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The unique functionality of the Oxidative Phosphorylation proteins in the rod disks offers new insights into rod-driven retinal degenerations

Abstract:

Rod photoreceptors, devoid of mitochondria, require significant chemical energy for visual processing. Biochemical analyses, proteomic and imaging studies of rod outer segment disks suggested that the metabolic support for phototransduction comes from ectopic oxidative phosphorylation (OxPhos) playing a key role in reactive oxygen species (ROS) production. Oxidative stress is associated with diabetic retinopathy and age-related macular degeneration. Studies on an ex vivo model of human retinal pigmented epithelium (RPE), ARPE-19 cells, examined the effects of phagocytosis of rod outer segments by cells maintained in normal versus high-glucose environments. ARPE-19 cells cultured in high glucose and treated with oxidized rod outer segments displayed altered intracellular trafficking and heightened oxidation markers compared to those treated with unoxidized rods. This data suggests that early oxidative damage in diabetic retinopathy may originate in the rods and subsequently impact the RPE, providing a new perspective to the current notion that retinal degeneration is solely dependent on redox alterations within the RPE. A proteomic and bioinformatic study comparing rod disks and retinal mitochondria identified differential enrichment of the OxPhos proteins in the disks versus retinal mitochondria. The rod disk proteins exhibited a stronger correlation than the mitochondrial proteins with the tricarboxylic acid cycle and OxPhos proteins. This indicates that OxPhos proteins represent a true component of the rod disk proteome, with different functionality. These findings shed new light on the pathogenesis of rod-driven retinal degenerative diseases and pave the way for new therapeutic approaches for these conditions.

Biography

Isabella Panfoli has completed her PhD in Biology from Genoa University School of Sciences and her M.D. degree from Genoa University School of Medicine (Italy). She is an associate professor of biochemistry at Genoa University School of Medical and Pharmaceutical Sciences, Department of Pharmacy, and a faculty member of the course on chemistry and pharmaceutical techniques in the same department. Dr. Panfoli is a member of various medical and scientific societies. She has published 163 papers in reputed journals and has been serving as an editorial board member of repute.