with conventional drugs such as low molecular weight compounds, high molecular weight compounds and nucleic acids, the concept of DDS that addresses the delivery of drugs to the target tissue should be propagated to cell-based therapy to improve the treatment outcomes. We apply the knowledge and technology that we have cultivated up to now, and are developing a method of controlling pharmacokinetics of mesenchymal stem cells. First, for the purpose of enhancing cell-cell adhesion to a therapeutic target cell, we are developing a method of modifying a ligand molecule on the cell membrane. In addition, we are also creating cells that exhibit therapeutic effects selectively at the treatment target site by changing their function in response to the micro environment in tissue.

Recent publications

- Rahimova N, et al., Development of mKO2 fusion proteins for real-time imaging and mechanistic investigation of the degradation kinetics of human IκBα in living cells. Biochim Biophys Acta Mol Cell Res. (2019) 1866(2),190-198.
- Babazada H, et al., Binding and structure-kinetic relationship analysis of selective TLR4-targeted immunosuppressive self-assembling heparin nanoparticles. Int J Pharm. (2018) 552(1-2), 76-83.
- Chantarasrivong C, et al., Synthesis and Functional Characterization of Novel Sialyl LewisX Mimic-Decorated Liposomes for E-selectin-Mediated Targeting to Inflamed Endothelial Cells. Mol Pharm. (2017) 14(5), 1528-1537.