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ICGEB International SEMINAR PROGRAMME 2017

Monday, 18 September 2017 | 12:00 noon | ICGEB Seminar Room, W building | Padriciano, 99, Trieste, ITALY

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More than 90% of the human genes undergo alternative splicing, a posttranscriptional mechanism that explains how one gene can give rise to multiple protein isoforms. It has become apparent that coordinated splicing networks regulate organ development and that alternative splicing has physiological functions in developmental processes (Baralle & Giudice, 2017 Nat Rev Mol Cell Biol). Most conserved and tissue-specific splicing occurs on striated muscle and brain, raising the question of how developmental and tissue-specific splicing influences protein function. We have previously found that membrane trafficking genes undergo splicing transitions during heart development (Giudice et al., 2014 Nat Commun). Alternative exons are gradually included in development in heart and skeletal muscles but not in other tissues, suggesting roles specific to striated muscle. We hypothesize that specific trafficking isoforms contribute to striated muscle biogenesis and cell architecture maintenance being important for cell type-specific functions. To start testing this hypothesis, we delivered morpholino antisense oligonucleotides into the flexor digitorum brevis muscles of adult mice to redirect splicing of four selected trafficking genes to fetal isoforms. Splicing switch results in structural and functional defects including T-tubule disruption and DHPR and RYR1 mislocalization impairing excitation-contraction coupling and proper calcium handling and force generation (Giudice et al., 2016 Cell Rep). Our results demonstrate previously unrecognized roles for trafficking proteins in muscle homeostasis and specific requirements for adult splice variants.

"Alternative splicing of intracellular trafficking genes in development and differentiation"

Host: F. E. Baralle

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