Genetic dissection of vertebrate sarcomere assembly

Talk by Derek L. Stemple (Wellcome trust Sanger institute, Cambridge) on 09/02/10 hosted by Dr. Robert Kelsh

The sarcomere is the repeating unit of the vertebrate striated muscle. The structure is comprised of 50-100 proteins which form thick and thin overlapping filaments. Nemaline myopathy type II is a hereditary muscle deformation condition caused by mutations in the Nebulin and Tropomodulin 4 (Tmod4) proteins. ENU screens produced a range of Zebrafish models with muscle wasting phenotypes. *Buzz off* was found to have a mutation in nebulin; in normal development, nebulin is required for the formation of nemaline rods which act as a template for actin polymerisation. In the buzz off mutant, actin was restricted to the cell boundaries and normal thin filaments did not form. Tmod4 mutants had impaired motility and an elongated phenotype; this was due to an increased polymerisation of some sarcomere proteins. Tmod4/nebulin double mutants also had a lengthened phenotype; the double mutant caused hypertrophy of nemaline rods leading to spontaneous filament breakage. This was compounded by an increase in actin polymerisation, and a loss of orientation of thin muscle filaments. This work has shown Zebrafish muscle impaired mutants to provide a versatile model for studying human muscle wasting diseases.

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