Biologists determine the Leep2 complex regulates macropinosome formation

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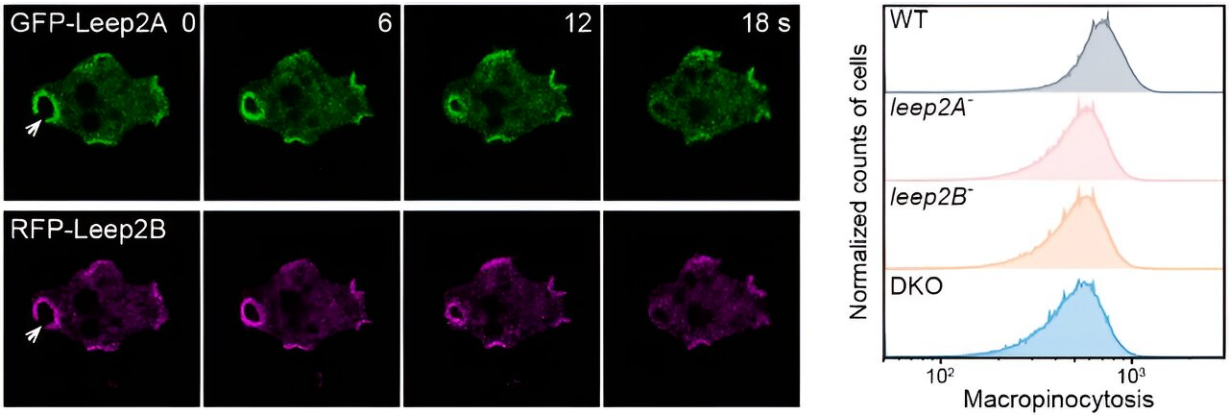

The Leep2A/2B RasGAP complex localizes to macropinocytic cups and regulate the cells' macropinocytic activity. Credit: Cai Huaqing's group

The social amoeba Dictyostelium discoideum is a valuable model to study the regulation of macropinocytosis. A research team led by Prof. Cai Huaqing from the Institute of Biophysics of the Chinese Academy of Sciences has recently used the Dictyostelium model system and a proteomics-based approach to reveal the molecular mechanism of macropinosome formation controlled by Ras signaling.

The study

was published in the *Journal of Cell Biology.*

Macropinocytosis is a specialized endocytic process that mediates the large-scale non-selective uptake of extracellular fluid by cells. The Ras gene, which is frequently mutated in tumors, is a key regulator of macropinocytosis. Understanding the spatiotemporal regulation of Ras signaling during macropinocytosis is therefore of great importance.

In this study, the researchers used

biochemical methods to screen for regulatory factors localized at macropinocytic cups and identified a protein complex called Leep2, composed of Leep2A and Leep2B.

The Leep2 complex functions as a Ras GTPase-activating protein that precisely regulates the activity of three small GTPases of the Ras family, thereby controlling the formation and closure of macropinosomes.

This study elucidates the critical regulatory role of maintaining a balance of Ras activity in macropinocytosis and paves the way for future investigations into how Ras-centered signaling pathways regulate macropinocytosis in tumor cells.

More information: Xiaoting Chao et al, Leep2A and Leep2B function as a RasGAP complex to regulate macropinosome formation, *Journal of Cell Biology* (2024). DOI: 10.1083/jcb.202401110

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