

P050 Structure and extension of fibrillin microfibrils

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Fibrillin-1, a 330kDa extracellular matrix glycoprotein, assembles to form fibrillin microfibrils which have a key role in elastic fibre formation and homeostasis. The microfibrils have a beads-on-a-string ultrastructure with 57nm period and mass of 2.4MDa per repeat. Mutations in fibrillin-1 cause Marfan syndrome, a heritable disorder with potentially fatal cardiovascular, ocular and skeletal defects; a major factor in the pathology of this disease is the dysregulation of TGFbeta signalling. Fibrillin microfibrils have occasionally been observed to increase their periodicity from 57nm up to 150nm, suggesting a role in tissue elasticity.

We have used single particle image analysis of transverse views of tissue microfibrils to identify eight molecules in cross-section through a microfibril. We have found that removing bound calcium at physiological salt concentrations results in microfibrils with a range of periodicities from 40nm – 150nm. Visualisation of these microfibrils with TEM and single particle image analysis has revealed a gross conformational change in the interbead region, from four thin filaments to two larger filaments, at periodicities greater than 80nm. These data suggest a large molecular rearrangement within the interbead of the microfibril when they are stretched.