Institut NeuroMyoGène

Lyon 1 Inserm cnrs

Seminar

Thursday May 26th 11.00

Salle Guillermond – Bâtiment l'Herbier – 9 rue Raphael DUBOIS –
Domaine Universitaire de la DOUA
(http://oscar.univ-lyon1.fr/appli-externe/plan/plans/plan_campus_ouest.html)

Francesco Zorzato

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"Pathophysiology of ryanodinopathies"

Abstract

Type 1 ryanodine receptor (RyR1) is preferentially expressed in skeletal muscle, and mutations in the gene have been associated with malignant hyperthermia, a pharmacogenetic disease, and with several congenital myopathies, including central core disease, multiminicore disease, centronuclear myopathy, congenital fibre type disproportion. Experimental data have indicated that RyR1 is also expressed in some areas of the central nervous system, in some cell types of the immune system and in smooth muscle cells. These results imply that mutations in the gene encoding RyR1 will not only affect skeletal muscles, but other tissues that express this calcium channel as well, thereby broadening the clinical spectrum of disorders due to RyR1 dysfunctions.

The RyR1 is of fundamental importance for the development of muscle force and a decrease in its content may be causally linked to the profound muscle weakness seen in patients with some forms of congenital myopathies linked to recessive RYR1 mutations. The protein composition of the junctional sarcoplasmic reticulum membrane encompassing the excitation-contraction coupling molecular complex (ECCMC) is extremely complicated. Polymorphic variants of the junctional sarcoplasmic reticulum protein JP45 have been shown to segregate in Malignant Hyperthermia Susceptible subjects of Malignant Hyperthermia families in the UK. Thus, some ECCMC accessory proteins may play a role not only in regulating excitation-contraction coupling but also as modifiers of the ryanodinopathies phenotype.

If you wish to meet Francesco Zorzato, please contact Bruno Allard (bruno.allard@univ-lyon1.fr).

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Selected recent publications:

Yasuda T, Delbono O, Wang ZM, Messi ML, Girard T, Urwyler A, Treves S, Zorzato F. (2013) JP-45/JSRP1 Variants Affect Skeletal Muscle Excitation-Contraction Coupling by Decreasing the Sensitivity of the Dihydropyridine Receptor. Hum Mut 34:184-190.

Mosca B, Delbono O, Messi ML, Bergamelli L, Wang ZM, Vukcevic M, Lopez R, Treves S, Nishi M, Takeshima T, Paolini C, Martini M, Rispoli G, Protasi F, Zorzato F (2013) Enhanced dihydropyridine receptor calcium channel activity restores muscle strength in JP45/CASQ1 double knock-out mice. Nat Commun 4:1541 doi: 10.1038/ncomms2496.

Vukcevic M, Zorzato F, Keck S, Tsakiris DA, Keiser J, Maizels RM, Treves S (2013). Gain of function of the immune system caused by a ryanodine receptor 1 mutation. J Cell Sci 126:3485-3492.

O. Rokach, N. D. Ullrich, M. Rausch, V. Mouly, H. Zhou, F. Muntoni, F. Zorzato and S. Treves (2013). Characterization of a human skeletal muscle- derived cell line: biochemical, cellular and electrophysiological characterization. Biochem J 455:169-177.

Pérez-Schindler J, Summermatter S, Santos G, Zorzato F, Handschin C (2013) The transcriptional coactivator PGC-1a is dispensable for chronic overload-induced skeletal muscle hypertrophy and metabolic remodeling. Proc Natl Acad Sci U S A 110:20314-20319.

Rokach O, Ullrich ND, Rausch M, Mouly V, Zhou H, Muntoni F, Zorzato F, Treves S (2013) Establishment of a human skeletal muscle-derived cell line: biochemical, cellular and electrophysiological characterization. Biochem J 455:169-177.

Sekulic-Jablanovic M, Palmowski-Wolfe A, Zorzato F, Treves S (2015) Characterization of excitation-contraction coupling components in human extraocular muscles. Biochem J 466:29-36.

Lopez RJ, Mosca B, Treves S, Maj M, Bergamelli L, Calderon JC, Bentzinger CF, Romanino K, Hall MN, Rüegg MA, Delbono O, Caputo C, Zorzato F (2015) Raptor ablation in skeletal muscle decreases Cav1.1 expression and affects the function of the excitation-contraction coupling supramolecular complex. Biochem J 466:123-135.

Li L, Mirza S, Richardson SJ, Gallant EM, Thekkedam C, Pace SM, Zorzato F, Liu D, Beard NA, Dulhunty AF (2015) A new cytoplasmic interaction between junctin and ryanodine receptor Ca^{2+} release channels. J Cell Sci 128:951-963.

Rokach O, Sekulic-Jablanovic M, Voermans N, Wilmshurst J, Pillay K, Heytens L, Zhou H, Muntoni F, Gautel M, Nevo Y, Mitrani-Rosenbaum S, Attali R, Finotti A, Gambari R, Mosca B, Jungbluth H, Zorzato F, Treves S (2015) Epigenetic changes as a common trigger of muscle weakness in congenital myopathies. Hum Mol Genet 24: 4636-4647.

Mosca B, Eckhardt J, Bergamelli L, Treves S, Bongianino R, De Negri M, Priori SG, Protasi F, Zorzato F (2016) Role of the JP45-calsequestrin complex on calcium entry in slow twitch skeletal muscles J Biol Chem In press.