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The giant muscle protein titin extends over one half of the muscle sarcomere. In its largest isoform titin comprises more than 38,000 residues and about 300 domains. Its structural complexity does not allow the application of classical structural biology methods to determine its overall architecture. Therefore, we have decided to chop the protein into smaller fragments and determine the high resolution structures of representative parts. Within this endeavor, we have also become interested to consider known ligands involved in the titin interactome for structural/functional analysis. Over the last decade, we determined structures of the N-terminal assembly complex (Zou et al., 2006), from the I-band (Mayans et al., 2001; Vega et al., unpublished) and from the A-band including the kinase domain and down-stream signaling complexes (Mayans et al., 1998; Muller et al., 2006; Muller et al., 2007; Muller et al., unpublished; Chen et al., unpublished). The available data allow modeling a large part of the titin proteome and to interpret available low resolution data of the entire titin filament. Combined with complementary functional data, our findings reveal key structural/functional relationships of titin and its interactions partners. Structural biology results from a related sarcomeric filament protein, myomesin (also known as mini-titin) will be presented in a separate contribution. Some of the data have been published recently (Pinotsis et al., 2008).

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Keywords: muscle proteins, protein/protein interactions, kinase structure

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Ion channel structures by single particle analysis using EM: Sodium and TRP channels, IP3 receptor

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Six-transmembrane (6-TM) type channels are plasmamembrane integral components of cellular signaling pathways conserved in almost all species including animals, plants, and some kinds of prokaryotes. These channels selectively permeate cations in response to various signals. In excitable and non-excitable mammalian cells, 6-TM cation channels play fundamental roles, including the generation of action potential and its transmission, the regulation of intracellular ion concentrations, and the activation of signaling cascades by humoral or mechanical pathways. We have recently determined the structure of four different 6-TM type cation channels: the voltage-sensitive sodium channel[1], the IP3 receptor[2], the TRPC3[3] and TRPM2[4] channels, using single particle analysis from cryo-EM images. The basic structure of the molecules was shown to be similar: a bell-like shape composed of a relatively small extracellular (or luminal) domain, a protein-dense transmembrane domain, and an expanded cytoplasmic domain. However in detail, the cytoplasmic architectures are quite different from each other and are diversely evolved to their specific physiological functions.

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Keywords: electron microscopy analysis, ion channel structures, three-dimensional, image reconstruction

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The assembly process of the double-layered capsids of phytoreoviruses

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Viruses in the family *Reoviridae* have an inner core with a large interior cavity that contains the 10 to 12 segmented double-stranded RNA as a genome, and a transcriptional complex that includes proteins with RNA polymerase, helicase, guanylyltransferase and transmethylase activities and an RNA-binding protein. The core particle is surrounded by one or two layers of outer capsid proteins. During X-ray crystallographic and Cryo-electorn microscopic studies of the structural organization of *Rice dwarf virus*, a member of the genus *Phytoreovirus* in the family *Reoviridae*, we have identified possible structural mechanisms that allow creation of a large cavity inside a double-layered spherical particle that consists of heterologous proteins with different lattices. The viral particle seems to be created in a genetically economical manner, with the sealing of joints between inner-layer proteins by a second layer of proteins, suggesting the organization of a rigid protein layer that separate from and, probably, protects the interior of the virus from the cytoplasmic environment within infected cells. Procedure of the virus assembly was analyzed combined with molecular cytopathological data in virus infected cells.

Keywords: virus assembly, viral structure and function, virus host interactions

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A new virus structure: The nucleosome-like organization of the filamentous archaeal virus AFV1

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