

Abnormal distribution of inositol 1,4,5-trisphosphate receptors in human muscle can be related to altered calcium signals and gene expression in Duchenne dystrophy-derived cells

Cárdenas, César

Jureti?, Nevenka

Bevilacqua, Jorge A.

García, Isaac E.

Figueroa, Reinaldo

Hartley, Ricardo

Taratuto, Ana L.

Gejman, Roger

Riveros, Nora

Molgó, Jordi

Jaimovich, Enrique

Inositol 1,4,5-trisphosphate (IP₃) receptors (IP₃R_s) drive calcium signals involved in skeletal muscle excitation-transcription coupling and plasticity; IP₃R subtype distribution and downstream events evoked by their activation have not been studied in human muscle nor has their possible alteration in Duchenne muscular dystrophy (DMD). We studied the expression and localization of IP₃R subtypes in normal and DMD human muscle and in normal (RCMH) and dystrophic (RCDMD) human muscle cell lines. In normal muscle, both type 1 IP₃R_s (IP₃R₁) and type 2 IP₃R_s (IP₃R₂) show a higher expression in type II fibers, whereas type 3 IP₃R_s (IP₃R₃) show uniform distribution. In DMD biopsies, all fibers display a homogeneous IP₃R₂ label, whereas $24 \pm 7\%$ of type II fibers have lost the IP₃R₁ label. RCDMD cells show 5-fold overexpression of IP₃R₂ and down-regulation of IP₃R₃ compared with RCMH cells. A tetanic stimulus induces IP₃-dependent slow Ca²⁺ transients significantly larger and faster in RCDMD ce