

Cse1: the Structure of an Exportin in its Closed, Cytosolic State

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Cse1 mediates nuclear export of importin-alpha, the nuclear localization signal (NLS) import adaptor. We report the 3.1Å resolution structure of cargo-free Cse1, representing this HEAT-repeat protein in its cytosolic state. Cse1 is compact, consisting of N- and C-terminal arches that interact to form a ring. Comparison with the structure of cargo-bound Cse1 shows a major conformational change leading to opening of the structure upon cargo binding.

The largest structural changes occur within a hinge region centered at HEAT repeat 8. This repeat contains a conserved insertion that connects the RanGTP and importin-alpha contact sites and that is essential for binding. In the cargo-free state, the RanGTP binding sites are occluded and the importin-alpha sites are distorted. Mutations that destabilize the N- to C-terminal interaction uncouple importin-alpha and Ran binding, suggesting that the closed conformation prevents association with importin-alpha.

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