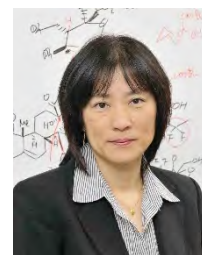


**Synthetic Organic Chemistry Laboratory**  
**Chief Scientist: Mikiko Sodeoka (D.Pharm.)**



**(0) Research field**

CPR Subcommittee: Chemistry, Biology

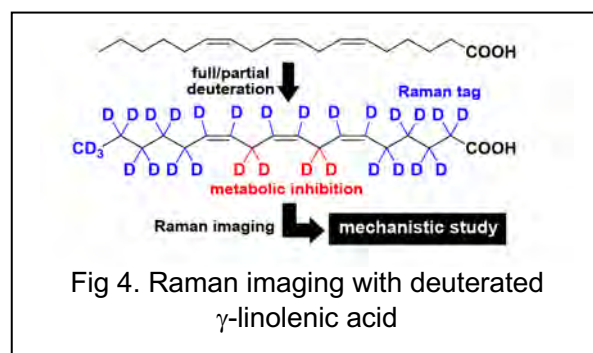
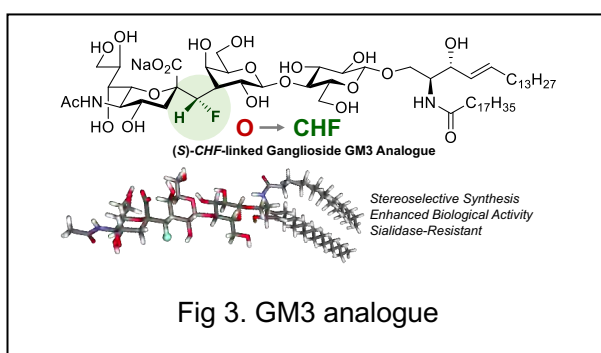
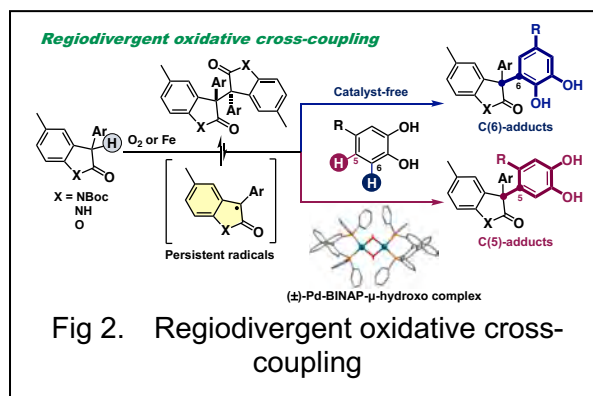
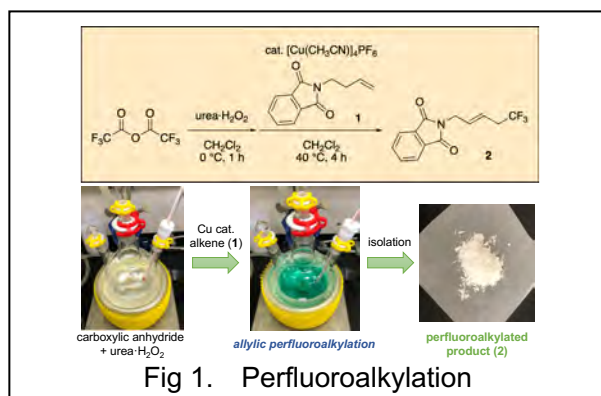
**Keywords:** Transition Metal Chemistry, Fluorine Chemistry, Bioactive Molecules, Chemical Biology

**(1) Long-term goal of laboratory and research background**

Our laboratory focuses on the following research areas based on synthetic organic chemistry: 1) development of new reactions and methodologies for the efficient synthesis of bioactive molecules, 2) design and synthesis of molecules having unique biological activity, 3) biological researches using these unique molecules as biological probes. Our research interests encompass from novel synthetic methods using transition metal-catalysts for fluorine-containing molecules and chiral compounds to the design and synthesis of intracellular signal transduction modulators and their application to cell biology research. In particular, we are focusing on enzymes in charge of chemical modification of proteins, such as phosphorylation and methylation. We are working on design and synthesis of selective inhibitors of such enzymes as well as development of new methods for analyzing chemical modification of proteins. Development of new chemical methodology for identification of target protein/binding site of small bioactive molecules and for their imaging. Clarification of the unknown molecular mechanism of cell death (necrosis) by using our original cell death control molecules is also currently underway.

**(2) Current research activities (FY2020) and plan (until Mar. 2025)**

In this fiscal year, the experimental procedure for our perfluoroalkylation of alkenes on a multi-gram scale was optimized. We have also developed a regiodivergent oxidative cross-coupling reaction of persistent tertiary-carbon radicals with catechols. We synthesized sialidase-resistant analogues of ganglioside GM3, leading to identification of (*S*)-CHF-linked GM3 analogue that exhibits greater cell proliferation activity than native GM3. We applied Raman imaging to the quantitative analysis of drug uptake in live cells. Furthermore, synthesis of deuterated  $\gamma$ -linolenic acid (GLA) and Raman imaging revealed that deuterated GLA showed tumor-selective cytotoxicity by the accumulation in lipid droplets. In addition, we also applied fluorescent affinity labeling method using *O*-NBD unit for the analysis of antitumor natural product rocaglamide A, leading to the identification of the second target protein DDX-3. We will continuously develop new fluoroalkylation reactions and cross-coupling reactions. We will also continue the research on the regulation mechanism of necrosis by developing novel analysis methods.



### (3) Members

#### (Chief Scientist)

Mikiko Sodeoka

#### (Senior Research scientist)

Kosuke Dodo, Yoshihiro Sohtome

#### (Research Scientist)

Shintaro Kawamura, Rajiv Kumar Verma

#### (Special Postdoctoral Researcher)

Syusuke Egoshi

#### (Postdoctoral Researcher)

Subha Bakthavatsalam, Takuma Tagami

#### (Technical Staff)

as of March, 2021

Naoki Terayama, Mai Akakabe, Kota Koike

#### (Visiting Technician)

Kanae Saito, Koshi Harada

#### (Assistant)

Izumi Saito

#### (Part-time Worker)

Xiuling Wang

#### (Student Trainee)

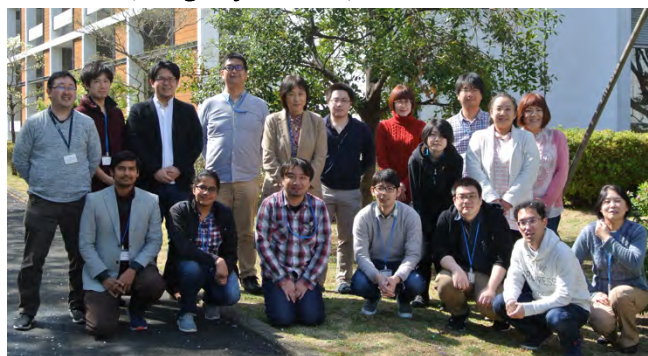
Yusuke Mitani (M2)

#### (Vice Chief Scientist)

Hiroyuki Koshino (Unit Leader of Center for Sustainable Resource Science)

### (4) Representative research achievements

1. "Regiodivergent Oxidative Cross-Coupling of Catechols with Persistent *tert*-Carbon Radicals", M. Sugawara, R. Ohnishi, T. Ezawa, M. Akakabe, M. Sawamura, D. Hojo, D. Hashizume, Y. Sohtome, and M. Sodeoka, *ACS Catal.* 10, 12770-12782 (2020).
2. "Quantitative drug dynamics visualized by alkyne-tagged plasmonic-enhanced Raman microscopy", K. Koike, K. Bando, J. Ando, H. Yamakoshi, N. Terayama, K. Dodo, N. I. Smith, M. Sodeoka, K. Fujita, *ACS Nano* 14, 15032-15041 (2020).
3. "Ganglioside GM3 Analogues Containing Monofluoromethylene-linked Sialoside: Synthesis, Stereochemical Effects, Conformational Behavior, and Biological Activities", G. Hirai, M. Kato, H. Koshino, E. Nishizawa, K. Oonuma, E. Ota, T. Watanabe, D. Hashizume, Y. Tamura, M. Okada, T. Miyagi, and M. Sodeoka, *JACS Au*, 1, 137-146 (2021).
4. "Development of deuterated derivatives of  $\gamma$ -linolenic acid and their application for biological studies: metabolic tuning and Raman imaging", A. Sato, Y. Tamura, S. Egoshi, K. Fujiwara, K. Oonuma, S. Nakao, K. Dodo, and M. Sodeoka, *Chem. Comm.* 57, 2180-2181 (2021).
5. "Cu-catalyzed Allylic Perfluoroalkylation of Alkenes by Using Perfluoro Acid Anhydrides: Preparation of *N*-(5,5,5-Trifluoro-2-penten-1-yl)phthalimide", Y. Aoki, S. Kawamura, and M. Sodeoka, *Org. Synth.* 98, 84-96 (2021).



### Laboratory Homepage

[https://www.riken.jp/en/research/labs/chief/synth\\_org\\_chem/index.html](https://www.riken.jp/en/research/labs/chief/synth_org_chem/index.html)

<http://soc.riken.jp/index-e.html>