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Why do peroxisomes associate with the cytoskeleton?☆

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ABSTRACT

Attachment of peroxisomes to cytoskeleton and movement along microtubular filaments and actin cables are essential and highly regulated processes enabling metabolic efficiency, biogenesis, maintenance and inheritance of this dynamic cellular compartment. Several peroxisome-associated proteins have been identified, which mediate interaction with motor proteins, adaptor proteins or other constituents of the cytoskeleton. It appears that there is a species-specific complexity of protein–protein interactions required to control directional movement and arresting. An open question is why some proteins with a specific role in peroxisomal protein import have an additional function in the regulation of cytoskeleton binding and motility of peroxisomes. This article is part of a Special Issue entitled: Peroxisomes edited by Ralf Erdmann.

1. Introduction

Peroxisomes exhibit a remarkable plasticity with respect to shape, size, abundance and metabolic function, often altered by changing environments [1]. The heterogenic appearance of peroxisomes became obvious with improvement of microscopic techniques. Electron microscopy revealed that peroxisomes are small, single-membrane bound organelles with varying diameters between 0.1 to 1.5 μm (Fig. 1A). Using fluorescent labeling techniques, the number of peroxisomes per cell was estimated to range between one and many hundred organelles depending on species, tissue, age and external stimuli. In mammalian cells, many peroxisomes are found in close proximity to the cytoskeleton (Fig. 1B). Live cell imaging of peroxisomes revealed striking dynamics of their intracellular distribution. Peroxisomes' motility involves oscillations, short range motions and long distance saltations in all possible directions (Fig. 1C). All organisms are supposed to require the cytoskeleton of both microtubules and microfilaments for peroxisome function, inheritance and maintenance. However, plant and yeast peroxisomes predominantly move along actin filaments, while animal cells preferentially use the microtubular network to transport peroxisomes, frequently over long distances. Recent progress has been made to understand the molecular basis of motility of peroxisomes and possible functions for each type of motion.

2. Myosin-driven transport of peroxisomes along actin filaments

In many organisms, the movement of organelles occurs along actin tracks by myosin motor proteins. Actin is a highly abundant and conserved protein found in virtually all eukaryotic cells. The monomeric form (G-actin) polymerizes to double-stranded, helical actin filaments (F-actin) in an ATP-dependent manner [2,3]. Actin is a central component in muscle contraction, cell motility and organelle movement [4,5]. Myosins are conserved motor proteins, which move along actin cables in eukaryotes [6]. The myosin superfamily is divided into as many as 37 classes [7,8]. In metazoa and fungi, class V myosins function as motors in organelle and vesicle movement, establishing cell polarity, mitotic spindle positioning, partitioning during cell division and mRNA localization [9–12]. Plant class XI myosins are closely related to class V myosins and share most of the functions [8,13]. While metazoan and fungi typically have one to three different class V myosins, plants usually have around a dozen different class XI myosins.

The yeast *Saccharomyces cerevisiae* (*S. cerevisiae*) divides asymmetrically by forming a bud from the mother cell. To ensure that peroxisomes and other organelles are inherited by daughter cells, this kind of cell division requires that the transport is tightly regulated [14]. Moreover, it has to be ensured that not all organelles are transported into the bud, but some need to be retained in the mother cell. The transport of different organelles into the bud is a highly ordered process [15–17]. Different cargoes are transported at different time points of the cell cycle. For example mitochondria are transported into the bud later than peroxisomes [18,19]. In *S. cerevisiae*, the movement of organelles to the bud occurs along actin tracks by the motor proteins Myo2 and Myo4.

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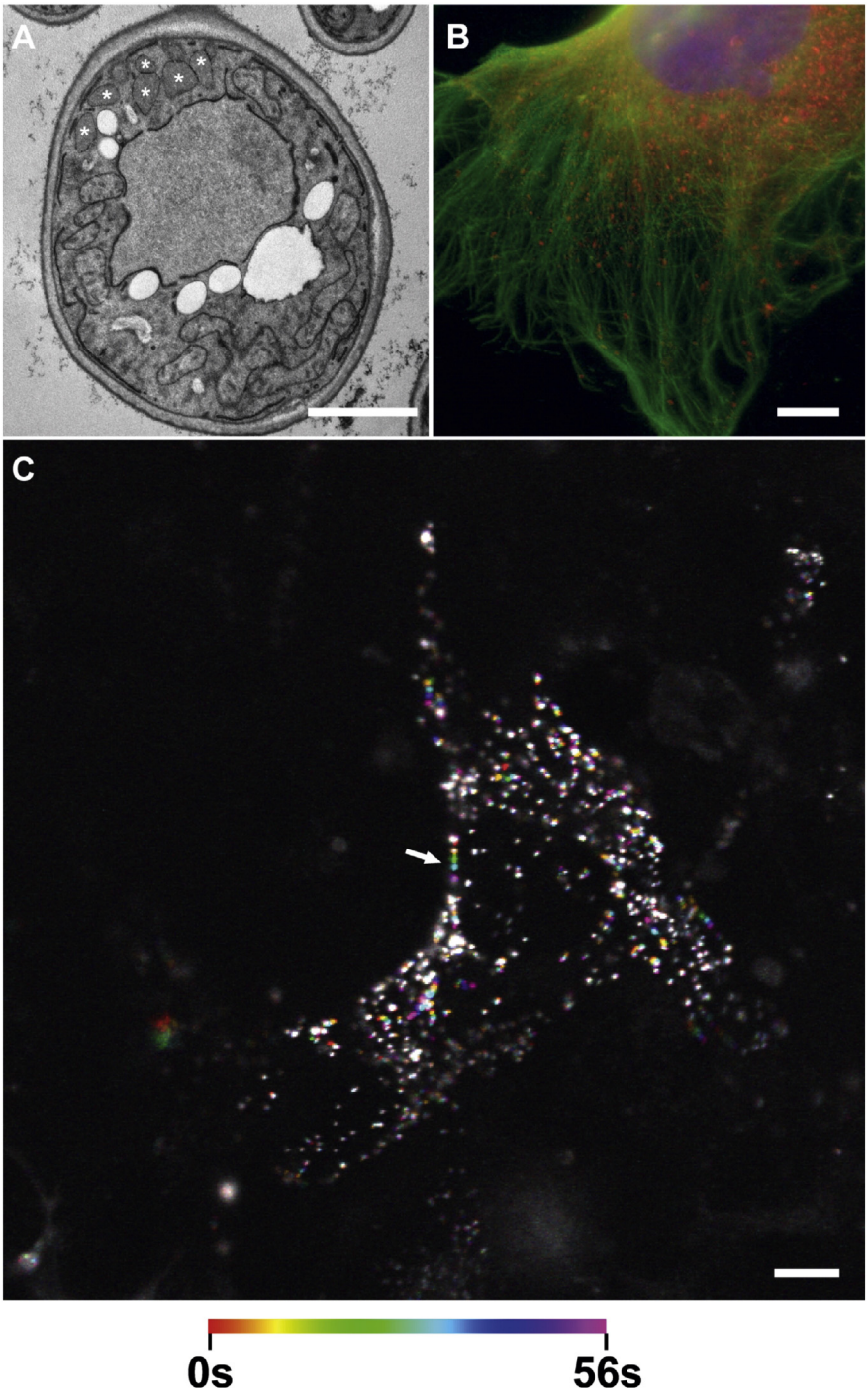

Fig. 1. Microscopy of peroxisomes (A) Electron micrograph of a *Saccharomyces cerevisiae* cell. Peroxisomes are marked with an asterisk. Scale bar: 1 μm. (B) Fluorescence microscopy of a human fibroblast labeled with DAPI (nucleus, blue), Pmp70 antibodies (peroxisomes, red) and TubStain-GFP (microtubules, green). Scale bar: 10 μm. Note that all peroxisomes are in close proximity to microtubules. (C) Live cell fluorescence microscopy showing movement of peroxisomes in a human fibroblast cell. Peroxisomes are labeled with GFP. Different time points are represented by different colors. Static peroxisomes are white, moving peroxisomes are visible as a row of dots with different colors (arrow). Scale bar: 10 μm.

While Myo4 transports the cortical ER and mRNAs, most other organelles including mitochondria and peroxisomes are moved by Myo2 [20–23]. The N-terminus of the homodimeric Myo2 contains the conserved motor domain, while the C-terminus contains the cargo-binding domain [24,25]. Specific adapter proteins have been identified for various organelles and secretory vesicles, which bind the C-terminus of Myo2 [14,26,27]. Like in yeast, plant peroxisomes predominantly move along actin as shown by confocal microscopy using fluorescent proteins to simultaneously visualize peroxisomes and actin [28–30]. Plant peroxisomes were found in close vicinity to actin and moved along the actin filaments [30]. Moreover, treatment of different plant cells with the actin destabilizing drugs cytochalasin and latruncilin B led to a reversible stop of peroxisomal movement [28–30].

3. Structural basis of peroxisome interactions with myosin and actin

In *S. cerevisiae*, the peroxisomal membrane Protein Inp2 plays a central role in peroxisome inheritance. Inp2 interacts directly with the

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