2026 CLS Seminar No. 9

Institute of SCIENCE TOKYO

Chemical Probes for Drug Discovery and Precision Medicine

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Activatable fluorogenic probes that remain weakly emissive until they encounter a defined biomolecular environment provide high-contrast readouts in living systems. Our work has focused on translating this principle into a wide range of chemical structures, from fluorescent amino acids[1] to peptides[2] and proteins[3]. The central design criteria are that these probes should be synthetically accessible while minimally perturbing the recognition features of the parent biomolecule, and switch on preferentially upon productive target engagement, thereby enabling wash-free imaging and improved signal-to-noise ratios in complex samples.[4]

Using this platform, we have developed fluorogenic probes for infection, inflammation and immunology that operate in live cells, human biosamples, in vivo models and fresh ex vivo biopsies. Recent advances include fluorescent amino acids for peptide-PAINT and super-resolution microscopy, which reduce linkage error while retaining strong environmental sensitivity,[5] and fluorogenic tags for functionally important immune proteins such as interleukins and chemokines.[6] The same molecular design principles have also been extended to nanobodies and antibodies, generating targeted imaging agents that preserve high affinity and biological function.[7]

Current efforts focus on controlling excited-state behaviour and activation pathways for therapeutic labelling and targeted imaging. By tuning fluorophore electronics, conformational freedom and microenvironment sensitivity, we have generated minimally perturbing labels that report internalisation and trafficking of antibody-drug conjugates in drug-discovery studies with pharmaceutical partners.[8] In parallel, we are extending beyond intensity-based outputs through biocompatible thermally activated delayed fluorescence (TADF) probes for highly multiplexed fluorescence lifetime imaging[9] and activity-based chemiluminescent reagents.[10] These complementary chemical platforms broaden the toolbox for cell-targeted imaging agents and precision-medicine studies in patient-derived samples with clinical collaborators.

[1] a) *Nat. Commun.* **2016**, *7*, 10940. b) *Angew. Chem. Int. Ed.* **2022**, *61*, e202117218. [2] a) *Nat. Commun.* **2020**, *11*, 4027. b) *Nat. Commun.* **2022**, *13*, 2366. [3] a) *ACS Cent. Sci.* **2024**, *10*, 143. b) Harel et al. *J. Am. Chem. Soc.* **2025**, 147, 42647. [4] a) *Nat. Rev. Chem.* **2020**, *4*, 275. b) *ACS Nano* **2023**, 17, 19478. c) *Curr. Opin. Chem. Biol.* **2024**, 80, 102458. [5] *Angew. Chem. Int. Ed.* **2023**, *62*, e202216231. [6] a) *J. Am. Chem. Soc.* **2025**, 147, 47783. b) *Chem. Sci.* **2026.** [7] a) *Nat. Commun.* **2024**, *15*, 7531. b) *J. Am. Chem. Soc.* **2024**, *46*, 30565. [8] *J. Am. Chem. Soc.* **2025**, *147*, 7578. [9] *Angew. Chem. Int. Ed.* **2026**, e21482. [10] *Nat. Biomed. Eng.* **2026.**

Time＆Date：Friday, July 24, 13:00 — 14:30

Place：Meeting room 1 , 2F, H-2 Building, Yokohama Campus

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