

Three fundamental mechanisms could distinguish the transportation of protein. The first is gated transport which includes cargo movement between cytosol and the nucleus through nuclear pore complexes. Second is protein translocation, transmembrane protein translocators directly transport specific proteins across a membrane from the cytosol into a topologically distinct space. The transported protein molecule usually must unfold to snake through the translocator. And the last one is vesicular transport. This includes the transport from the ER to other organelles since the transport proteins do not cross a membrane.

In vesicular transport, each mode of protein transfer is usually guided by sorting signals in the transported protein, which are recognised by complementary sorting receptors—signal sequences and sorting receptors direct proteins to the correct cell address. A signal peptide could be added to the N terminal which usually induces protein from the ER to the Golgi body. And N terminal signal peptide-induced protein returns to the ER.

The transport of molecules between the nucleus and the cytosol.

The nuclear envelope encloses the DNA and defines the nuclear compartment. This envelope consists of two concentric membranes penetrated by nuclear pore complexes. The small molecules which smaller than 5000daltons can freely diffuse through the nuclear pores. Large proteins, however, diffuse in much more slowly, and the larger a protein, the more slowly it passes through the NPC. Proteins larger than 60k daltons cannot pass enter by passive diffusion, which means they need active transport. Sorting signals called nuclear localization signals (NLSs) are responsible for the selectivity of this active nuclear import process.

To initiate nuclear import, most nuclear localization signals must be recognized by nuclear import receptors. Which belongs to the karyopherin family. The import receptors are soluble cytosolic proteins that bind both to the nuclear localization signal on the cargo protein and to the FG repeats which could prevent the dissociation of the receptor-cargo complex. Once go through NPC and inside the nucleus, the import receptors dissociate from their cargo and return to the cytosol. Nuclear export works like nuclear import but in reverse. The transport system relies on nuclear export signals on the macromolecules to be exported, as well as on complementary nuclear export receptors. These receptors bind to both the export signal and NPC proteins to guide their cargo through the NPC to the cytosol.

The GTP-bound form of the monomeric GTPase Ran is required for both nuclear import and export since going through NPCs increases order in the cell. The cytosol contains mainly Ran-GDP and the nucleus contains mainly Ran-GTP. In the import, when the cargo-receptor complex goes through the NPC, the Ran-GTP binds to them causing the receptors to release their cargo. Because the Ran-GDP in the cytosol does not bind to import receptors, unloading occurs only on the nuclear side of the NPC. In this way, the nuclear localization of Ran-GTP creates the directionality of the import process. The empty import receptor with Ran-GTP is transported back through the NPC to the cytosol. There, Ran-GAP triggers Ran-GTP to hydrolyze its bound GTP, thereby converting it to Ran-GDP, which dissociates from the receptor. The receptor is then ready for another cycle of nuclear transport. Nuclear export occurs by a similar mechanism, except that Ran-GTP in the nucleus promotes cargo binding to the export receptor, rather than promoting cargo dissociation. Once the export receptor moves through the pore to the cytosol, Ran-GTP converts to Ran-GDP and releases both its cargo and Ran-GDP in the cytosol. Free export receptors are then returned to the nucleus to complete the cycle.

mitochondria precursor proteins are imported as unfolded polypeptide chains

Many proteins entering the matrix space contain a signal sequence at their N-terminus that a signal peptidase rapidly removes after import. They all form an amphiphilic alpha-helix in which positively charged residues cluster on one side of the helix, while uncharged hydrophobic residues cluster on the opposite side. Multisubunit protein complexes that function as protein translocators mediate protein movement across mitochondrial membranes. The TOM complex transfers proteins across the outer membrane and two TIM complexes transfer proteins across the inner membrane.

Mitochondrial precursor proteins do not fold into their native structures after they are synthesized; instead, they remain unfolded in the cytosol through interactions with the chaperone protein such as the hsp70 family protein. The N-terminal signal sequence of mitochondrial precursor protein is recognized by receptors of the TOM complex. The protein is then translocated through the TIM 23 complex so that it transiently spans both mitochondrial membranes. The signal sequence is cleaved off by a signal peptidase in the matrix space to form the mature protein. ATP is needed as an energy supply for the release of newly synthesized polypeptides from the chaperone proteins and binds with the TOM complex. Once the signal sequence has passed through the TOM complex and is bound to a TIM complex, further translocation through the TIM translocation channel requires the electrochemical H^+ gradient across the inner membrane. Mitochondrial hsp70 also plays a crucial part in the import process. The hsp70 has a high affinity for unfolded polypeptide chains and it binds tightly to an imported protein chain as soon as the chain transfers to TIM. The hsp70 then undergoes a conformational change and releases the protein chain in an ATP-dependent step, pulling force on the protein being imported. And hsp60 protein helps the unfolded polypeptide chain to fold correctly by using the energy of ATP hydrolysis.

For protein transport into the inner membrane, a hydrophobic amino acid sequence, strategically placed after the N-terminal signal sequence, acts as a stop-transfer sequence, preventing further translocation across the inner membrane. In the transport route of the inner membrane intermembrane space, the TIM23 complex initially translocates the entire protein into the matrix space, then is removed by signal peptidase and the new hydrophobic N-terminal signal is exposed. The signal sequence guides the protein to the OXA complex, which inserts the protein into the inner membrane.