Division of Biochemistry
– Chemical Biology –

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HÖEG, Finn Lukas — The University of Hamburg, Germany, 6 April, 2022–30 September, 2022
LATOS, Krystian — Jagiellonian University, Poland, 22 August, 2022–14 October, 2022

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 that these basic studies open new avenues for small-molecule applications in a range of fields.

KEYWORDS

Chemical Biology
Chemical Genetics
Self-Assembly
Immunology
Chemical Library

Recent Selected Publications

Toh, K.; Nishio, K.; Nakagawa, R.; Egoshi, S.; Abo, M.; Perron, A.; Sato, S.; Okumura, N.; Koizumi, N.; Dodo, K.; Sodeoka, M.; Uesugi, M., Chemoproteomic Identification of Blue-Light-Damaged Proteins, *J. Am. Chem. Soc.*, **144,** 20171-20176 (2022).

Jin, S.; Zhuo, S.; Takemoto, Y.; Li, Y.; Uesugi, M., Self-Assembling Small-Molecule Adjuvants as Antigen Nano-Carriers, *Chem Commun.*, **58,** 12228-12231 (2022).

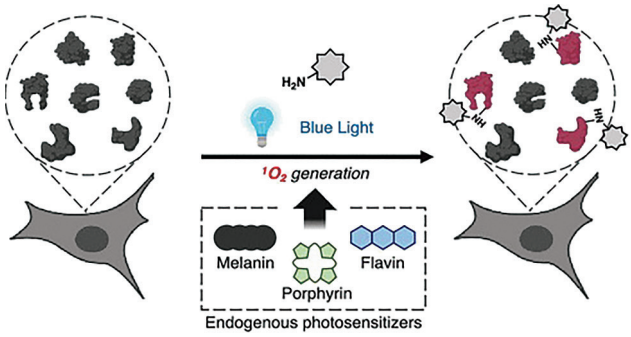
Nishio, K.; Toh, K.; Perron, A.; Goto, M.; Abo, M.; Shimakawa, Y.; Uesugi, M., Magnetic Control of Cells by Chemical Fabrication of Melanin, *J. Am. Chem. Soc.*, **144,** 16720-16725 (2022).

Ado, G.; Noda, N.; Vu, H.; Perron, A.; Mahapatra, A.; Arista, K.; Yoshimura, H.; Packwood, D.; Ishidate, F.; Sato, S.; Ozawa, T.; Uesugi, M., Discovery of a Phase-Separating Small Molecule That Selectively Sequesters Tubulin in Cells, *Chemical Science*, **13,** 5760-5766 (2022).

Mendoza, A.; Takemoto, Y.; Cruzado, K.; Masoud, S.; Nagata, A.; Tantipanjaporn, A.; Okuda, S.; Kawagoe, F.; Sakamoto, R.; Odagi, M.; Mototani, S.; Togashi, M.; Kawatani, M.; Aono, H.; Osada, H.; Nakagawa, H.; Higashi, T.; Kittaka, A.; Nagasawa, K.; Uesugi, M., Controlled Lipid β-Oxidation and Carnitine Biosynthesis by a Vitamin D Metabolite, *Cell Chemical Biology,* **29,** 660-669 (2022).

Chemoproteomic Identification of Blue-Light-Damaged Proteins

Visible light, particularly in the blue region of the spectrum, can cause cell dysfunction through the generation of singlet oxygen, contributing to cellular aging and age-related pathologies. Although photooxidation of nucleic acids, lipids, and amino acids has been extensively studied, the magnitude and span of blue-light-induced protein damages within proteome remain largely unknown. The Uesugi group took a chemoproteomic approach to mapping blue-light-damaged proteins in live mammalian cells by exploiting a nucleophilic alkyne chemical probe. A gene ontology enrichment analysis revealed that cell surface proteins are more readily oxidized than other susceptible sets of proteins, including mitochondrial proteins. In particular, the integrin family of cell surface receptors (ITGs) was highly ranked in the mammalian cells tested, including human corneal endothelial cells. The blue-light-oxidized ITGB1 protein was functionally inactive in promoting cell adhesion and proliferation, suggesting that the photodamage of integrins contributes to the blue-light-induced cell dysfunction. Further application of our method to various cells and tissues should lead to a comprehensive analysis of light-sensitive proteins.



Magnetic Control of Cells by Chemical Fabrication of Melanin

Melanin is an organic material biosynthesized from tyrosine in pigment-producing cells. The Uesugi group developed a simple method to generate tailored functional materials in mammalian cells by chemically fabricating intracellular melanin. Our approach exploits synthetic tyrosine derivatives to hijack the melanin biosynthesis pathway in pigment-producing cells. Its application was exemplified by synthesizing and using a paramagnetic tyrosine derivative, m-YR, which endowed melanoma cells with responsiveness to external magnetic fields. The mechanical force generated by the magnet-responsive melanin forced the cells to elongate and align parallel to the magnetic power lines. Critically, even non-pigment cells were similarly remote-controlled by external magnetic fields once engineered to express tyrosinase and treated with m-YR, suggesting the versatility of the approach. The present methodology may potentially provide a new avenue for mechanobiology and magnetogenetic studies and a framework for magnetic control of specific cells.