Division of Biochemistry
– Chemical Biology –

http://www.scl.kyoto-u.ac.jp/~uesugi/e/index.php

Prof
UESUGI, Motonari
(D Pharm Sc)

Assoc Prof
OHKANDA, Junko
(D Chem)

Assist Prof
SHIMOGAWA, Hiroki
(D Sc)

Proj Res*
SATO, Shinichi
(D Eng)

Proj Res**
HIRATA, Nao
(D Eng)

Proj Res**
WATANABE, Mizuki
(D Pharm Sc)

Proj Res**
JIN, Guihua
(D Med Sc)

Proj Res***
KUO, Ting-Fang
(D Sc)

Proj Res***
KATSUDA, Yousuke
(D Sc)

Proj Res**
TAKENOYA, Mihoko
(D Eng)

Proj Res***
PERRON, Amelie
(Ph D)

Guest Res Assoc
PARVATKAR, Prakash Tukaram
(Ph D)

Researcher

WATANABE, Haruhi

Assist Res Staff

NAKASHIMA, Mitsue****

Students

FRISCO, Heidie Laya (D3)
MAO, Di (D2)
TAKAYA, Junichiro (D2)
WANG, Chenyu (M2)
MBENZA, Mbambi Naasson**** (RS)

* Program-Specific Research Center Assist Prof of iCeMS
** Res (WPI) of iCeMS
*** PD (NEXT Program) of iCeMS
**** iCeMS

Visiting Researcher

Assoc Prof HOW, Siew Eng Universiti Malaysia Sabah, Malaysia, 1 May-31 October

Scope of Research

KEYWORDS
Cell Therapy
Chemical Biology
Small Molecules
Chemical Library
Chemical Genetics

Chemical biology is an interdisciplinary field of study that is often defined as "chemistry-initiated biology." As biological processes all stem from chemical events, it should be possible to understand or manipulate biological events by using chemistry. Our laboratory has been discovering or designing unique organic molecules that modulate fundamental processes in human cells. Such synthetic organic molecules often serve as tools for basic cell biology. Discovery or design of small molecules with unique biological activity permits small-molecule initiated exploration of complex cellular events. Our mission is to create a new world of bioactive synthetic molecules: their new way to use, their new shapes, and their new sizes. We hope to open new avenues for small-molecule applications in a range of fields, including future concepts in drug discovery and use of small molecules for cell therapy.

Selected Publications

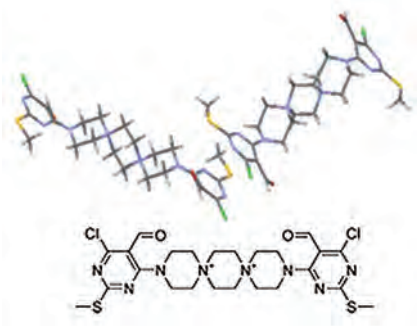
Sakano, D.; Shiraki, N.; Kikawa, K.; Yamazoe, T.; Kataoka, M.; Umeda, K.; Araki, K.; Mao, D.; Matsumoto, S.; Nakagata, N.; Andersson, O.; Stainier, D.; Endo, F.; Kume, K.; Uesugi, M.; Kume, S., VMAT2 Identified as a Regulator of Late-stage Beta Cell Differentiation, *Nat. Chem. Biol.*, **10,** 141-148 (2014).

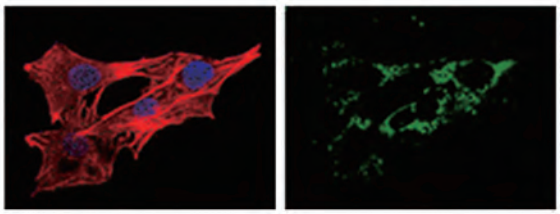
Takemoto, N.; Suehara, T.; Frisco, H.; Sato, S.; Sezaki, T.; Kusamori, K.; Kawazoe, Y.; Park, S.; Yamazoe, S.; Mizuhata, Y.; Inoue, R.; Miller, G.; Hansen, S.; Jayson, G.; Gardiner, J.; Kanaya, T.; Tokitoh, N.; Ueda, K.; Takakura, Y.; Kioka, N.; Nishikawa, M.; Uesugi, M., Small Molecule-induced Clustering of Heparan Sulfate Promotes Cell Adhesion, *J. Am. Chem. Soc.*, **135 (30),** 11032-11039 (2013).

Minami, I.; Yamada, K.; Otsuji, T. G.; Yamamoto, T.; Shen, Y.; Otsuka, S.; Kadota, S.; Morone, N.; Barve, M.; Asai, Y.; Tenkova-Heuser, T.; Heuser, J. E.; Uesugi, M.; Aiba, K.; Nakatsuji, N., A Small Molecule That Promotes Cardiac Differentiation of Human Pluripotent Stem Cells under Defined Cytokine- and Xeno-free Conditions, *Cell Reports*, **2(5),** 1448-1460 (2012).

Small Molecule-induced Clustering of Heparan Sulfate Promotes Cell Adhesion

Adhesamine is an organic small molecule that promotes adhesion and growth of cultured human cells by binding selectively to heparan sulfate on the cell surface. The Uesugi research group combined chemical, physicochemical, and cell biological experiments, using adhesamine and its analogues, to examine the mechanism by which this dumbbell-shaped, non-peptidic molecule induces physiologically relevant cell adhesion. The results suggest that multiple adhesamine molecules cooperatively bind to heparan sulfate and induce its assembly, promoting clustering of heparan sulfate-bound syndecan-4 on the cell surface. A pilot study showed that adhesamine improved the viability and attachment of transplanted cells in mice. Further studies of adhesamine and other small molecules could lead to the design of assembly-inducing molecules for use in cell biology and cell therapy.





Small-molecule Inhibitors of SREBP Activation–potential for New Treatment of Metabolic Disorders

Sterol regulatory element-binding proteins (SREBPs) are transcriptional factors that control lipid and cholesterol metabolism. Activation of SREBPs in response to a decrease in cellular sterols results in acceleration of the synthesis of fatty acids, triglycerides, and cholesterol. Aberrant SREBP activity has been linked to metabolic disease states, such as obesity, fatty liver, insulin resistance, hyperlipidemia, and atherosclerosis. Thus, inhibition of SREBP activation is a potential therapeutic approach to treating metabolic disorders. Our laboratory recently discovered a number of inhibitors of SREBP activation, including fatostatin and FGH10019. Our analysis indicates that these two synthetic molecules exert their biological activities by directly interacting with SCAP (SREBP cleavage-activating protein).