

Department of Pharmaceutics
Division of Biopharmaceutics
School of Pharmaceutical Sciences

Outline

The department investigates practical pharmacy issues of biochemistry and physical pharmaceutics. The department shares education of pharmaceutics and social pharmacy.

Faculty members

Professor: Yoshihiko Shibayama, Ph.D.

Keywords: Clinical pharmaceutics, Pharmacology, Molecular biology, Pharmacokinetics, Cancer chemotherapy, MicroRNA, Functional foods

Research content

Clinical questions about pharmaceutical care are studied using culture cells, animal, and human samples.

Specialty areas are as follows:

Functions of microRNA in the cells, Study of molecular biology, Study of functional foods

Associate professor: Tsutomu Nakagawa, Ph.D

Keywords: Biochemistry, Pharmaceutics

Research contents:

#1 Identification of the novel, glucose-insensitive nuclear localization signals of ChREBP.

#2 The effect of O-GlcNAc modification on ChREBP activity.

#3 The effect of glycosylation on apico-basal distribution of GLUT2.

Assistant Professor: Yoshitada Kubo, Ph.D.

Keywords: Pharmaceutics, Generic drugs, Dispersion, Stability of drugs

Research content

#1 Resolvability and bioavailability of pharmaceuticals with poor solubility is being advanced by the solid dispersion system.

#2 Specialty areas are evaluation of the quality of and stability of pharmaceuticals.

Main research in progress

- 1) Reportedly, pharmaceutical profiles differ between the original drug and generic drugs. Quality, efficacy, and safety profiles of generic drugs were not elucidated in detail. Thus, we have reported on the pharmaceutical profiles of generic drugs.
- 2) Reportedly, insoluble drugs were limited by the step of absorption in the intestine. The solubility profile of insoluble drugs in the intestine should affect variance of bioavailability among individual and physiological differences. We have previously reported on improvement of solubility and bioavailability of insoluble drugs used with a hydrophilic polymer carrier as a dispersed solid system.
- 3) Carbohydrate response element binding protein (ChREBP, Also known as MLXIPL: MLX interacting protein like) is a transcription factor that plays a critical role in glucose-mediated induction of genes involved in hepatic glycolysis and lipogenesis. Circulating blood glucose levels regulate ChREBP activity in hepatocytes; however, the detailed underlying mechanism for this remains unclear. In our previous study, we found that the nuclear import of ChREBP is regulated in a glucose-dependent manner. We are currently identifying the novel, glucose-insensitive nuclear localization signals of ChREBP, responsible for its basal activity. Moreover, we are investigating the effect of O-GlcNAc modification on DNA-binding of ChREBP.
- 4) Micro RNA (miR) is a non-coding RNA, which consists of about a 20mer short-chain nucleotide sequence. MiRs play crucial roles in cell functions by inhibiting complementary RNAs, depending on RNA interference. We have previously reported on prognoses and responses to chemotherapies in

patients with cancer using biopsies, sera, and cultured cells. We investigate molecular and cellular mechanisms of cancer using molecular biology, statistics, bioinformatics, and genome editing.

- 5) The effect of anticancer drugs on expression levels of drug transporters have been evaluated using cultured cells and animals.
- 6) Expression levels of NAD-dependent deacetylase SIRT1 are increased by calorie restriction. SIRT1 is a key regulator of several aspects of metabolism and aging. Furthermore, SIRT1 regulates functions of tumors, genomic stability, the endocrine system, and cognition; facilitation of SIRT1 and Pgc-1 α , Igfbp extends the life span. We have reported a new function of Kurozu, traditional vinegar made from rice; Kurozu treatment stimulated expression of SIRT1 and Pgc-1 α , Igfbp, which improves genes' senescence.

Current publications

Shibayama Y, Nagano M, Fujii A, Hashiguchi K, Morita S, Kubo Y, Nakagawa T. Effect of concentrated Kurozu, a traditional Japanese vinegar, on expression of hepatic miR-34a, -149-3p, and -181a-5p in high-fat diet-fed mice. *Foods in Health & Disease*, **10**: 1-17 (2020)

Shibayama Y, Kubo Y, Nakagawa T, Iseki K. MicroRNA-101-5p Suppresses the Expression of the Ras-Related Protein RAP1A. *Biol Pharm Bull*. 42: 1332-1336 (2019)

Shibayama Y, Nagano M, Hashiguchi K, Fujii A, Iseki K. Supplementation of concentrated Kurozu, a Japanese black vinegar, reduces the onset of hepatic steatosis in mice fed with a high-fat diet. *Functional Foods in Health & Disease*, **9**: 276-296 (2019)

Sato S., Jung H., Nakagawa T., Pawlosky R., Takeshima T., Lee W. R., Sakiyama H., Laxman S., Wynn R. M., Tu B. P., MacMillan J. B., De Brabander J. K., Veech R. L., Uyeda K. Metabolite Regulation of Nuclear Localization of Carbohydrate-response Element-binding Protein (ChREBP): ROLE OF AMP AS AN ALLOSTERIC INHIBITOR. *J. Biol. Chem.* **291**: 10515-27 (2016)

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