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Abstract

Altered signal transduction and cellular permeability in retinal bipolar cells caused by mutated TRPM1 and MYO7A could reveal new insights of retinal degeneration pathways

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Abstract:

The earliest step of the visual processing is the generation of parallel information channels responding to increases versus decreases in light intensity. Such ON and OFF responses begin at the first retinal synapse where two classes of postsynaptic bipolar cells react with opposite polarities to glutamate released by photoreceptors. While dendrites of OFF-bipolar cells contain ionotropic glutamate receptors of the AMPA/kainite class, the ON-bipolar cell dendrites express a unique metabotropic glutamate receptor 6 (mGluR6). TRPM1 is a component of the transduction cation channel negatively regulated by the mGluR6 cascade in ON bipolar cells, and forms a macromolecular complex with other proteins including the just cited mGluR6, GPR179, nyctalopin, and the regulator of G protein signaling proteins. Mutations of human TRPM1 are associated with hereditary and acquired diseases in which the retinal ON pathway is selectively affected, such as congenital stationary night blindness. It represents a clinically and genetically heterogeneous group of retinal disorders, whose affected patients lack rod function and suffer from night blindness starting in early childhood. We present data coming from whole exome sequencing of a family in which 2 sons were diagnosed for an orphan form of retinal dystrophy, even if characterized by two different phenotypes. Both patients presented a causative mutation of Usher Syndrome in MYO7A gene, but only one showed a causative mutation of CSNB in TRPM1 gene (c.470C>T, Ser157Phe). We evaluated possible consequences of identified variants on each corresponding protein, analyzing their possible interaction and biological processes that their alterations could impair.

Biography:

Luigi Donato, PhD in "Applied Biology and Experimental Medicine", frequents the Labs of Molecular Genetics of University of Messina, Italy. He is a researcher of the IEMEST institute in Palermo, Italy. He published more than 40 papers in reputed journals and participated in more than 25 national and international congresses, also being in the Organizing Committee in three of them. He was a member of ARVO and he is a member of AIBG. He joined the Editorial Board of several journals, also acting as Guest Editor for "Antioxidants". His main research fields are retinal dystrophies and omics approaches.

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