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Defaults in the cellular transport machinery have frequently associated with many human pathologies, including cancer. Our work focuses on elucidating the various aspects of the regulation of vesicular transport and membrane trafficking. Toward this objective, we are using a combination of approaches, including live cell imaging, micro-patterning and reconstitution of transport events using model membranes.

Function of Rab GTPases (Bruno Goud)

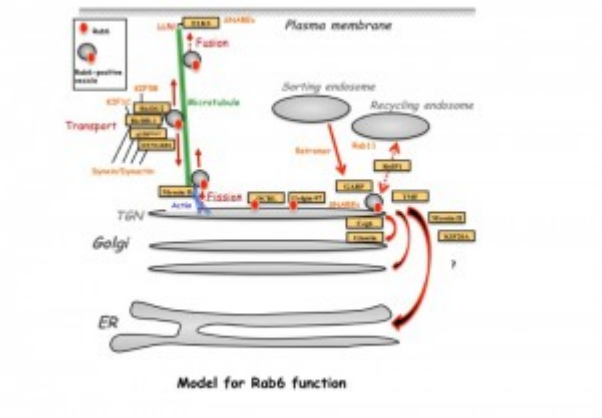

Fig. 1: Model for Rab6 function

Rab GTPases (>60 in man) virtually regulate all transport steps between cellular organelles, i.e. budding of transport vesicles from donor membranes, their movement along the actin and microtubule cytoskeleton and their targeting/fusion with acceptor membranes. We are focusing on Rab6, a Golgi-associated Rab GTP-ase that coordinates several transport pathways at the level of this organelle (Fig. 1), and on Rab proteins that share common effectors with Rab6, such as Rab8, Rab11 and Rab39. In particular, our recent work has highlighted a role of myosin II in the fission of Rab6 positive vesicles from Golgi membranes and the identification of multiple Rab-binding domains on Myosin Va. Ongoing projects concern the *in vitro* reconstitution of myosin II-driven fission process, the role of

Rab6/Rab8/myosin Va/b in post-Golgi transport events, the role of Rab11 in trafficking of APP (amyloid precursor protein) and BACE-1 in neuronal cells and the characterization of the Rab11/Rab25-mediated signaling pathways associated bladder cancer progression.

Physical parameters that underlie transport processes (Jean-Baptiste Manneville)

To unravel physical parameters such as membrane tension or membrane curvature underlying transport events, we have developed for several years the use of *in vitro* systems based on giant unilamellar vesicles (GUVs) from which membrane tethers are pulled with kinesin motors or optical tweezers. Our recent work has been focused on how the incorporation of polyunsaturated fatty acids modifies membrane properties and on the role of BIN1/M-amphiphysin2 in lipid clustering. We have also developed a novel approach to probe Golgi mechanics in living cells using polystyrene beads internalized in cultured cells and trapped with optical tweezers (Fig. 2).

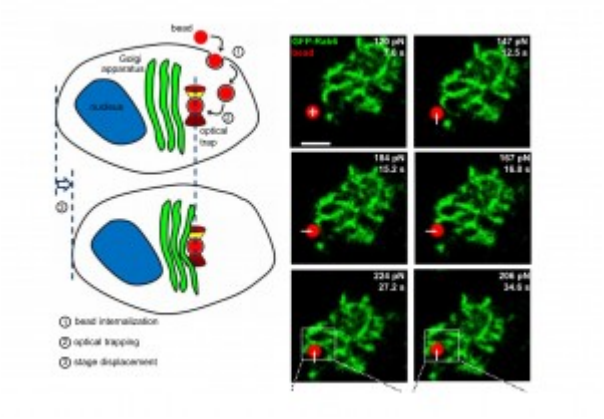

Fig. 2: Experimental set-up for probing Golgi mechanics in vivo

Understanding the global organization of endomembranes (Kristine Schauer)

We have developed a computational tool based on the micropatterning technique and density estimation using kernel-based algorithms to visualize the global organization of endomembranes. Our recent work using this approach has highlighted the role of cell adhesion in the topology of endocytosis and signaling. Ongoing studies aim at identifying molecular motors of the myosin and kinesin families that sustain the steady-sate organization of endomembranes and at detecting changes of this organization in cancer cells.

Function of myosins in membrane traffic (Evelyne Coudrier)

Our recent work has shown that the single-headed non-processive myosin 1 (myosin 1b) regulates the formation of tubules emanating from the trans-Golgi-Network (TGN) and can

extract membrane tubes along bundles of actin filaments in a minimal reconstituted system. Our current and future research aim at understanding the role of myosin 1b at the plasma membrane and the interplay between myosins and the actin network in the Golgi region to achieve their role in cargo transport.

Key publications

Year of publication 2019

Lou Fourriere, Amal Kasri, Nelly Gareil, Sabine Bardin, Hugo Bousquet, David Pereira, Franck Perez, Bruno Goud, Gaelle Boncompain, Stéphanie Miserey-Lenkei (2019 May 31)
RAB6 and microtubules restrict protein secretion to focal adhesions.
The Journal of cell biology : DOI : 10.1083/jcb.201805002

Year of publication 2018

Jean-Marie Carpier, Andres E Zucchetti, Laurence Bataille, Stéphanie Dogniaux, Massiullah Shafaq-Zadah, Sabine Bardin, Marco Lucchino, Mathieu Maurin, Leonel D Joannas, Joao Gamelas Magalhaes, Ludger Johannes, Thierry Galli, Bruno Goud, Claire Hivroz (2018 Feb 15)
Rab6-dependent retrograde traffic of LAT controls immune synapse formation and T cell activation.
The Journal of experimental medicine : 1245-1265 : DOI : 10.1084/jem.20162042

Year of publication 2017

Stéphanie Miserey-Lenkei, Hugo Bousquet, Olena Pylypenko, Sabine Bardin, Ariane Dimitrov, Gaëlle Bressanelli, Raja Bonifay, Vincent Fraisier, Catherine Guillou, Cécile Bougeret, Anne Houdusse, Arnaud Echard, Bruno Goud (2017 Nov 3)
Coupling fission and exit of RAB6 vesicles at Golgi hotspots through kinesin-myosin interactions.
Nature communications : 1254 : DOI : 10.1038/s41467-017-01266-0

Anand Patwardhan, Sabine Bardin, Stéphanie Miserey-Lenkei, Lionel Larue, Bruno Goud, Graça Raposo, Cédric Delevoye (2017 Jun 14)
Routing of the RAB6 secretory pathway towards the lysosome related organelle of melanocytes.
Nature communications : 15835 : DOI : 10.1038/ncomms15835

Year of publication 2016

Jean-Baptiste Brault, Cécile Khou, Justine Basset, Laure Coquand, Vincent Fraisier, Marie-Pascale

Frenkiel, Bruno Goud, Jean-Claude Manuguerra, Nathalie Pardigon, Alexandre D Baffet (2016 Jul 26)
Comparative Analysis Between Flaviviruses Reveals Specific Neural Stem Cell Tropism for Zika Virus in the Mouse Developing Neocortex.
EBioMedicine : DOI : S2352-3964(16)30323-1

Laura Picas, Frederique Gaits-Iacovoni, Bruno Goud (2016 Apr 20)
The emerging role of phosphoinositide clustering in intracellular trafficking and signal transduction.
F1000Research : DOI : 10.12688/f1000research.7537.1