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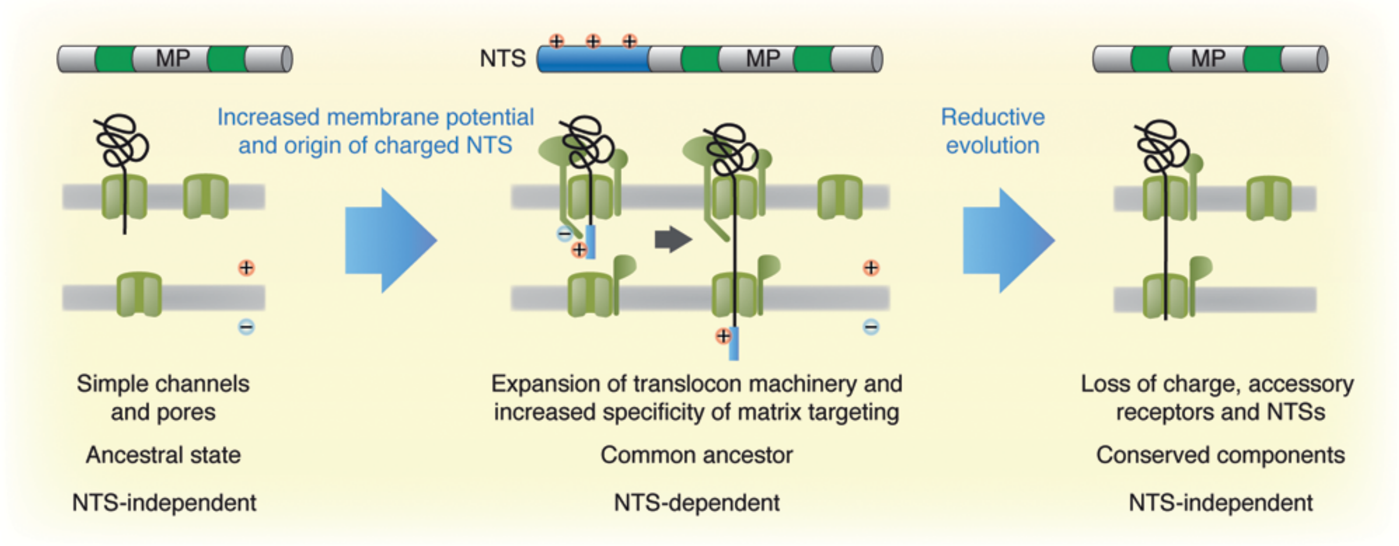
Protein import into the mitochondrial and hydrogenosomal matrix

Cells, the basic unit of life, can be divided into two major classes: the prokaryotes (cells that have their genetic information freely floating with them) and eukaryotes (cells with internal compartments, one of which holds the genetic information). Mitochondria, the electrically charged powerhouses of the cell, were key to the transition from prokaryote to eukaryote. The evolution of protein import into the double membrane bound mitochondria is central to understanding its origin and function in all eukaryotes. Eukaryotic cells are extremely elaborate, resembling a bustling city, busy with constant traffic of proteins between various compartments. Getting things to their proper destination is essential for cell survival. Just like letters find their destination by way of an address, proteins destined to the mitochondrion find their way by virtue of a small succession of charged amino acids at the beginning of each protein's amino acid sequence. This sequence is called the “transit peptide”. These “transit peptides” have corresponding gates (translocases) at the membrane that specifically recognize these transit peptides and only let proteins with the correct address in. In many cases these gates are aided by gatekeepers (accessory receptor proteins) to ensure proper identification of the “transit peptides”. How did such subcellular targeting systems arise during the emergence of the eukaryotic cell? In the current study we focus on the evolution of the “transit peptides”.

For 30 years it has been known that “transit peptides” are positively charged, for 20 years it has been known that the positive charge helps protein cross the negatively charged inner mitochondrial membrane by electrophoresis. Recent studies however, have shown that in organisms that contain highly reduced mitochondria (hydrogenosomes) the “transit peptides” are dispensable for targeting. We propose a hypothesis to explain the origin of these “transit peptides” and why some organisms do not require them.



Top section: Schematic architecture of peptides recognized by the mitochondria during various stages of evolution. The unknown internal motifs are shown in *dark green* while the charged “transit peptide” is shown in *blue*. *Bottom Section* The two membranes of the mitochondria showing the gates and gatekeepers (shown in *light green*) involved in transporting proteins across membranes (shown in *grey*).

The electrochemical gradient across the inner membrane of mitochondria require a positively charged transit peptide for selective protein import. “Uncharged” hydrogenosomes do not require charged transit peptides to recognize their proteins for import; they recognize their cargo by a mechanism of currently unknown nature. Our observations indicate that these unknown targeting motifs are also present in eukaryotes with canonical “charged” mitochondria. This conservation uncovers the ancestral state of protein targeting, which initially depended on yet unidentified signals and was then supplemented by charged “transit peptides” in response to charged mitochondria. Subsequently, loss of the charge in mitochondria (due to evolutionary reduction) resulted in proteins reverting to use these ancestral internal motifs. We conclude that during evolution the sensing of intracellular electrical charge played a role in protein targeting to the mitochondria. Before electricity, a simpler address was used, which is just now being uncovered.

Publication

Conservation of transit peptide-independent protein import into the mitochondrial and hydrogenosomal matrix.
Garg S, Stölting J, Zimorski V, Rada P, Tachezy J, Martin WF, Gould SB
Genome Biol Evol. 2015 Sep 2. pii: evv175.