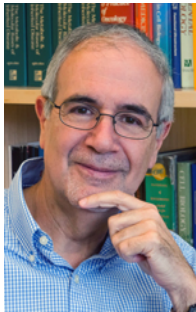




Department of Anatomy & Cell Biology



On the move: mechanisms and functions of lysosome positioning

Dr. Juan Bonifacino

National Institute of Health (NIH), USA

Distinguished Investigator & Associate Scientific Director
Cell Biology & Neurobiology Branch

Lysosomes are membrane-bound organelles whose main function is the degradation of biomacromolecules delivered by way of endocytosis, biosynthetic transport and autophagy. In addition, lysosomes participate in many other cellular processes, including lipid homeostasis, cell adhesion and migration, plasma membrane repair, detoxification, apoptosis, metabolic signaling and gene regulation. In my presentation, I will describe recent work from my laboratory on a novel aspect of lysosome biology: their positioning and motility within the cytoplasm. Indeed, lysosomes move back and forth between the center and the periphery of the cells. Outward movement is driven by kinesins, whereas inward movement is driven by dynein. The mechanisms by which lysosomes are coupled to these microtubule motors are incompletely understood. We obtained unexpected insights into the coupling of lysosomes to kinesins in the course of our studies on the BLOC-1 complex that is defective in some types of the hypopigmentation and bleeding disorder Hermansky-Pudlak syndrome (HPS). Affinity purification and mass spectrometry analyses using the BLOS2 subunit of BLOC-1 as bait led us to discover a related eight-subunit complex named BORC (for BLOC-one-related complex). We found that BORC associates with the lysosomal membrane, where it functions to recruit the small GTPase Arl8. This initiates a chain of interactions that promotes kinesin-dependent movement of lysosomes toward the plus ends of microtubules in the cell periphery. Further studies showed that BORC-dependent dispersal of lysosomes is required for autophagy, cholesterol transport, cell adhesion and migration, and nutrient signaling. These experiments thus uncovered a molecular machinery involved in moving lysosomes to the cell periphery, and highlighted the importance of this machinery in the regulation of many critical cellular processes.

Wednesday, April 19, 2017

11:30 am

**Strathcona Anatomy Building
3640 University Street
Room 2/36**

www.mcgill.ca/anatomy/seminars
anatomysec.med@mcgill.ca