# Abstract of Presentation

Presentation Title

**Regulation of nucleocytoplasmic protein transport and its significance to cell functions**

Name (Underline the family name)

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Abstract

In eukaryotic cells, cell functions are maintained through the continuous traffic of various molecules between the nucleus and the cytoplasm. Functional molecules move between the nucleus and the cytoplasm through the nuclear pore complexes (NPCs) which penetrate a double membrane, the nuclear envelope. Most karyophilic proteins have specific nuclear localization signals (NLSs) within their amino acid sequences, and many of the proteins exported from the nucleus to the cytoplasm contain nuclear export signals (NESs). There are multiple transport factors such as importin alpha and importin beta with cargo-specificity determined by the NLS or NES signals of the cargo molecules. NPCs consist of ~30 different proteins called nucleoporins. A small GTPase Ran ensures the directionality of nucleaocytoplasmic transport.

We studied to know how the transport factors, NPC components (nucleoporins) and Ran cycle are involved in cell functions such as cell differentiation. We have shown that importin alpha subtype switching triggers neural differentiation of ES cells. Furthermore, we found a novel cell-fate determination mechanism by which importin alpha1 functions as a dominant-negative regulator of nuclear import of a specific set of transcription factors such as Oct6 and Brn2 inducing differentiation to help maintain the undifferentiated state of ES cells. In addition, using mouse C2C12 cells, we found that NPC remodeling occurs during muscle differentiation and that it plays a crucial role in skeletal myogenesis. In particular, the nucleoporin NUP358/RanBP2 stoichiometry within individual NPCs was altered during muscle differentiation of C2C12 cells. Nuclear export rate in myotubes was higher than that in myoblasts. Furthermore, siRNA-mediated depletion of NUP358 in myoblasts dramatically suppressed myotube formation without affecting cell viability. These findings indicate that the NPC is architecturally and functionally variable during cell differentiation and suggest that NPC remodeling has a great impact on skeletal muscle differentiation. Furthermore, using RanBP1-knockout mice, we found that the drastic decrease in “RanBP” activity from the stage of elongating spermatids impaired spermatogenesis, demonstrating the physiological importance of proper RanGTPase cycle regulation in mammalian organism.