Department of Pharmaceutical Chemistry
School of Pharmaceutical Sciences

Faculty members

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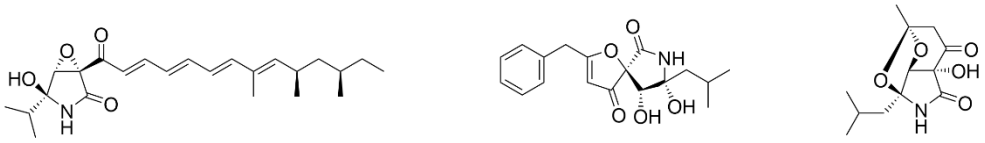
Research Interests

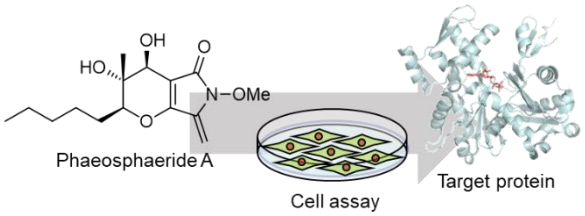
Our research fields are chemistry, biology, and pharmaceutical sciences, including (a) total synthesis of biologically active molecules, (b) bioorganic studies of the biologically active natural products, and (c) development of small-molecule kinase inhibitors.

(a) A large part of our research has focused on the total synthesis of biologically important natural products. To achieve them, we also strive to develop the highly stereoselective reactions.
We have successfully developed the diastereoselective Darzens reaction, enabling us to complete the total synthesis of L-755,807 as a bradykinin binding inhibitor, berkeleyamide D as a caspase-I and matrix metalloprotease III inhibitor, and rubrobramide with antifungal, cytotoxic, and nematicidal activities.

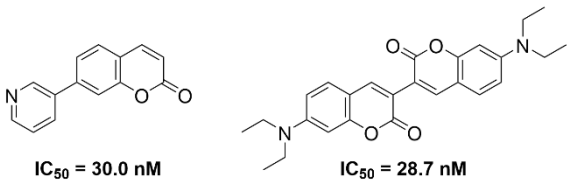


L-755,807 **Berkeleyamide D** **Rubrobramide**

(b) We strive to evaluate anti-cancer activity of the synthetic and isolated compounds from natural sources, and to elucidate the target biomolecules of natural products with significant biological activities. These researches are usually regarded as “chemical biology”, which covers the interdisciplinary area of chemistry and biology. In other words, our research aims to elucidate the biological phenomena using chemistry as a starting point.
The bioorganic study of phaeosphaerides is one of our ongoing projects, aiming to identify the target protein of phaeosphaerides with STAT3 inhibitory activity.



(c) Our research interests involve the development of the small-molecule kinase inhibitors against CYP, BACE1, or DGAT1. We are recently dedicated to disclose the structure–activity relationship of heterocyclic compounds with CYP inhibitory effects.
Significantly, we discovered some coumarin analogs with a pyridyl substituent and dimeric coumarins as highly potent inhibitors of 19A1 (aromatase). Aromatase inhibitors are well known to be effective for the treatment of estrogen-dependent human breast cancer.



IC_{50} = 30.0 nM IC_{50} = 28.7 nM

Publications (2020–)

1. Synthesis and Biological Evaluation of Coumarin Derivatives as Selective CYP2A6 Inhibitors
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   Bioorg. Med. Chem. Lett. **2023**, *86*, 129206.
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3. Advancing the Biosynthetic and Chemical Understanding of the Carcinogenic Risk Factor Colibactin and Its Producers.
   Hirayama, Y.; Sato, M.; Watanabe, K.
   Biochemistry **2022**, *61*, 2782-2790.
4. Enantioselective Total Synthesis of (+)-Rubrobramide, (+)-Talaramide A, and (–)-Berkeleyamide D by a Skeletal Diversification Strategy.
   Tanaka III, K.; Kobayashi, K.; Kogen, H.
   Chem. Commun. **2021**, *57*, 9780-9783.
5. Isolation of New Colibactin Metabolites from Wild-Type *Escherichia coli* and *In Situ* Trapping of a Mature Colibactin Derivative.
   Zhou, T.; Hirayama, Y.; Tsunematsu, Y.; Suzuki, N.; Tanaka, S.; Uchiyama, N.; Goda, Y.; Yoshikawa, Y.; Iwashita, Y.; Sato, M.; Miyoshi, N.; Mutoh, M.; Ishikawa, H.; Sugimura, H.; Wakabayashi, K.; Watanabe, K.
   J. Am. Chem. Soc. **2021**, *143*, 5526-5533.
6. Concise Synthesis of the Major Metabolite M8 from Ticagrelor and Simultaneous Determination of Ticagrelor and M8 by a Novel LC/MS Method.
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   Tanaka III, K.; Kogen, H.; Kobayashi, K.
   Heterocycles **2021**, *102*, 1235-1285.
8. Genotyping of a Gene Cluster for Production of Colibactin and in vitro Genotoxicity Analysis of *Escherichia coli* Strains Obtained from the Japan Collection of Microorganisms.
   Kawanishi, M.; Shimohara, C.; Oda, Y.; Hisatomi, Y.; Tsunematsu, Y.; Sato, M.; Hirayama, Y.; Miyoshi, N.; Iwashita, Y.; Yoshikawa, Y.; Sugimura, H.; Mutoh, M.; Ishikawa, H.; Wakabayashi, K.; Yagi, T.; Watanabe, K.
   Gene Environ. **2020**, *42*, 12.
9. Novel *o*-Toluidine Metabolite in Rat Urine Associated with Urinary Bladder Carcinogenesis.
   Tajima, Y.; Toyoda, T.; Hirayama, Y.; Matsushita, K.; Yamada, T.; Ogawa, K.; Watanabe, K.; Takamura-Enya, T.; Totsuka, Y.; Wakabayashi, K.; Miyoshi, N.
   Chem. Res. Toxicol. **2020**, *33*, 1907-1914.