

Keynotes

Plenary Lecture

Order from Disorder: Towards molecular architecture of the muscle Z-disk assembly by integrative structural biology

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Sarcomeres are the smallest contractile units found in cardiac and skeletal muscle, where actin and myosin filaments move past each other to generate tension. This molecular machinery is supported by a subset of highly organised cytoskeletal proteins that perform architectural, mechanical, and signalling functions. The ultrastructure of a sarcomere is highly ordered and bordered by Z-disks, which play an important role in mechanical stability, force transmission and signalling.

In the Z-disks – the lateral boundaries of the sarcomere machinery – the protein α -actinin-2 cross-links antiparallel actin filaments from adjacent sarcomeres, and additionally serves as a binding platform for a number of other Z-disk proteins. In striated muscle cells, the Z-disk represents a highly organized three-dimensional assembly containing a large directory of proteins orchestrated in a multi-protein complex centred on its major component α -actinin, with still poorly three-dimensional interaction map. To investigate the structural architecture of the Z-disk, the assembly hierarchy, and structure-function relationships, we are employing an integrative structural biology strategy, combining molecular biophysics, structural, and biochemical approaches.

In this presentation, I will share our findings on the dynamic, flexible, and fuzzy complexes formed by the primary Z-disk protein α -actinin and its interactome. I will discuss these findings in the context of the asymmetric sorting of α -actinin, the architecture and assembly of sarcomeric Z-disks, and the potential role of membrane-less compartmentalisation in this process.