

MicroRNA-211 Regulates Oxidative Phosphorylation and Energy Metabolism in Human Vitiligo

Authors : Anupama Sahoo, Bongyong Lee, Katia Boniface, Julien Seneschal, Sanjaya K. Sahoo, Tatsuya Seki, Chunyan Wang, Soumen Das, Xianlin Han, Michael Steppie, Sudipta Seal, Alain Taieb, Ranjan J. Perera

Abstract : Vitiligo is a common, chronic skin disorder characterized by loss of epidermal melanocytes and progressive depigmentation. Vitiligo has a complex immune, genetic, environmental, and biochemical etiology, but the exact molecular mechanisms of vitiligo development and progression, particularly those related to metabolic control, are poorly understood. Here we characterized the human vitiligo cell line PIG3V and the normal human melanocytes, HEM-I by RNA-sequencing, targeted metabolomics, and shotgun lipidomics. Melanocyte-enriched miR-211, a known metabolic switch in non-pigmented melanoma cells, was severely downregulated in vitiligo cell line PIG3V and skin biopsies from vitiligo patients, while its novel predicted targets transcriptional co-activator PGC1- α (PPARGC1A), ribonucleotide reductase regulatory subunit M2 (RRM2), and serine-threonine protein kinase TAO1 (TAOK1) were reciprocally upregulated. miR-211 binds to PGC1- α 3'UTR locus and represses it. Although mitochondrial numbers were constant, mitochondrial complexes I, II, and IV and respiratory responses were defective in vitiligo cells. Nanoparticle-coated miR-211 partially augmented the oxygen consumption rate in PIG3V cells. The lower oxygen consumption rate, changes in lipid and metabolite profiles, and increased reactive oxygen species production observed in vitiligo cells appear to be partly due to abnormal regulation of miR-211 and its target genes. These genes represent potential biomarkers and therapeutic targets in human vitiligo.

Keywords : metabolism, microRNA, mitochondria, vitiligo

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