

Department of Organic and Medicinal Chemistry

Professor Hiroyuki Kagechika

Associate Professor
Tomoya HiranoAssistant Professor
Shuichi MoriAssistant Professor
Mari YuasaTechnical Specialist
Hiroyuki Masuno

Drug discovery based on molecular structure and function

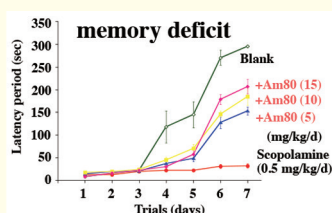
1. Medicinal chemistry of retinoids and nuclear receptors
2. Development of novel modulators of gene transcription or signaling pathways for clinical applications in intractable diseases
3. Development of novel fluorophores and fluorescent sensors
4. Aromatic architecture based on amide conformational properties

1. Ando F, Mori S, Yui N, Morimoto T, Nomura N, Sohara E, Rai T, Sasaki S, Kondo Y, Kagechika H, Uchida S: AKAPs-PKA disruptors increase AQP2 activity independently of vasopressin in a model of nephrogenic diabetes insipidus, *Nature Commun* 9, 1411, 2018.
2. Yokoo H, Ohsaki A, Kagechika H, Hirano T: Unique properties of 1,5-naphthyridin-2(1H)-one derivatives as environmental-polarity-sensitive fluorescent dyes, *Eur J Org Chem* 2018, 679-687.
3. Mori S, Hirano T, Takaguchi A, Fujiwara T, Okazaki Y, Kagechika H: Selective reagent for detection of N- ϵ -monomethylation of a peptide lysine residue through SNAr reaction, *Eur J Org Chem* 2017, 3606-3611.
4. Fujii S, Masuno H, Taoda H, Kano A, Wongmayura A, Nakabayashi M, Ito N, Shimizu M, Kawachi E, Hirano T, Endo Y, Tanatani A, Kagechika H: Boron cluster-based development of potent non-steroidal vitamin D receptor ligands: Direct observation of hydrophobic interaction between protein surface and carborane, *J Am Chem Soc* 133, 20933-20941, 2011.
5. Kagechika H, Shudo K: Retinoids: Recent developments concerning structure and clinical utility, *J Med Chem* 48, 5875-5883, 2005.

Our group is working on the development of various functional molecules based on organic chemistry and its application in the field of drug discovery and material sciences. In particular, we focus on medicinal chemistry and chemical biology research to elucidate the functions and clinical utility of hydrophobic signaling molecules, such as steroid hormones and active vitamins.

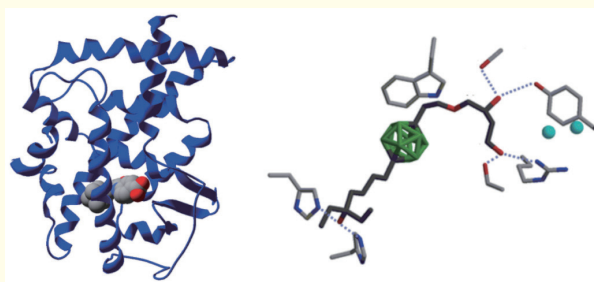
Medicinal chemistry of retinoids

Retinoids – the natural and synthetic analogs of retinoic acid – regulate various biological phenomena. We are developing novel synthetic retinoid agonists and antagonists, and examining their clinical applications in the fields of cancer, autoimmune diseases, neurodegenerative diseases, and others. Among our compounds, Am80 (tamibarotene) was approved as a drug for relapsed acute promyelocytic leukemia (APL) in Japan, and the study of further clinical applications for Am80 is ongoing.



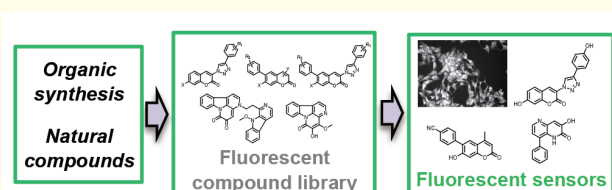
Medicinal chemistry of nuclear receptors

Nuclear receptors are ligand-inducible transcription factors, responsible for the biological activities of hydrophobic hormones. We are developing novel ligands for various nuclear receptors by using unique hydrophobic pharmacophores, such as carboranes (boron clusters).



Development of fluorescent molecules

Fluorescent molecules applicable to biological research and medical diagnosis have been developed based on a fluorescent compound library derived from organic synthesis and natural compounds.



Development of aromatic foldamers

Based on our finding that N-methylated aromatic amides and ureas exist in cis conformation, we have constructed aromatic foldamers with unique structures and functions.

