Cryo-EM structure of the Imp7:Impβ:H1.0 complex

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Transport of proteins through the nuclear pore complex (NPC) is mediated by transport receptors. A majority of proteins require a single transport receptor to pass through the NPC. Highly charged proteins that interact with nucleic acids and are prone to aggregation, such as linker histones (H1) and some ribosomal proteins, require two independent receptors for their transport through the NPC. How transport receptors form a complex with their cargo remains unclear. Here, we studied the nuclear import of linker histones which require the formation of a heterodimeric transport complex, consisting of two members of the importin β family, importin β (Impβ) and importin 7 (Imp7) [1]. The Imp7:Impβ complex is also necessary for nuclear import of several ribosomal proteins and HIV virus integrase [2].

We have determined the cryo-EM structure of the Imp7:Impβ:H1.0 complex [3]. Two importins pack together and form a cradle which accommodates the linker histone. The structure shows that the H1.0 globular domain is bound by Impβ, while acidic residues in both Impβ and Imp7 bind and chaperone the positively charged C-terminal tail of H1, revealing why both importins are required for H1 import. Moreover, the structure shows that the H1 tail is required for the shape of the entire complex, which is supported by cross-linking mass spectrometry data.

Furthermore, we have observed that another disordered region, the Imp7 C-terminus, has conserved GGxxF and FxFG motifs, which are a hallmark of FG-nucleoporins. We show that these motifs are essential for complex formation between Impβ and Imp7, as well as several other importins indicating that this is a common mechanism for importin dimerization.

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