【Grant-in-Aid for Transformative Research Areas（B）】

Trogocytosis: Elucidating a New Principle of Intercellular Communication via Cellular Nibbling

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Project Information	Project Number : 26B305　Project Period (FY) : 2026-2028 Keywords : Trogocytosis, Immune cells, Microglia, *Entamoeba histolytica*, Nanopipette

Purpose and Background of the Research

●Outline of the Research

Traditionally, cell–cell communication has been studied mainly through signaling by secreted factors such as hormones and cytokines. Recently, trogocytosis, a newly recognized form of phagocytosis, has emerged as an alternative mode of communication. While conventional phagocytosis involves engulfing and digesting an entire cell (Fig. 1, upper left panel A), trogocytosis refers to the process by which a cell "bites off" and internalizes a portion of another cell, including its membrane (Fig. 1, upper left panel B). Trogocytosis is considered an evolutionarily conserved mechanism observed from unicellular protozoa to multicellular organisms. However, because studies have been conducted separately across different fields, its fundamental principles and physiological roles remain unclear. To address this gap, this research area integrates immunology, neuroscience, and parasitology to analyze trogocytosis in a cross-disciplinary manner, aiming to define its shared mechanisms and functional significance.

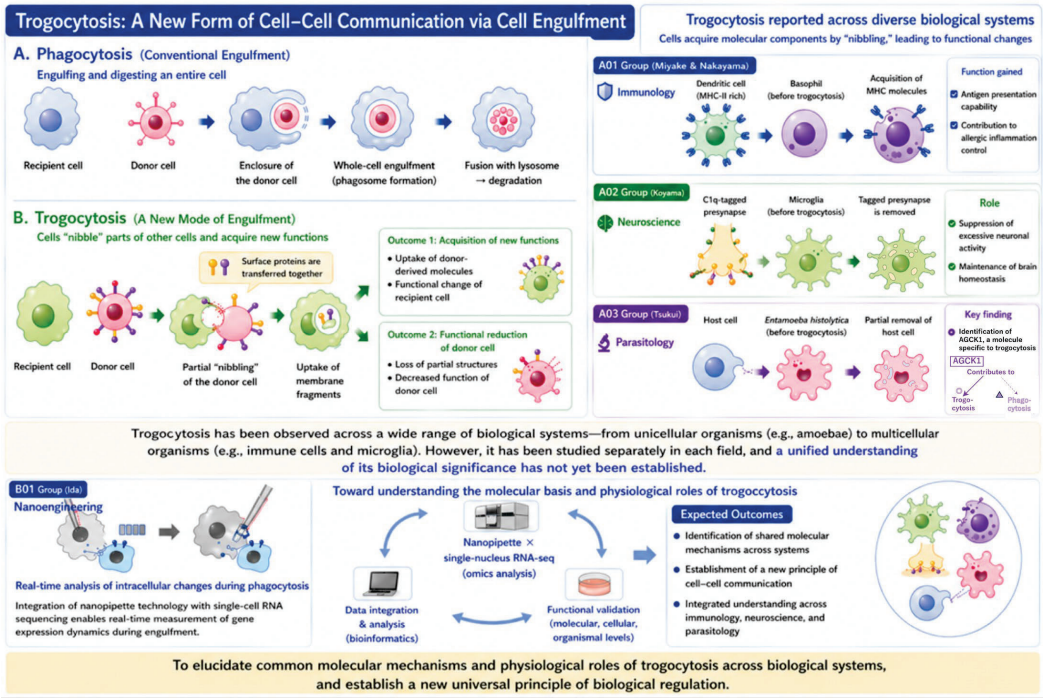

Figure 1. Establishment of Trogo Biology

●Establishing a New Modality for Trogocytosis Research

A major challenge in trogocytosis research is the lack of a common analytical platform across fields. Because donor-derived components are internalized into recipient cells, conventional methods cannot distinguish their origins. Moreover, trogocytosis is a rapid process, making it difficult for standard RNA sequencing to capture dynamic changes. To address this, this project will establish a new analytical platform based on nanotechnology.

The B01 research group will develop nanopipette-based methods that enable real-time observation and precise extraction of nuclear or intracellular components from cells undergoing trogocytosis. This approach will allow time-resolved analysis of molecular dynamics during the process. By applying this platform across disciplines, we aim to elucidate the common molecular principles of trogocytosis (Fig. 2).

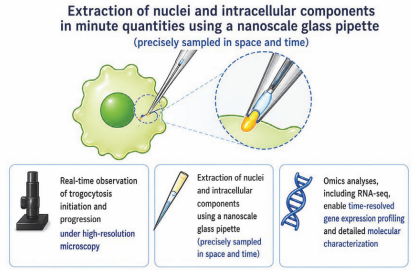

Figure 2. Trogocytosis research using nanopipette technology

Expected Research Achievements

●Research Plan and Methods

This project aims to identify shared mechanisms of trogocytosis across diverse systems by comparing mouse immune cells, microglia, and amoebae. We will integrate flow cytometry, super-resolution microscopy, and omics analyses to achieve a cross-disciplinary understanding.

Research Group A01 (Miyake & Nakayama): Trogocytosis in Immune cells
Identify key genes and mechanisms underlying MHC transfer using single-cell RNA-seq and CRISPR screening.

Research Group A02 (Koyama): Trogocytosis in Microglia
Test the hypothesis that microglia maintain neural homeostasis via selective mitochondrial removal using 3D culture (GNU) and imaging.

Research Group A03 (Tsukui): Trogocytosis in Amoebae
Elucidate molecular mechanisms in *Entamoeba histolytica* through comparison with *E. dispar* and evaluate host responses using Colon-on-Chip.

Research Group B01 (Ida): Nanopipette technology
Establish real-time extraction and analysis of nuclei during trogocytosis and enable precise functional perturbation. This platform will be shared across the project.

Through these cross-disciplinary comparative analyses and the development of innovative technologies, this project aims to elucidate the universal principles of cell–cell communication mediated by "cellular nibbling" via trogocytosis. Establishing the concept of trogocytosis as a mechanism of biological regulation may ultimately lead to the creation of a new research field: "biological regulation through phagocytosis," integrating trogocytosis with other related processes.

Website(s)	https://trogo-biology.jp/