Drug Design Chemistry (Molecular Design)

1. Staffs and Students (April 2009)

Associate Professor	Tomoya Hirano	
Assistant Professor	Shigeru Ito	
Research Promotion Technician	Akiko Sugimoto	
Graduate Student	Gao Pei,	Shusakui Kobayashi,
	Aya Suzuki,	Yuki Yamada

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 fluorophores

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 for some post-translational modifications of tyrosine residues or the visualization of some receptor proteins.

3) Development of histone methyltransferase inhibitors

Post-translational modification of histone proteins plays an important role in the regulation of gene expression, and can be controlled by histone modifying enzymes, such as histone methyltransferase (HMT). We are developing some inhibitors against these HMTs.

4) Studies of anti-tumor substances in the spores of *Ganoderma lucidum* (Reishi Houshi)

During our isolation of biologically active substances from the spores of *Ganoderma lucidum* (Reishi Houshi) guided by the inhibitory activity on HL-60 cell proliferation, NMR and Mass data indicate the substances contain several fatty acids. In particular, the fatty acids having odd carbon number show potent inhibitory activity. We are now identifying the responsible structures for the activity.

4. Publications

Original articles

1. Hirano T, Akiyama J, Mori S, Kagechika H: Modulation of Intramolecular Heterodimer-induced Fluorescence Quenching of Tricarbocyanine Dye for the Development of Fluorescent Sensor. Org Biomol Chem. 8: 5568–5575, 2010.
2. Mori S, Iwase K, Iwanami N, Tanaka Y, Kagechika H, Hirano T: Development of Novel Bisubstrate-type Inhibitors of Histone Methyltransferase SET7/9. Bioorg Med Chem.18: 8158–8166, 2010.
3. Ito S, Hirano T, Sugimoto A, Kagechika H, Takechi S, Yamaguchi T: Latent Enamine Functionality of 5-Methyl-2,3-dihydropyrazines. Chem Pharm Bull. 58: 922–977, 2010.
4. Ito S, Takechi S, Nakahara K, Kashige N, and Yamaguchi T: Phenyl-Substituted Dihydropyrazines with DNA Strand-Breakage Activity. Chem Pharm Bull. 58: 825-828, 2010.

Review articles

1. Hirano T, Kagechika H: Thyromimetics: a Review of Recent Reports and Patents (2004 – 2009). Exp Op Ther Patents. 20: 213–228, 2010.