

# Bio Phys TO

## Lunchtime Seminar Series

### WHEN?

April 10, 2025

12:00-1:00PM

### WHERE?

McLennan Physical Laboratories

255 Huron Street

Rm. 606

### WHY?

Join us for pizza and an opportunity to learn and engage with members of the UofT Biophysics community!

### SPEAKER

## Sergey Plotnikov

*Department of Cell and Systems Biology*

### A TRPV4-dependent calcium signaling axis governs lamellipodial actin architecture to promote cell migration



Cell migration is crucial for development and tissue homeostasis, while its dysregulation leads to severe pathologies. Cell migration is driven by the extension of actin-based lamellipodia protrusions, powered by actin polymerization, which is tightly regulated by signaling pathways, including Rho GTPases and  $\text{Ca}^{2+}$  signaling. While the importance of  $\text{Ca}^{2+}$  signaling in lamellipodia protrusions has been established, the molecular mechanisms linking  $\text{Ca}^{2+}$  to lamellipodia assembly are unknown. Here, we identify a novel  $\text{Ca}^{2+}$  signaling axis involving the mechano-gated channel TRPV4, which regulates lamellipodia protrusions in various cell types. Using  $\text{Ca}^{2+}$  and FRET imaging, we demonstrate that TRPV4-mediated  $\text{Ca}^{2+}$  influx upregulates RhoA activity within lamellipodia, which then facilitates formin-mediated actin assembly. Mechanistically, we identify CaMKII and TEM4 as key mediators relaying the TRPV4-mediated  $\text{Ca}^{2+}$  signal to RhoA. These data define a molecular pathway by which  $\text{Ca}^{2+}$  influx regulates small GTPase activity within a specific cellular domain – lamellipodia – and demonstrate the critical role in organizing the actin machinery and promoting cell migration in diverse biological contexts.

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