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I E C B

Involvement of phosphatidylinositol-5 monophosphate (PtdIns5P) and Rho GTPases in the assembly of functional invadosomes in hematopoietic cells.

Frédérique GAITS-IACOVONI
Institut des Maladies Métaboliques et Cardiovasculaires (I2MC)
INSERM UMR 1048, Université Paul Sabatier, Toulouse, FRANCE

PtdIns5P has been the subject of many studies over the last decade but its functions as a signaling molecule are still poorly understood. Early studies reported production of PtdIns5P in the nucleus upon stress where it regulates apoptosis by binding the chromatin-regulator ING2. Cell fractionation demonstrated that while the majority of basal PtdIns5P is present in the plasma membrane, it is also enriched in endomembrane compartments. Our group pioneered studies demonstrating PtdIns5P is produced upon bacterial infection of epithelial cells by the human pathogen *Shigella flexneri*. In this model, PtdIns5P activates EGFR without ligand to stimulate the PI 3-kinase/Akt survival pathway. Elevation of PtdIns5P levels profoundly alters trafficking and leads to abolition of receptor degradation. Importantly, we detected PtdIns5P pools in early endosomes, where it impacted vesicular maturation. In anaplastic lymphomas, we demonstrated that PtdIns5P was produced through activation of the lipid kinase PIKfyve, involved in vesicular homeostasis and regulated invasiveness through structuration of invadopodia. This talk will focus on molecular aspects suggesting that PtdIns5P might integrate signals regulating both actin and trafficking to affect cellular fate and drive 3D-chemotaxis.