Poster Presentation

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Netrin4 and laminin gamma-1 interacts via their N-terminal globular domains

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Laminin is a heterotrimeric molecule composed of an alpha, a beta and a gamma chain. It interacts with various ligands at the extracellular matrix and plays a pivotal role in many biological processes. Netrin4, one of the four secreted netrins, specifically interacts with the laminin gamma-1 chain (Schneiders et al. 2007). We recently highlighted the biological significance of this complex using ex vivo and in vivo studies (Reuten et al. 2016). Furthermore, we also solved a structure of netrin4 at 3.1 Å that allowed us to reason why netrin4 and our previously reported structure of netrin1 (Grandin et al. 2016) interact with different binding partners. To implicate the structure of netrin4/laminin gamma-1 complex and its biological functions, we employed a multidisciplinary approach where we combined the low-resolution shape information of netrin4/laminin gamma-1 complex with the high-resolution structure information of each component to obtain a high-resolution model of the complex. This approach revealed that the N-terminal globular domains of netrin4 and laminin gamma-1 are required for the interaction (Reuten et al. 2016). The interaction sites were validated using structure-guided mutations that provided detailed insights on the biological relevance of this complex (Reuten et al. 2016). The high-resolution model of the netrin4/laminin gamma-1 complex was validated by comparing the experimentally derived hydrodynamic properties with those calculated from the structures.

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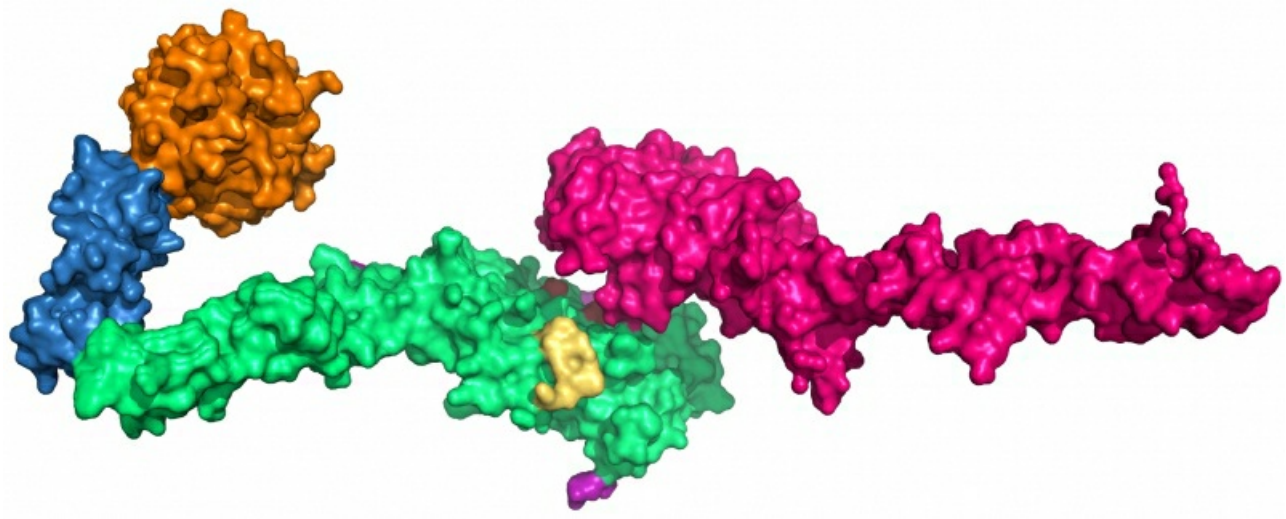

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