CHAPTER 7

Regulation of Nuclear Import and Export of Proteins in Plants and Its Role in Light Signal Transduction

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The nuclear envelope separates the theatres of two major cellular processes in eukaryotes: transcription takes place in the nucleus whereas proteins are synthesized in the cytoplasm. The localization of these processes in two different compartments of the cell implies that macromolecules must be exchanged very rapidly and efficiently between the nucleus and the cytoplasm in order to ensure proper regulation of signaling and metabolism of a living cell.

All transport processes across the nuclear envelope take place at very large multi-protein complexes called nuclear pore complexes (NPCs), which provide the gates between the nucleus and the cytoplasm. It has been known for many years that nucleo-cytoplasmic transport processes of macromolecules are receptor-mediated, but only in the last few years was it revealed that most of the nuclear transport processes depend on importin β-like protein receptors.[1,2] The genes encoding these receptors constitute a small gene family, and they are named after the member that was first identified at the molecular level. These receptor proteins share limited sequence identity, they can interact with the regulatory GTPase Ran in its GTP-bound form, they are able to interact with nucleoporins, and they shuttle continuously between the nucleus and the cytoplasm.[3] For every class of the many different macromolecular transport cargos, like proteins, mRNA, tRNA, ribosomal subunits, snRNPs, there exists a specific receptor, or a combination of receptors.

Nuclear Import of Proteins

Karyophilic proteins that contain a classical basic nuclear localization signal (NLS), whether monopartite (SV40-like) or bipartite, are imported into the nucleus by the import receptor importin β (also called karyopherin β; see Fig. 1A). However, importin β does not bind directly to these import substrates. In these cases, importin α (also called karyopherin α) serves as an adapter between the cargo protein and the nuclear import receptor itself.[4] Therefore, the first step in the nuclear import of a NLS-containing protein is the specific recognition of the NLS in the cytoplasm by importin α, which constitutes the soluble NLS receptor.[5] Importin β binds co-operatively to the basic amino terminus of importin α called importin β-binding (IBB) domain.[6,7] This leads to the formation of the triple import complex consisting of importin α, importin β and the NLS-containing protein, which then docks as a single entity

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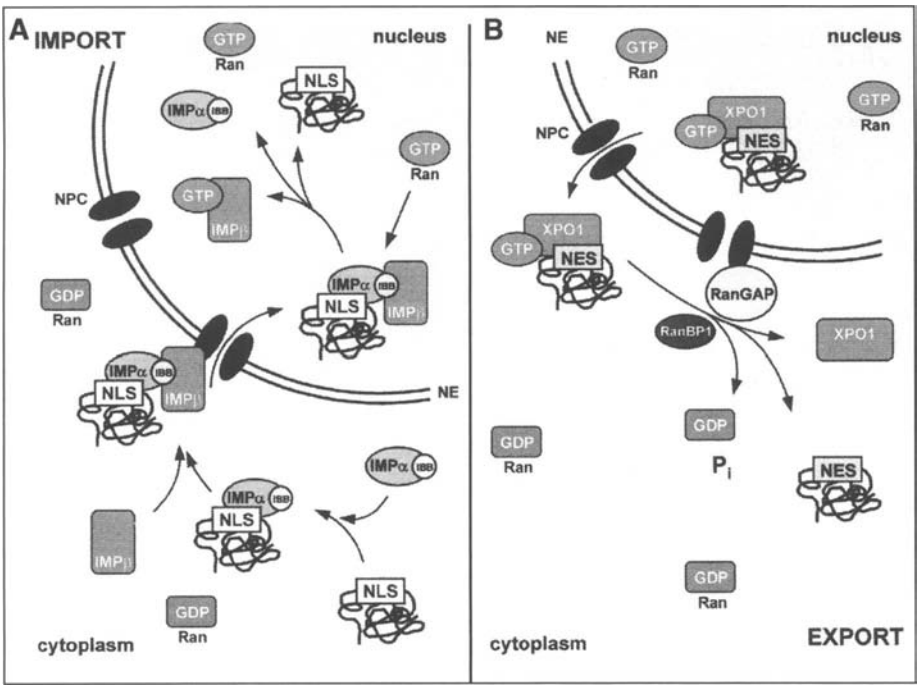

Figure1. Comparison of nuclear import and nuclear export of proteins. A) Nuclear import of NLS-containing proteins by importin α/ importin β (IMPα/IMPβ) is initiated by the specific recognition of the NLS within a protein by the NLS receptor importin α in the cytoplasm. The nuclear import receptor importin β binds co-operatively to the importin α/cargo protein complex to form the triple import complex that docks to the nuclear pore complex (NPC) via importin β. After translocation into the nucleus, it is dissociated by the interaction of Ran-GTP with importin β, leading to the release of the import cargo protein into the nucleoplasm. B) Nuclear export of proteins that contain a leucine-rich NES is accomplished by the export receptor exportin 1 (XPO1), which directly and specifically binds to the NES and to Ran-GTP in a co-operative manner in the nucleoplasm. After translocation of this triple export complex through the NPC into the cytoplasm, the co-ordinated action of the cytosolic proteins RanBP1 and RanGAP leads to the dissociation of the export complex and to the hydrolysis of GTP on Ran and hence to the release of the export cargo into the cytoplasm.

to the NPC via importin β and is subsequently translocated into the nucleus. Within the nucleus, the concentration of Ran-GTP is high.[8] Since the binding sites on importin β for Ran-GTP and importin α overlap, Ran-GTP is competing with importin α for the binding to importin β, which leads to the dissociation of the triple import complex and hence to the release of the import cargo in the nucleus.[9] Importin β is recycled to the cytoplasm in complex with Ran-GTP, although there is also evidence that it may leave the nucleus in a Ran-independent manner.[10] After hydrolysis of GTP on Ran in the cytoplasm, Importin β is ready for a new import cycle. Importin α is exported to the cytoplasm by a specific export receptor, termed CAS, which is also a member of the importin β family.[11-14]

Although most of the proteins that are imported by importin β depend on recognition by importin α, there are also proteins that do not need this adapter. These proteins bind directly to the import receptor importin β and contain a more archaical nuclear localization signal that resembles the IBB domain of importin α. There are also many other proteins that are imported into the nucleus and that contain neither such an import signal nor a classical basic NLS (for a