Molecular trafficking between the nucleus and the cytoplasm flows through nuclear pore complexes (NPCs). Molecules and macromolecules roughly smaller than 40 kDa can diffuse freely through NPCs, while bulkier macromolecules must go through a well-regulated process of facilitated diffusion in which they bind to soluble transport receptors of either the karyopherin or soluble transport receptors of either the karyopherin 

Yoshimura and colleagues show that HEAT proteins that are involved in diverse cellular functions may facilitate their own translocation through the nuclear pore complex, owing to their structural similarity to nuclear transport receptors of the karyopherin β family.

Certain ARM repeat proteins such as β-catenin were previously reported to cross the pore without interacting with Kaps (Fagotto et al., 1998). It was also shown that hydrophobic surface regions may increase the passive transport rate of proteins (Naim et al., 2009) and that nucleoporins Nup188 and Nup192, HEAT/ARM proteins that form a part of the NPC scaffold, could diffuse through the pore independently of Kaps (Andersen et al., 2013) but are outcompeted by high concentrations of importin-β.

In this issue of Structure, Yoshimura et al. (2014) report that numerous HEAT repeats that are otherwise too large to cross the NPC can interact with FG repeats and cross the pore independently of Kaps (Figure 1B). Moreover, they can interact with other proteins to mediate transport on their own. This raises the tempting possibility that HEAT proteins can bypass the classic route of transport, making use of their structure similarity to Kap-β and adapting their HEAT repeats to interact with the NPC.

Yoshimura et al. (2014) examine the role of flexibility in both importin-β and non-kap HEAT proteins and demonstrate that impaired flexibility prevents efficient nucleocytoplasmic translocation in either class. This is expected of Kap-β proteins, which are known to assume different conformations when they interact with different partners, possibly playing a role in allosteric release of cargo when exiting the pore (Conti et al., 2006). However,
New Binding Face of C-type Lectin-like Domains

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C-type lectin-like receptor 2 (CLEC-2) is a member of the C-type lectin (like) receptor (CLR) family that uses a Ca²⁺ binding domain to bind specific glycans. However, in this issue of Structure, Nagae and colleagues report on how the structures of CLEC-2 in complex with a glycopeptide podoplanin and a snake venom protein, rhodocytin, show a different mode of binding.

Cell surface receptors play a critical role in mediating cell-cell interactions and regulating numerous physiological events. They are also targeted by microbes that hijack them during the infection process. In turn, the host cells use their cell surface receptors as the front line defense to recognize and eliminate infectious microorganisms. Immune cell surface receptors are largely comprised of immunoglobulin (Ig) and C-type lectin (like) receptor (CLR) families (Kuroki et al., 2014).