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 Eng)

Senior Lect
PERRON, Amelie
(Ph D)

Assist Prof
TAKEMOTO, Yasushi
(D Eng)

Proj Res*
SATO, Shinichi
(D Eng)

Proj Res**
KATSUDA, Yousuke
(D Sc)

Proj Res**
TAKASHIMA, Ippei
(D Pharm Sc)

Proj Res**
TAKENOYA, Mihoko
(D Eng)

Researchers

FURUTA, Tomoyuki****
OKUDA, Satoshi****

Proj Res

GOETZE, Sebastian Andreas (Ph D) ***
TANTIPANJAPORN, Ajcharapan***

Researchers(pt)

AKIZUKI, Maika
QIN, Ying****

Assist Techn Staff

MAO, Di****
TAKAYA, Junichiro (D Med Sc) ****

Assist Res Staff

NAKASHIMA, Mitsue****

*Assoc Prof of iCeMS **PD of iCeMS ***Guest Res Assoc of iCeMS ****iCeMS

Students

ASANO, Risa (D3)
LIAO, Youqi (D3)
PUNZALAN, Louvy Lynn (D2)
YATSUZUKA, Kenji (D2)
MENDOZA, Aileen de-Leon (D1)
JUNG, Yejin (D1)
CHUNG, Watson Xie Khim (M2)
KOTAKE, Kenjiro (M1)
TAJIRI, Ken (M1)
HAKARIYA, Hayase (M1)
YOSHIDA, Hiroki (M1)
PE, Kathleen Beverly Alog (M1)
VU, Hue Thi (M1)
LE, Toan Khanh (RS)

Scope of Research

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 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 activities permits small-molecule-initiated exploration of complex cellular events. Our mission is to create a new world of bioactive synthetic molecules: new modes of activity, new shapes, and 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.

KEYWORDS
Cell Therapy
Chemical Biology
Small Molecules
Chemical Library
Chemical Genetics

Selected Publications

Katsuda, Y.; Sato, S.; Asano, L.; Morimura, Y.; Furuta, T.; Sugiyama, H.; Hagihara, M.; Uesugi, M., A Small Molecule That Represses Translation of G-quadruplex-Containing mRNA, *J. Am. Chem. Soc.*, **138,** 9037-9040 (2016).

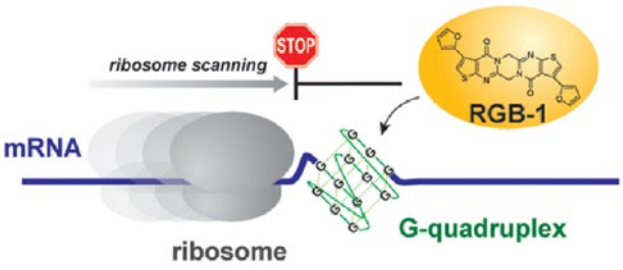
Takaya, J.; Mio, K.; Shiraishi, T.; Kurokawa, T.; Otsuka, S.; Mori, Y.; Uesugi, M., A Potent and Site-Selective Agonist of TRPA1, *J. Am. Chem. Soc.*, **137,** 15859-15864 (2015).

Parvatkar, P.; Kato, N.; Uesugi, M.; Sato, S.; Ohkanda, J., Intracellular Generation of a Diterpene-Peptide Conjugate that Inhibits 14-3-3-Mediated Interactions, *J. Am. Chem. Soc.*, **137,** 15624-15627 (2015).

Sato, S.; Watanabe, M.; Katsuda, Y.; Murata, A.; Wang, D. O.; Uesugi, M., Live-cell Imaging of Endogenous mRNAs with a Small Molecule, *Angew. Chem. Int. Ed.*, **54,** 1855-1858 (2015).

A Small Molecule That Represses Translation of G-Quadruplex-Containing mRNA

The G-quadruplexes form highly stable nucleic acid structures, which are implicated in various biological processes in both DNA and RNA. Although DNA G-quadruplexes have been studied in great detail, biological roles of RNA G-quadruplexes have received less attention. In this study, a screening of a chemical library permitted identification of a small-molecule tool that binds selectively to RNA G-quadruplex structures. The polyaromatic molecule, RGB-1, stabilizes RNA G-quadruplex, but not DNA versions or other RNA structures. RGB-1 intensified the G-quadruplex-mediated inhibition of RNA translation in mammalian cells, decreased expression of the NRAS proto-oncogene in breast cancer cells, and permitted identification of a novel sequence that forms G-quadruplex in NRAS mRNA. RGB-1 may serve as a unique tool for understanding cellular roles of RNA G-quadruplex structures.



A Potent and Site-Selective Agonist of TRPA1

TRPA1 is a member of the transient receptor potential (TRP) cation channel family that is expressed primarily on sensory neurons. This chemo-sensor is activated through covalent modification of multiple cysteine residues with a wide range of reactive compounds including allyl isothiocyanate (AITC), a spicy component of wasabi. The present study reports on potent and selective agonists of TRPA1, discovered through screening 1,657 electrophilic molecules. In an effort to validate the mode of action of hit molecules, we noted a new TRPA1-selective agonist, JT010 (molecule 1), which opens the TRPA1 channel by covalently and site-selectively binding to Cys621 (EC50 = 0.65 nM). The results suggest that a single modification of Cys621 is sufficient to open the TRPA1 channel. The TRPA1-selective probe described herein might be useful for further mechanistic studies of TRPA1 activation.