Molecular Basis of the Myomesin Dimerisation: Implications for the Sarcomeric Assembly of the M-band

Nikos Pinotsis[a], Stephan Lange[b,c], Matthias Wilmanns[a], *[a]EMBL-Hamburg, Notkeststrasse 85, D-22603 Hamburg, Germany, [b]The Randall Centre and Cardiovascular Divisions, Muscle Cell Biology, King's College London, Guy's Campus, London, SE1 1UL, UK, [c]ETH Zurich Hoenggerberg, CH-8093 Zurich, Switzerland.* E-mail: pinotsis@embl-hamburg.de

Myomesin is an essential component of the sarcomeric M-band expressed in every type of vertebrate striated muscle analyzed so far. It is composed of 7 Ig-like and 5 Fn(III) domains. A unique sequence at the N-terminal part anchors myosin, while the central Fn(III) domains interact with the M4 domain of titin and the muscle-type creatine Kinase. These features favour specific lattice orientations and models of the M-band. A consistently important characteristic of myomesin that recently has been reported is its dimerisation via domain 13. We determined the structure of domains 12 and 13 revealing an antiparallel orientation of domain 13. Both domains 12 and 13 are Ig-like of type I. They are connected through a 22-residue helix that orients them to an almost vertical position. The overall assembly was confirmed *in vitro* by small angle X-ray scattering. For the *in vivo* confirmation of the assembly, we used a novel protein-complementation method utilizing truncated YFP mutants fused either to the N- or C-terminus of the myomesin dimerisation domain. Reconstitution of the intrinsic YFP-fluorescence could only be observed for the antiparallel orientation of the myomesin dimers, whereas constructs fused only N-terminally to myomesin displayed no fluorescence signal.

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