## RETINAL MIRNA PROFILE AND ELECTRORETINOGRAPHY IN DYSBINDIN-1NULL MUTANT ALBINO MICE: IMPLICATIONS IN HERMANSKY-PUDLAK SYNDROME 7

**Giovanni Luca Romano[1], Chiara Bianca Maria Platania[2], Gian Marco Leggio[2], Sebastiano Alfio Torrisi[2], Salvatore Salomone[2], Michele Purrello[2], Marco Ragusa[2], Cristina Barbagallo[2], Federica Conti[2], Rosa Mastrogiacomo[3], Francesca Managò[3], Maurizio Cammalleri[4], Francesco Papaleo[3], Filippo Drago[2], Claudio Bucolo[2]**

*[1]University of Miami, Miami - USA, [2]Dipartimento di Scienze Biomediche e Biotecnologiche, Catania - Italy, [3]Istituto Italiano di Tecnologia, Genoa - Italy, [4]Università di Pisa, Pisa - Italy*

**Purpose:** Deletion of the dystrobrevin binding protein 1gene (DTNBP1, dysbindin-1protein) has been linked to Hermansky-Pudlak syndrome type 7(HPS-7), a rare disease characterized by oculocutaneous albinism, which affects retinal function. In order to shed light on the pathogenic mechanism leading to defects on retinal neurodevelopment we focused our research on dysbindin-1null mutant mice ($Dys^{-/-}$), as a model of HPS-7. We analyzed the expression of a focused set of miRNAs in the retina of wild type (WT), $Dys^{+/-}$ and $Dys^{-/-}$ mice. We also investigated the retinal function of these mice through electroretinography (ERG) assessment.

**Material and methods:** The first step included the prediction of newly disrupted or created miRNA-binding sites upon mutation of the dysbindin gene through access to the miRSNPs database. Predictions were carried out by filtering for European Caucasian ancestry. Bioinformatic analysis was carried out with the Diana miRPath v 3.0 tool [25] to predict a focused miRNA set, to be further analyzed in wt, Dys $^{+/-}$ and $Dys^{-/-}$ mice. ERG was recorded in each mouse in the three experimental groups: WT, $Dys^{+/-}$ and $Dys^{-/-}$.

**Results:** We analyzed the expression of a focused set of miRNAs in the retina of wild type (WT), $Dys^{+/-}$ and $Dys^{-/-}$ mice. We also investigated the retinal function of these mice through electroretinography (ERG) assessment. In the retina of $Dys^{-/-}$ mice, six miRNAs were up-regulated, while ERG showed an increased in b-wave, compared to WT mice. Furthermore, a gene-dose effect was highlighted both for miR-186-5p increased expression and ERG b-wave increased amplitude in $Dys^{-/-}$ mice compared to $Dys^{+/-}$ and WT mice. A post-hoc bioinformatic approach was applied to understand the link between differential expression of the six miRNAs in the retina of $Dys^{-/-}$ mice and the putative pathogenic mechanisms behind retinal neurodevelopment defects.

**Discussion and conclusions:** This approach evidenced that dysregulated miRNAs (miR-101-3p, miR-137, miR-186-5p, miR-326, miR-382-5p and miR-876-5p) in $Dys^{-/-}$ mice retina could target genes and pathways involved in synaptic plasticity and regulation of dopaminergic signaling, which, when dysregulated, affect retinal functions. Overall, the data indicate potential mechanisms underlying ocular albinism and retinal abnormalities in $Dys^{-/-}$ mice, which may have translational significance in HSP-7patients, both in terms of diagnostic/prognostic biomarkers and novel pharmacological targets.