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Review

The role of the cytoskeleton and molecular motors in endosomal dynamics

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ABSTRACT

The endocytic pathway is essential for processes that define how cells interact with their environment, including receptor signalling, cell adhesion and migration, pathogen entry, membrane protein turnover and nutrient uptake. The spatial organisation of endocytic trafficking requires motor proteins that tether membranes or transport them along the actin and microtubule cytoskeletons. Microtubules, actin filaments and motor proteins also provide force to deform and assist in the scission of membranes, thereby facilitating endosomal sorting and the generation of transport intermediates.

Contents

1. The endosomal system: an overview

The early endosome, characterised by the presence of rab5 and EEA1, acts as the major sorting station on the endocytic pathway (Fig. 1). Several populations of endocytic vesicle deliver content to the early endosome from the plasma membrane. At least two of these are generated by a clathrin-dependent pathway; APPL1-positive [1] and SNX15-positive [2] vesicles. The early endosome also receives vesicles derived from the TGN. From the endosome, cargo is sorted: for degradation, via a pathway comprised of multivesicular bodies (MVBs), during which endosomes mature and then fuse with the lysosome; or for recycling back to the plasma membrane or TGN [3]. Recycling to the plasma membrane occurs via slow or fast pathways. "Fast" recycling takes material directly from an early endosome back to the plasma membrane, and is regulated by Rab4 and Rab35 [4,5]. In contrast, "slow" recycling transits through Rab11-positive recycling endosomes [6–8]. The major pathways and important molecular components are shown in Fig. 1. How each motor associates with various endocytic compartments and contributes to endocytic function (detailed below) is summarised in Table 1.

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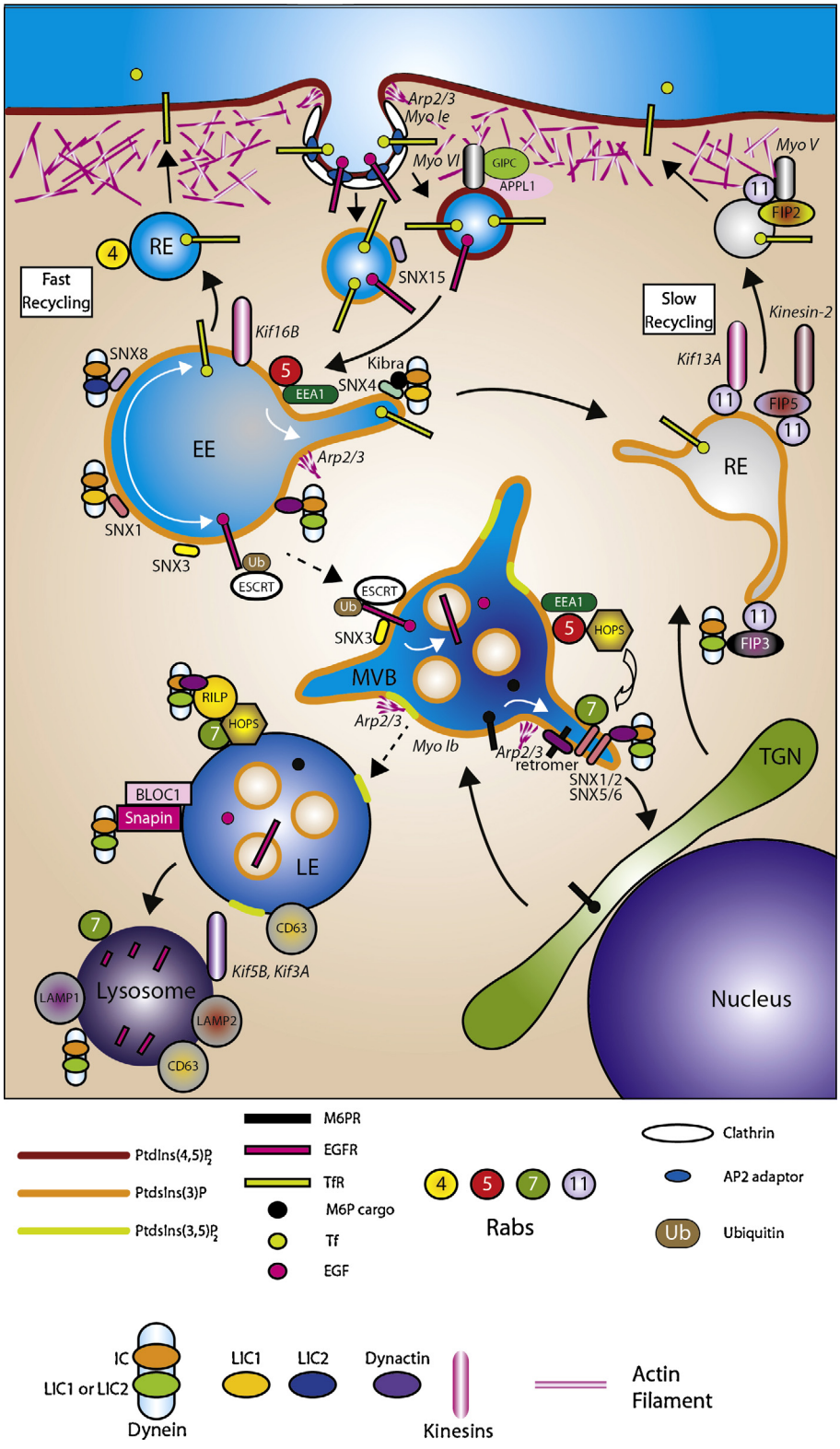

Fig. 1. Overview of the endocytic pathway and the cytoskeleton. Transport steps are shown using solid arrows, maturation steps are shown using broken arrows.

2. Motor proteins

Microtubules support intracellular transport in a manner that is dependent on their intrinsic polarity. They possess a dynamic plus end that, in most cells, grows towards the periphery and a minus end that is anchored in the microtubule organising centre, normally located near the nucleus in non-dividing cells. Microtubules support both short- and long-range movements, using two types of motors: kinesins, with a few exceptions, move towards plus ends [9], whilst cytoplasmic

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