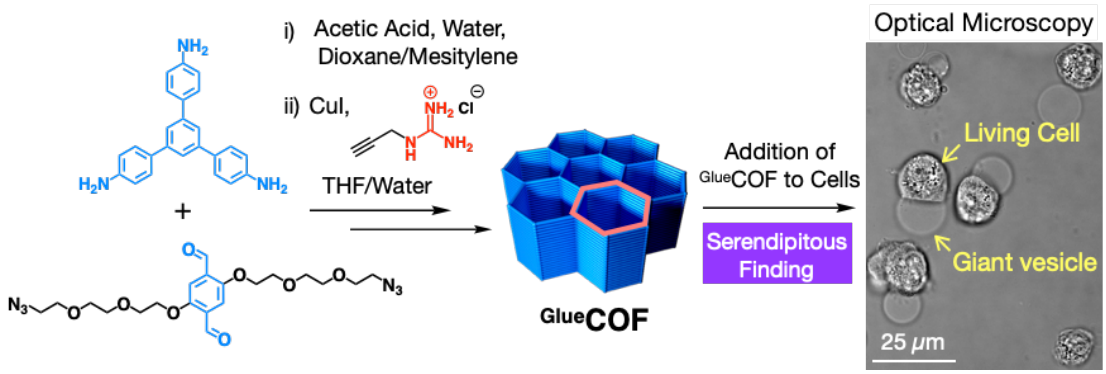
Giant Extracellular Vesicles Formed through the Interaction of Living Cells with Covalent Organic Frameworks Decorated with Guanidinium Moieties

([1]*The Univ. of Tokyo*) ○Young Kyoung Hong[1], Hyuna Jo[1], Takayuki Miki[1], Takuzo Aida[1]
Keywords: Artificial Extracellular Vesicle, Molecular Glue, Covalent Organic Framework

Extracellular vesicles (EVs), packed with biological information, offer exciting promises for biomarker discovery and applications in therapeutics and non-invasive diagnostics.[1] These specialized vesicles can serve as potent carriers of biologically important contents, including microRNAs which play crucial roles in gene regulation and cellular signaling. The use of EVs containing bioactive materials holds immense promise in diagnostics, where specific profiles in EVs can serve as non-invasive biomarkers for disease detection and monitoring. Despite such promise, there remains two major limitations in the use of engineered EVs for wider applications: (1) Production efficiency and (2) Composition control.[2] Thus, an innovative technology for scalable production of EVs with improved loading efficiency of cellular components must be developed to meet the clinical demand for cargo-loaded EVs.

We have recently observed the emergence of remarkably giant EVs (10-15 μm), almost reaching the size of the parent cell, triggered by the introduction of bio-adhesive covalent organic frameworks (^{Glue}COFs)[3]. The adhesive characteristics of ^{Glue}COF stem from its abundant guanidinium ion pendants, enabling the formation of multivalent salt-bridges with oxyanionic units on the cell membrane. This unprecedented stimulation of EV production by COFs, a phenomenon not previously documented, unveils opportunities for the facile generation of artificial EVs.



1) A. M. Vargason, A. C. Anselmo, S. Mitragotri, *Nat. Biomed. Eng.* **2021**, 5, 951. 2) I. K. Herrmann, M. J. A. Wood, G. Fuhrmann, *Nat. Nanotechnol.* **2021**, *16(7)*, 748–759. 3) H. Jo, T. Kitao, A. Kimura, Y. Itoh, T. Aida, K. Okuro, *Angew. Chem. Int. Ed.* **2021**, *60*, 8932–8937.