doi:10.1017/S1431927610054176
Microsc. Microanal. 16 (Suppl 2), 2010

Identification of Mitochondrial Derived Vesicles.

P. Rippstein, M. Neuspiel, A. Schauss, V. Soubannier, E. Braschi and H.M. McBride.

Stewart Whitman Core Histopathology Laboratory, Rm H2102, Rm H445A.
University of Ottawa Heart Institute, 40 Ruskin Street, Ottawa, Ontario, K1Y 4W7, Canada.

Mitochondrial morphology with its two membrane system, intricate cristae architecture and numerous links to the endoplasmic reticulum and other organelles has been well characterized by electron microscopists throughout the ages. Studies initially directed towards the dissection of mitochondrial division ultimately led to the identification of small mitochondrial fragments which appeared to carry only select proteins. Given the previous assumption that mitochondrial protein import should be equal in all organelles, the appearance of structures demonstrating only certain specific proteins was unusual. Ultrastructural analysis of these structures in intact cells revealed previously uncharacterized, vesicular profiles emanating from the sides of otherwise intact mitochondria. The formation of these vesicles did not depend on the known mitochondrial fission machinery, consistent with a novel machinery. Indeed, the edges of these structures appeared electron dense, suggesting some coat-related structure, and were of uniform size, between 70-120 nm in diameter. Pre-embedded immunogold labeling for the mitochondrial marker protein MAPL (mitochondria-anchored protein ligase), shown to transport in vesicles to the peroxisome, demonstrated that many of the vesicles carry both single and double membranes. Further experimentation revealed that vesicles that did not contain MAPL instead carry oxidized proteins that are subsequently delivered to the lysosomes for degradation. In vitro generation of mitochondrial derived vesicles allowed their separation by sucrose density gradients, and subsequent ultrastructural analysis of the fractions demonstrated the enrichment of single vs. double membrane structures at unique buoyant densities. Taken together, the combination of confocal, EM and biochemical reconstitution has revealed the presence of a novel vesicular transport route between the mitochondria, peroxisomes and lysosomes.

References:

[1] **Neuspiel, M., Schauss, A.C., Braschi, E., Zunino, R., Rippstein, P.**, Rachubinski, R.A., Andrade-Navarro, M.A., and **McBride, H.M.** *Cargo-selected transport from the mitochondria to peroxisomes is mediated by vesicular carriers.* **Current Biology.** 18(2), 102-108, 2008.

[2] **Zunino, R., Rippstein, P.**, Andrade-Navarro, M., and **McBride, H.M**. *The SUMO protease SenP5 is required to maintain mitochondrial morphology and function.* **Journal of Cell Science**, 120(7):1178-1188, 2007

[3] **Zunino, R., Rippstein, P.**, Andrade-Navarro, M., and **McBride, H.M**. *The SUMO protease SenP5 is required to maintain mitochondrial morphology and function.* **Journal of Cell Science**, 120(7):1178-1188, 2007