The nuclear pore complex

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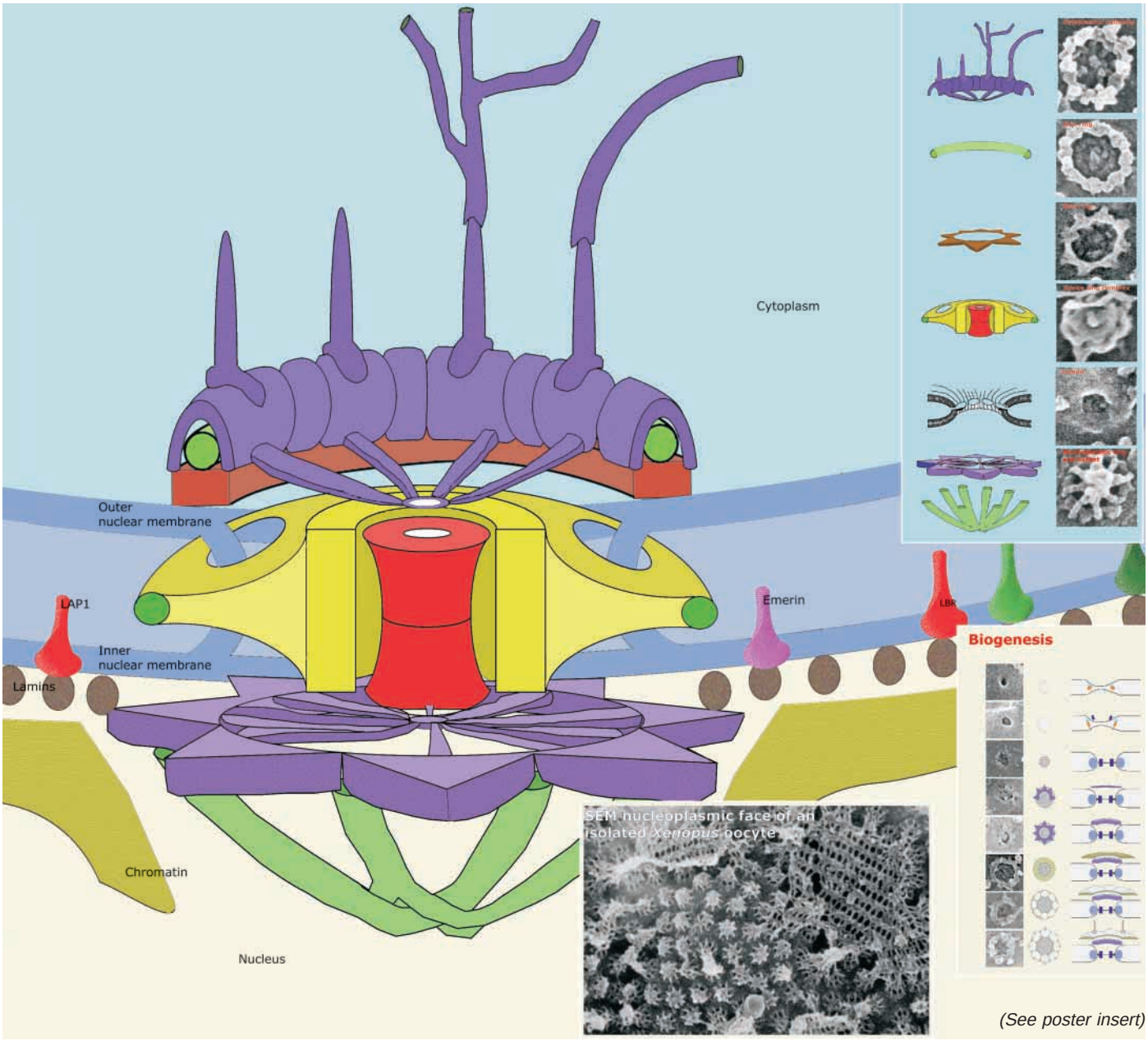
All transport between the nucleus and the cytoplasm passes through the nuclear pore complex (NPC) (**Functions**). Small (20-40 kDa) molecules passively diffuse through the NPC, whereas there are a series of signal- and temperature-dependent mechanisms for large molecules. Major import traffic includes nuclear proteins, ribosomal proteins and mature snRNPs, and export traffic includes mRNAs, tRNAs, snRNAs and pre-ribosomes. NPCs are large supramolecular structures that have a molecular mass of 50 MDa in yeast and 120 MDa in vertebrates. They comprise ~30 structural nucleoporin proteins in yeast and 50-100 in vertebrates. Transmission electron microscope sections (**TEM section**) cut normal to the nuclear envelope (NE) show continuity of the outer NE membrane with the endoplasmic reticulum, and also reveal that the inner and outer NE membranes are fused to accommodate the pore structure. Field emission in-lens scanning electron microscopy (**SEM cytoplasmic**) visualises the surface structure of the NPC and its eightfold radial symmetry: eight filaments project into the cytoplasm at the nuclear surface, which contrasts with the characteristic nuclear pore basket structure at the nucleoplasmic face of the NE (**SEM nucleoplasmic**). In amphibian oocytes, an additional fibrous protein organisation, the nuclear envelope lattice, is located on the distal region of the nuclear pore baskets.

Internal NPC structure has been directly visualised by field emission in-lens SEM



(See poster insert)

through successive exposure of the NPC multiple ring substructure by mechanical fracture or gentle proteolysis. The **Exploded view** of the NPC shows the cytoplasmic filaments, which insert into the cytoplasmic coaxial ring. Between this and the outer nuclear membrane lie the thin ring and star ring. A set of internal filaments join the cytoplasmic coaxial ring to the entrance of the transporter, which sits in the centre of the spoke ring complex and fills the space between the inner and outer nuclear envelope membranes. Similar structures are replicated at the nucleoplasmic membrane, where the nucleoplasmic coaxial ring supports the NPC basket. Each separate component observed on the cytoplasmic face of the NPC has also been observed during the formation of pore complexes both in vitro and in vivo. Nuclear pore **Biogenesis** is initiated by dimpling of the outer nuclear membrane, which leads to the formation of a stabilised pore; this is followed by the appearance of internal structures (the spoke ring complex), the addition of the star ring and the successive incorporation of further pore complex structure and, finally, the cytoplasmic filaments. In both yeast and vertebrate NPCs, characterisation of specific nucleoporins and their specific locations is ongoing (**Protein localisation**). On the inner aspect of the internal nuclear envelope membrane, a variety of fibrous proteins associate with both the NE and peripheral chromatin, such as the lamins and their associated proteins.

The classical view of the steps of nuclear **Import** involves the importin (karyopherin) super family, which has multiple members. These transport receptors (e.g. importin α) recognise nuclear-localisation sequences (NLSs) on proteins destined for nuclear import; these sequences are usually a short stretch of amino acids enriched in basic residues. Importin α binds to importin β, and the cargo is translocated into the nucleus, where it is dissociated from the importins by Ran, a small GTPase, in its GTP-bound form. RanGTP binds to importin β and recycles it back to the cytoplasm, where GTP hydrolysis of Ran by the GTPase-activating protein RanGAP occurs; this releases importin β for the next round of import. Cytoplasmic RanGDP is taken back into the nucleus by nuclear transport factor 2 (NTF2); RCC1 (RanGEF) then stimulates exchange of Ran-bound GDP for GTP, which converts Ran to its GTP-bound form. Importin α is recycled to the cytoplasm complexed with CAS (the product of the cellular apoptosis susceptibility gene) and RanGTP. Thus Ran exists mainly as its GDP-bound form in the cytoplasm, and its GTP-bound form in the nucleus. Both nuclear **Import** and **Export**, which involves nuclear export signals (NESs) are linked to the Ran GTPase cycle, although the actual process of nucleotide hydrolysis is not necessarily required for transport. The differential locations of RanGTP (nuclear) and RanGDP (cytoplasmic) may serve to provide positional information for transport. Other influences on nuclear transport may involve phosphorylation-sensitive components of the transport machinery, probably at the NPC itself. This would provide a mechanism for negative regulation of entire transport pathways, potentially leading to global control of cellular activity through modulation of nucleocytoplasmic trafficking.

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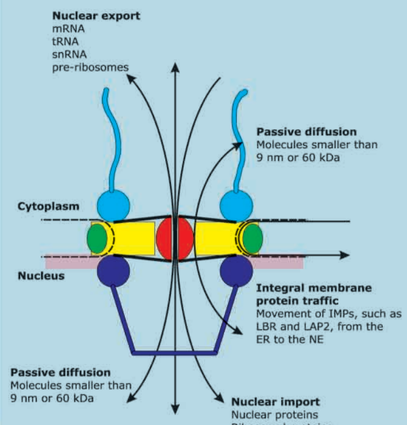
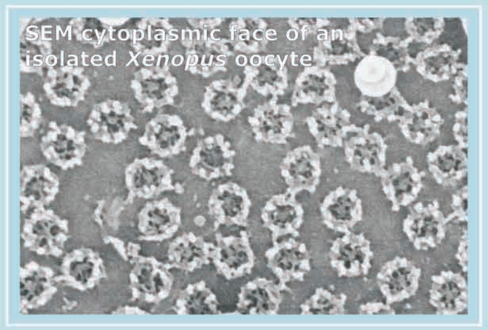
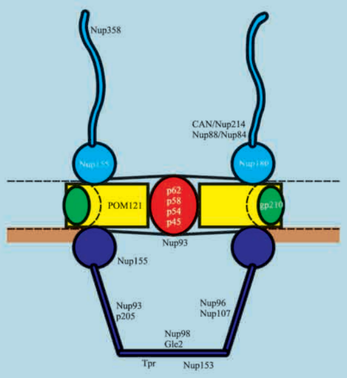
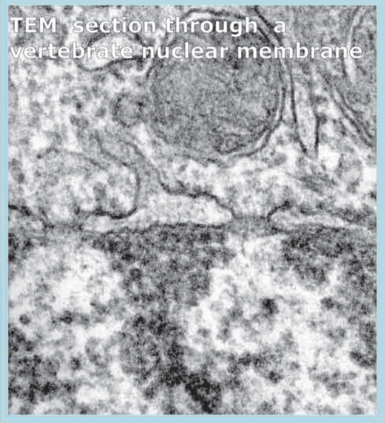
Functions



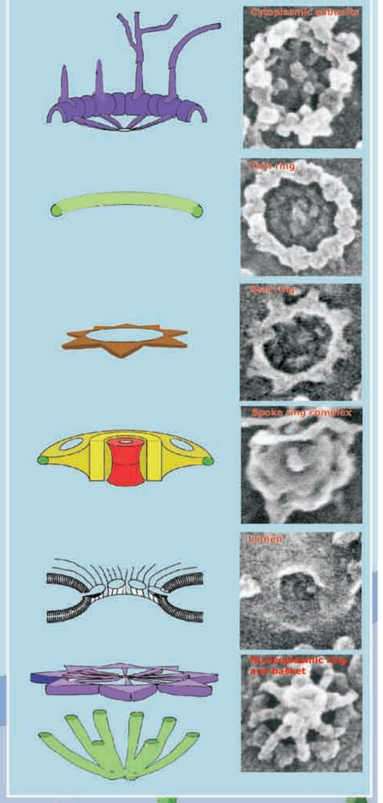


Protein localisation

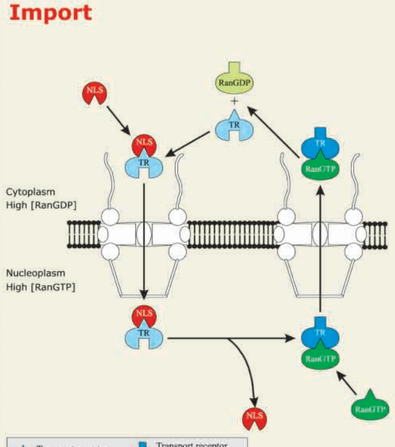




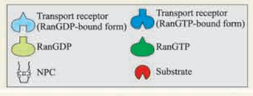
Exploded view



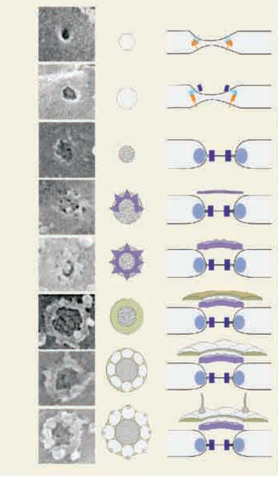
Import



Export



Biogenesis



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