Regulation of Protein Interaction in Protein Nuclear Transport and Its Function

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Abstract: Protein nuclear transport is an important process in eukaryotic cells, and is closely related to the normal function of cells. Normally, protein nuclear transport is accomplished by nuclear receptor mediation, which requires the participation of multiple proteins. Therefore, protein nuclear transport cannot be separated from the interaction between proteins. In this paper, the relationship between protein interaction and protein nuclear transport is studied, and its effects on cellular and physiological functions are analyzed from many aspects.

1. Introduction

The nucleus is the main component of eukaryotic cells, and the gene replication, protein translation and modification of cells are inseparable from the nucleus. In the process of normal life activities of cells, the nuclear membrane has stringent requirements for substances entering and leaving, especially macromolecular substances such as proteins. Some studies have shown that protein nuclear transport is accomplished by nuclear receptor mediation. The interaction between proteins in the process occupies an important position, and needs to be paid attention to. The research on the regulation of protein interaction for protein nuclear transport should be strengthened, and its effects on biological and physiological functions should be comprehensively analyzed.

2. Main component of the nuclear membrane

2.1 Nuclear pore complexes

The nuclear membrane is generally composed of lipid bilayer on both sides, and a nuclear pore complex (NPC) is present thereon. The nuclear pore complex is the main component of the nuclear membrane. Generally, its diameter is 25 nanometers, and the most central diameter of the channel is 9 nanometers [1-3]. Nuclear pore complex plays an important role in screening biological molecules and is also an important basis for the exchange of substances on both sides of the nuclear membrane.In general, molecules with a relative molecular mass between 40K and 50K can pass through the nuclear pore complex freely. Molecules with molecular mass above 50K and more than 6 nanometers in diameter, such as nucleic acids and proteins, need to pass through the nuclear pore complexes under the promotion of energy. The most common active transport of macromolecules is mediated by soluble transport receptor proteins such as cytosol.

2.2 Nuclear transport receptor

Active transport of macromoleculeslike proteins is inseparable from nuclear transport receptors. In the process of active transport of macromoleculeslike proteins, nuclear transport receptor proteins actively

bind to nuclear pore complexes for a short time to open up pathways for active transport of macromoleculeslike proteinsand generate energy to promote active transport of macromoleculeslike proteins. Normally, nuclear transporter receptors are divided into *Importin α* and *Importin β*[4-5]. The former acts as a junction protein in the process of active transport of macromoleculeslike proteins. When macromoleculeslike proteins need to pass through nuclear pore complexes, one end of *Importin α*will directly bind to the protein molecule, and the other end will connect to the homologues of *Importin α* and *Importin β* to help the active transfer of macromoleculeslike proteins. The protein family of *Importin α* contains many members, and the difference between different members lies in the cell type and differentiation status. Different *Importin α* proteins have certain selectivity and play different roles in the active transport of macromoleculeslike proteins.For the active transport of some special protein molecules, *Importin α* protein will play a functional compensation role to smoothly realize the active transport of special protein molecules. The white blood cells corresponding to different members ofprotein familyof *Importin α* are shown in Table 1. The protein family of *Importin β*is the main receptor protein for nuclear transport in eukaryotic cells. The members of protein family of *Importin β*are more than that of *Importin α*[6].Generally, mammals contain more than 20 pieces of *Importin β* proteins. The relative mass of these proteins is between 95K and 145K, and the functions of different members of*Importin β* are similar. When playing a role in nuclear transport, a member of the protein family of *Importin β* can correspond to a variety of macromolecules such as proteins that need to be transported. The reason for this situation is that the *Importin β* protein is rich in HEAT Repeats supercoiled domainwith abundant binding sites, which can complete junctions with a variety of proteins and other macromolecular substances [7-8]. Most *Importin β* proteins have the ability to recognize and actively transport macromoleculeslike proteins directly, while a small number of *Importin β* proteins need special transformation to effectively recognize and actively transportproteins according to the needs. Generally, it is excessive to combine substrates with typical localization signals.

Table 1 Protein family members of *Importin α* and some substrates

Importin & family	Example of cargoes
Importin α 1	Conatining Proteins
Importin α 2	Transcriptional factors and many viral proteins
Importin α 3	DNA binding proteins
Importin α 4	NF-rB
Importin α 5	Statl and stat3
Importin α 6	Unknow
Importin α 7	Stat3

3. Protein entry mechanism mediated by nuclear transport receptor

According to whether nuclear transport receptors are needed, protein entry mechanism mediated by nuclear transport receptorcan be divided into two categories, and protein entry mechanism relying on nuclear transport receptors is the most common one. The corresponding protein is bound by the nuclear transport receptor, and the protein is transported in the nucleus. The nuclear localization signal on the target protein is more important in the nuclear transport mechanism, which is the basis for the effective binding of the albumin by the nuclear transport receptor and completing the protein entry into the nucleus. Therefore, the nuclear transfer mechanism relying on the nuclear transport receptor can only achieve the active transport of albumin with nuclear localization signal.If thealbumin is diseased, the nuclear localization signal will be lost. It will be difficult to enter the nucleus normally [9-10]. The mechanism of protein entry into the nucleus, which does not require the participation of Importinα, is relatively rare.*Importin β* protein can directly recognize protein molecules that need to be actively transported, and directly mediate the smooth entry of protein into the nucleus. This protein entry mechanism also requires nuclear localization signals, but the nuclear localization signals on

albumin are lack of regularity and are often randomly distributed on the surface of leukocyte. In addition to the above two cases, the active transport of some proteins does not require the participation of *Importin β* protein and its homologues. Only the *Importin α* protein can complete the entry of the protein into the nucleus.CaMKIV is the most common one. *Importin α* protein can complete the transport of CaMKIV alone, and*Importin β* is not involved in the entire active transport process.

4. Regulation of protein interaction in nucleartransport

It can be said that the whole process of protein nuclear transport is inseparable from the interaction between proteins, including albumin and nuclear transport receptor proteins.Studies have shown that the use of RNA to interfere with *Importin α* protein will affect the nucleation of albumin in the process of binding with albumin. The main reason for this kind of situation is that the normal function of *Importin α* protein after interference is affected, and the interaction point between *Importin α* protein and albumin is problematic [11-12], which leads to the obstruction of subcellular localization. Eventually, the interaction between proteins is affected and the pathway of albumin into the nucleus is blocked. In addition, phosphorylation regulation also affects protein nuclear transport, and the phosphorylated serum and glucocorticoid-regulated kinase binds significantly to the *Importin α* receptor, and its ability to enter the nucleus is significantly increased.The nuclear entry ability of protein is proportional to the phosphorylation degree of serum/glucocorticoid-regulated kinase,and the higher the level of phosphorylation, the stronger the nuclear transport ability of the protein.

Some studies have shown that the concentration of calcium ion can affect the interaction between nuclear localization receptors and leukocyte, interfering with the nuclear transport of proteins. Jacob, as the main component of the nucleus, belongs to an important protein in the nucleus. Generally, it is highly expressed in the limbic system and cortex of the brain. Jacob has the ability to transmit receptor signals. When the concentration of calcium ions reaches to a certain level, the calcium binding protein binds to the nuclear localization signal on Jacob and forms a competitive relationship with the nuclear transport receptor. With the increasing of calcium concentration, it will be difficult for nuclear transport receptors to bind to leukocyte smoothly. Finally, it will affect subcellular localization and protein nuclear transport [13]. Researches have shown that not only nuclear-localized receptor proteins, but also subcellular localization of target cells is affected whenever a binding protein changes slightly, leading to abnormal nuclear transport of proteins.

Common proteins can interact with a variety of nuclear transport receptors during nuclear transport. Once such proteins have binding problems during nuclear transport, the remaining nuclear transport receptors can be directly compensated to ensure protein nuclear transport. Differences in subcellular localization between different nuclear transport receptors require more elaborate subcellular localization regulation during the binding process.For example, LKB1 is a serine/threonine kinase that regulates cell polarity, metabolism, and cell growth. The activity and cellular distribution of LKB1 is determined by its cofactors STRADα and M025. STRADαinduces repositioning of LKB1 from nucleus to plasma and stimulates its chemical activity.M025 stabilizes the interaction of STRADα/LKB1. Although LBKI is transported into the nucleus by nuclear transport receptors, and STRADα and M025 passively spread between the cytoplasm of the nucleus, STRADα induces LKB1 to shuttle between the cytoplasmic cytoplasm. STRAD α induces the nuclear output of LKB1 by helping the binding of LBK1 with nuclear output factors CRMI and exopinn7.STRADα inhibits nuclear import of LBK1 by competing with LKB1 and by the combination of mIopirtna.Mo25 stabilizes the STRADα/LKB1 complex, but it does not promote nuclear shuttle, and the localization of LKB1 is regulated by a variety of factors.

It can be seen that the interaction between the receptor and the target cell can regulate the nuclear transport of the protein. When the interaction between proteins is subtly regulated and modified, the interaction between proteins and he subcellular status of target cellswill change significantly,which affects the nuclear transport of proteins.

5. Conclusion

Protein nuclear transport is a relatively complex process. In the process of transport, a variety of proteins, such as nuclear pore complexes and nuclear transport receptors, are involved. Each step of the interaction between multiple proteins helps the target cells to successfully complete the active transport. So the interaction between proteins is the basis for the successful completion of nuclear transport of proteins. The dynamic equilibrium relationship between a large number of proteins is the key to the successful completion of protein nuclear transport, and has an important regulatory role for protein nuclear transport. Strengthening the study of the mutual interaction of proteins can effectively analyze the mechanism of protein, and study the organism's life activities. It plays an important role in elucidating the mechanism of disease, and is conducive to the development of new diagnostic methods and new therapeutic drugs.

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