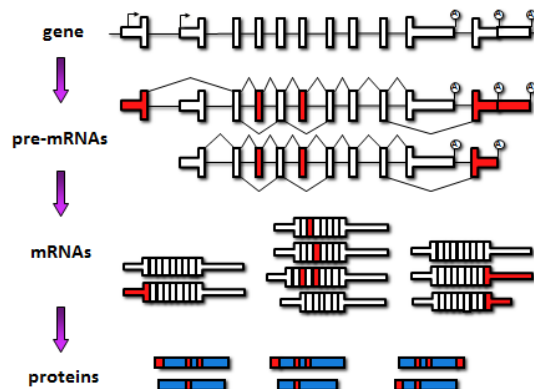




Alternative splicing regulatory networks in development and their disruption in disease



Regulation of alternative splicing during postnatal heart and skeletal muscle development results in fetal-to-adult protein isoform transitions with little change in overall gene expression. A network of developmental transitions are regulated by the RNA binding protein CELF1 which decreases 10-fold during this time period due to changes in protein stability and miRNA repression. Genes that undergo postnatal splicing transitions are enriched for vesicular trafficking functions indicating a previously unknown role for splicing regulation in striated muscle development. The network of splicing transitions identified during postnatal development is disrupted in the disease, myotonic dystrophy, resulting in mis-expression of fetal isoforms in adult heart and skeletal muscle leading to disease features. An understanding of the pathogenic mechanisms in myotonic dystrophy has resulted in promising therapeutic strategies currently in Phase II trials.

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Host: Dr. Ben Blencowe

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Time: 11AM

Place: Donnelly Centre, 160 College Street, Red Seminar Room