

Drug Design Chemistry (Molecular Design)

1. Staffs and Students (April 2009)

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2. Purpose of Education

Drug Design Chemistry covers several aspects of organic chemistry, analytical chemistry, medicinal chemistry and chemical biology. Through this course, students are expected to understand and train the experimental techniques related to those scientific fields.

Our laboratory is working on the developments of functional molecules, which can “modulate” or “sense” the physiological functions, such as enzyme inhibitors and fluorescent sensors for elucidating intracellular or extracellular signal transduction pathway. In addition, we also focus on the development of novel drug and diagnostic tools for various diseases.

3. Research Subject

1) Construction of a facile method to develop various fluorescent sensors for elucidating physiological functions

We construct a facile method to develop various fluorescent sensors, which can sense the change of the concentration or activity of each biologically important analyte.

2) Development of fluorescent sensors by modulating the complex formation of fluorophore

The control of intermolecular or intramolecular complex formation between two fluorophores or between a fluorophore and another molecular species has been utilized for the development of fluorescent sensors.

3) Development of various enzyme inhibitors based on the chemical structure of coenzymes or natural products

Coenzyme, such as ATP, is commonly utilized by most of enzymes in the specific enzyme family, such as protein kinase family or histone methyltransferase family. By derivatization of the structure of such coenzyme, we develop novel inhibitor for each enzyme. In addition, based on the chemical structure of natural products, saponins, isolated from soybean hypocotyls by our group, we develop novel inhibitors for matrix metalloproteinase (MMP), which is related to the metastasis of cancer.

4) Elucidation and application of antioxidant system *in vivo*

Reactive oxygen species (ROS) causes various kinds of sickness. Though a lot of materials having antioxidant action *in vivo* are reported, a role of the antioxidant action still remains to be elucidated. Bilirubin (BR) acts as a scavenger of ROS *in vivo* and converted to oxidative degradation products. Using these products, we study a mechanism of antioxidant action and develop a stress checker applying the mechanism.

4. Publications

Original articles

- Hirano T, Osaki T, Fujii S, Komatsu D, Azumaya I, Tanatani A, Kagachika H: Fluorescent Visualization of the Conformational Change of Aromatic Amide or Urea Induced by N-methylation. *Tetrahedron Lett.* 50: 488–491, 2009.
- Kudo M, Hanashima T, Muranaka A, Sato H, Uchiyama M, Azumaya I, Hirano T, Kagechika H, Tanatani A: Identification of Absolute Helical Structures of Aromatic Multilayered Oligo(m-phenylurea)s in Solution. *J Org Chem.* 74: 8154–8163, 2009.
- Eshima K, Fukaya S, Sugimoto A, Mori T, Yokoi H, Yamamoto Y, Sugiura S, Honda S, Masuko N, Murakami K, Yamasaki Y, Kagechika H: Contribution of AP-1 interference induced by TAC-101 to tumor growth suppression in a hepatocellular carcinoma model. *Tumor Biol.* 30: 1-7, 2009.
- Kadoma Y, Ito S, Atsumi T, Fujisawa S: Mechanisms of cytotoxicity of 2- or 2,6-di-tert-butylphenols and 2-methoxyphenols in terms of inhibition rate constant and a theoretical parameter. *Chemosphere* 74: 626-632, 2009.
- Gurbuz I, Yesilada E, Ito S: An anti-ulcerogenic flavonol diglucoside from *Equisetum palustre L.* *J Ethnopharmacology*, 121: 360-365, 2009.
- Murakami Y, Ishii H, Hoshina S, Takada N, Ueki A, Tanaka S, Kadoma Y, Ito S, Machino M, Fujisawa S:

Antioxidant and Cyclooxygenase-2-inhibiting activity of 4,4'-biphenol, 2,2'-biphenol and phenol. *Anticancer Res* 29: 2403-2410, 2009.

Review articles

1. Hirano T, Kagechika H. Construction of Coumarin Library for Development of Fluorescent Sensors. In *Combinatorial Methods for Chemical and Biological Sensors*, Edited by Radislav A. Potyrailo and Vladimir M. Mirsky. Chapter 18, Springer, pp 441-451, 2009.
2. Kadoma Y, Murakami Y, Atsumi T, Ito S, Fujisawa S. Cloves(Eugenol). Molecular targets and therapeutic uses of species: Modern uses for ancient medicine. 2009, 117-148. World Scientific Publishing Co. Pte. Ltd. Singapore.