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Spliceosomal snRNPs Repeatedly Cycle through Cajal Bodies

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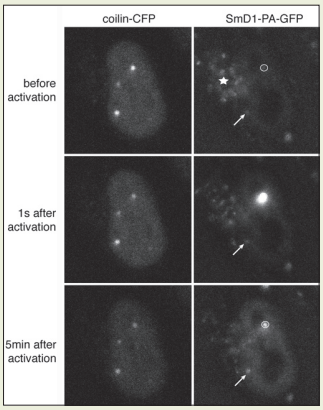
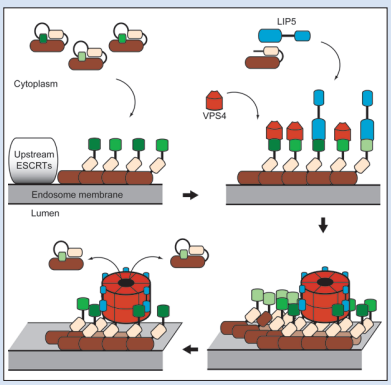


Spliceosomes, the pre-mRNA splicing machinery, are assembled from multiple snRNP complexes (e.g., U4, U6, and U5 snRNPs) that accumulate within Cajal bodies (CBs), subnuclear structures first observed over a hundred years ago. Recent findings have shown that the final biogenesis and assembly of new snRNPs occurs in CBs, although splicing by the mature spliceosome occurs in the nucleoplasm. By analyzing the dynamics of snRNP components labeled with photoactivatable or color-maturing fluorescent proteins, the authors show that CBs contain mainly mature snRNPs that repeatedly cycle through and between them. Inhibition of the spliceosomal cycle, i.e., the cyclic assembly of active snRNPs and their disintegration during splicing, by depletion of factors involved in spliceosome recycling led to a specific accumulation of U4/U6 snRNP assembly intermediates while the level of the U5 snRNP was reduced. These data indicate that regeneration of the U4/U6•U5 tri-snRNP after splicing also occurs in CBs, which thus emerge as the snRNP recycling center of the cell nucleus.



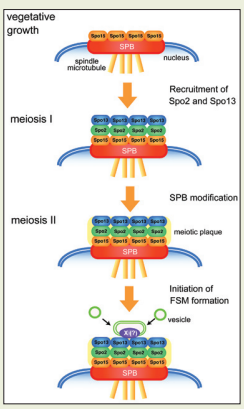
Novel Interactions of ESCRT-III with LIP5 and VPS4 and Their Implications for ESCRT-III Disassembly

Soomin Shim, Samuel A. Merrill, and Phyllis I. Hanson

The cellular machinery responsible for multivesicular body biogenesis is important for receptor down-regulation, viral budding, and cell abscission. ESCRT-III (**e**ndosomal **c**omplex **r**equired for **t**ransport III) is believed to drive these budding events, while the ATPase VPS4 recycles ESCRT-III with the aid of LIP5, a cofactor. LIP5 also interacts with CHMP5, a protein related to ESCRT-III, but the role of these interactions is unknown. Here the authors report that LIP5 binds directly to several ESCRT-III proteins at their C-termini, overlapping with sites previously implicated in binding VPS4. However, a second, unexpected binding site for VPS4 was identified in ESCRT-III proteins that might allow simultaneous binding of VPS4 and LIP5. Interestingly, LIP5 interacts with CHMP5 in a fundamentally different manner from its interaction with the other ESCRT-III proteins, such that CHMP5 might negatively regulate LIP5 for engagement with ESCRT-III and VPS4. This study adds new insight into how LIP5 and VPS4 cooperate in the pathway leading to multivesicular body formation.

Meiotic Spindle Pole Bodies Acquire the Ability to Assemble the Spore Plasma Membrane by Sequential Recruitment of Sporulation-specific Components in Fission Yeast

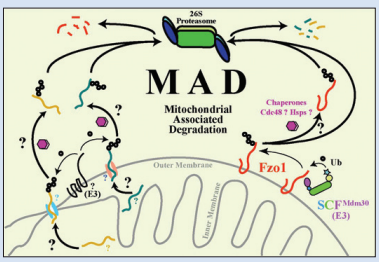
Yukiko Nakase, Michiko Nakamura-Kubo, Yanfang Ye, Aiko Hirata, Chikashi Shimoda, and Taro Nakamura



Sporulation in the fission yeast *Schizosaccharomyces pombe* is an alternative mode of cell division, equivalent to gametogenesis. A double unit membrane called the forespore membrane is formed de novo within the cytoplasm of mother cells during meiosis and develops into the plasma membrane of newborn spores. This unique membrane assembly begins at the spindle pole body (SPB), a centrosome-equivalent structure. In meiotic cells, the SPB is structurally modified to bear additional electron-dense outer plaques on the cytoplasmic side that appear to nucleate forespore membrane assembly. Here the authors identify two novel SPB components, Spo2 and Spo13, that are specifically expressed in meiosis, recruited to the cytoplasmic side of the SPB, and implicated in outer plaque formation. Spo2 and Spo13 localize to and closely contact the nascent forespore membrane and are essential for its assembly. These results provide new insights into the role of the meiotic machinery, the SPB, in de novo membrane biogenesis during gametogenesis of lower eukaryotes.

Ubiquitin-Proteasome–Dependent Degradation of a Mitofusin, a Critical Regulator of Mitochondrial Fusion

Mickael M. J. Cohen, Guillaume Leboucher, Nurit Livnat-Levanon, Michael H. Glickman, and Allan M. Weissman



Appropriately timed fusion and fission of the mitochondrial network is essential for respiration and requires a cohort of mitochondrion-associated GTPases. Modulating the levels of these GTPases alters the fusion/fission ratio. The authors show that the mitofusin Fzo1p is targeted for ubiquitylation by a complex cytosolic ubiquitin ligase, SCF^{Mdm30}, while still embedded in the mitochondrial outer membrane. Modification of Fzo1p with K48-linked polyubiquitin chains targets it for proteasomal degradation. These findings set the stage for a greater understanding of the means by which mitochondrial morphology is conditioned to meet cellular needs. Based on their work and previous findings, the authors propose a process of **m**itochondrial-**a**ssociated **d**egradation (MAD) reminiscent of the well-studied process of endoplasmic reticulum–associated degradation. In MAD, mitochondrial proteins would be ubiquitylated by specific E3s, extracted from mitochondria by specific chaperones, and targeted for destruction by cytosolic proteasomes. Alternatively, proteasomes may directly degrade the ubiquitylated target at the mitochondrion. ■