

Modularity and homology: the complete modelling of titin the type II module family

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The homology modelling of the structures of the 162 type II modules from the giant multi-domain protein titin is reported. The package Modeller was used and implemented in an automated fashion using four experimentally solved structures as templates. Validation of the models was addressed in terms of divergence from the template and consensus of the alignments. The homology within the whole family of type II modules as well as with the templates is relatively high (30-40% identity and ca. 60% similarity). Comparison between the models of domains for which an NMR structure has been solved with the experimental solution gives an estimate of the quality. Our results allow us to distinguish a number of structurally relevant residues that are therefore conserved in the whole family and buried in the hydrophobic core from those residues that are exposed and conserved. These will be functionally relevant. Comparison of exposed conserved patches for modules in different regions of the titin molecule suggests potential interaction surfaces. Our results may be tested directly for those modules whose binding partner is known.