CONICET- ANPCyT- SECyT UNC - Argentina

Palavras-chave: Epigenetic|Sex chromosomes|Brain development|DNA Methyltransferases|Histone deacetylases

13. NEUROGENESIS, NEURAL DEVELOPMENT AND EVOLUTION OF THE NERVOUS SYSTEM

KCNQ4 channel is required for outer hair cell survival, postnatal maturation and efferent innervation.

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INTRODUÇÃO:

KCNQ4 is a voltage-gated K^+ channel essential for hearing. Impairment of its function produces a chronic depolarization of hair cells (HC) leading to cell death, and hearing loss (HL). The mechanism of cell death remains unknown. A protective pathway is carried out by the efferent system by the activation of its synapses, restoring membrane potential. However, its contribution to KCNQ4-related HL is unknown.

OBJETIVOS:

Our aim is to evaluate the molecular, tissue and functional alterations of HCs and their efferent connectivity in a mouse model of HL, which is a knock-out for the KCNQ4 channel (*Kcnq4*$^{-/-}$) (Nº083/2016).

MÉTODOS:

In the WT and *Kcnq4*$^{-/-}$ mice we performed immunofluorescence (IF) combined with superresolution-confocal microscopy, quantitative PCR (qPCR), Auditory brainstem response (ABR) and Distortion product of otoacoustic emissions (DPOAE) assays.

RESULTADOS:

In 4 postnatal-weeks-old (W) *Kcnq4*$^{-/-}$ animals, using IF, we found an increase of cleaved CASPASE-3 expression in outer hair cells (OHC) from the basal turn. Moreover, qPCR analysis revealed that the expression ratio between the pro- and anti-apoptotic factors *Bax*/*Bcl2* was ~76-fold higher. We also found mislocalization of the membrane protein PRESTIN and of the efferent synapses (~30%) that contact OHC. Furthermore, we

found no changes in terminals volume but a 40% decrease in the number of synapses/OHC in *Kcnq4*$^{-/-}$ mice. By contrast, both genotypes at 2W exhibited the same immature wiring pattern. To test the hearing function, we performed ABR showing a significant threshold shift of 20-48 dB SPL in the 5.6-45.25 kHz frequency range. Besides, DPOAE test revealed a threshold shift of ~12-20 dB SPL in the 8-45.25 kHz range.

CONCLUSÕES:

We found new insights into the mechanism of HL in the *Kcnq4*$^{-/-}$ mice. While the basal OHCs die by apoptosis, hearing function is impaired in all cochlear regions.

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Palavras-chave: Hearing|Deafness|Channel|Maturation|KCNQ4

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13. NEUROGENESIS, NEURAL DEVELOPMENT AND EVOLUTION OF THE NERVOUS SYSTEM

Patched-related is required for the development of the Drosophila melanogaster embryonic nervous system

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INTRODUÇÃO:

Patched-related (*Ptr)* gene, primarily classified as a neuroectodermal gene, encodes for an 1169 amino acid protein of 12 putative transmembrane alpha-helices and a sterol-sensing domain that is similar to the topology and domain organization of Patched (Ptc), the canonical receptor of Hedgehog (Hh), a molecule essential for pattern formation, axon guidance and neuronal differentiation.

OBJETIVOS:

To know the physiological function of Ptr during the embryonic development of the *Drosophila melanogaster* nervous system.

MÉTODOS:

Generation of *Ptr* null mutant, knockdown and gain-of-function lines, embryo collections, immunofluorescence, immunohistochemistry, and light and confocal imaging to analyze the developing central and peripheral nervous systems as well as morphological parameters of adult wings.