LS-14-P-3189 The neurodegenerative phenotype Trembler-J mouse model of CMT1E shows differences associated with PMP22 mutation, T1703C, in the extracellular matrix of peripheral nerve fibers

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General information:
The extracellular matrix (ECM) of mammal peripherals nerve fibers plays an important role in Schwann cell (SC) development, proliferation, adhesion and extension. The ECM seems to be also involved in the modulation of myelination and, as a consequence, in the structural and functional nerve fibers integrity. The fiber ECM anchoring has been ensured by joints in trans from SC, connected in cis with the subcortical glial actin cytoskeleton. The structural dynamic, ensures signal transduction through the modulation of the cytoarchitecture, responding the axon to radial progress offered by Schwann cell.

Specific information:
We have recently signaled, by Atomic Force Microscopy (AFM) and confocal microscopy (Rosso et al, 2012), molecular differences on peripheral nerve fibers ECM constitution and organization associated to Trembler-J genotype, a murine model to human Charcot-Marie-Tooth (CMT1E) neuropathy. This differences are also related to the actin cytoarchitecture, giving specific differences on mechanical properties associated to wild type (+/+ ) and Trembler-J (TrJ/+ ) genotype (Kun et al, 2012).

Our approach:
The peripheral nerve fibers from (+/+ ) and (TrJ/+ ) genotype were studied by scanning electron microscopy (SEM). Metallized fibers showed specific ECM genotype differences, similar in appearance to that we have recently noted by AFM.

This difference appears to be supported at least partly in the absence of collagen IV in mice (TrJ/+ ).

The study of ECM on nonmetalized fibers also showed specific genotypic differences, apparently associated to underlining subcellular domains (node of Ranvier, Schmit-Lanterman clefts, cell nuclei), suggesting a coordinated and hierarchical structure of the basement membrane and ECM, which is present on wild type fibers and absent on (TrJ/+ ) that looked a more homogeneous organization of their constituents.

Along with the structural differences, the SEM microanalysis carried on nonmetalized fibers revealed significant differences in the composition and atomic ratio of both genotypes.

In our knowledge, such findings have not been reported before in the literature.
Fig. 1: Wild type fiber without gold coating showing depressions

Fig. 2: Mutant fiber (Trembler) without gold coating. Depressions are not observed