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MIRNA PROFILING IN VITREOUS HUMOR, VITREAL EXOSOMES AND SERUM FROM UVEAL MELANOMA PATIENTS: PATHOLOGICAL AND DIAGNOSTIC IMPLICATIONS

Michele Reibaldi; Teresio Avitabile; Andrea Russo; Antonio Longo; Mario Damiano Toro; Caterina Gagliano; marco ragusa; Santo Stella; Vincenza Bonfiglio; Cesare Mariotti

+ Author Affiliations & Notes

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Abstract

Purpose: Uveal melanoma (UM) is the second most common form of melanoma, as it represents approximately 5-6 % of all melanoma diagnoses. Actual therapeutic impact on patients survival is debatable at best, given that up to 50% of patients succumb to their disease. Although several methods are available, accurate diagnosis is not always easily feasible due to potential accidents (e.g., intraocular hemorrhage). Accordingly, there is a great need for improved, minimally invasive diagnostic methods for UM. Based on the assumption that the profile of circulating miRNAs is often altered in human cancers, we sought to verify whether UM patients show different serum or vitreous humor (VH) miRNAs profiles respect to healthy controls.

Methods: By using TaqMan Low Density Arrays, we analysed 754 miRNAs from VH, vitreal exosomes, and serum of 6 UM patients and 6 healthy donors.

Results: Our data demonstrate that VH miRNAs profile from UM patients is unique and only partially overlaps with that from serum of the same patients.Moreover, 90% of miRNAs are shared between VH and vitreal exosomes. Interestingly, also the alterations of miRNAs expression profiles in VH and vitreal exosomes of UM patients overlap in a statistically significant manner. This could suggest that miRNAs profile alterations in VH result from the dysregulation of the exosomal molecular cargo. We reported 32 miRNAs differentially expressed in UM patients in at least two different types of samples analyzed. Comparable modifications were detected in an independent cohort of twelve ocular melanoma patients. Most alterations were common to VH and vitreal exosomes. Interestingly, miR-146a was upregulated in the serum of UM patients. Upregulation of miR-21 and miR-146a was also detected in formalin-fixed and paraffin-embedded UM, suggesting that VH and serum alterations in UM patients could be the consequence of molecular mutations arising in tumoral cells. Computational functional analysis on miR-146a (the only miRNA dysregulated according to all biological matrices) showed an overrepresentation of biological functions related to cancer and immunity.

Conclusions: Our findings suggest the possibility to screen the blood of UM patients to identify diagnostic miRNAs released by the affected eye: based on this, miR-146a could be considered a potential non invasive blood marker of UM.