Vitreous proteomics correlates with gene expression profiling in uveal melanoma

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Purpose:
Uveal melanoma (UM) is marked by excellent local tumor control but high risk of metastatic disease. Gene expression profile (GEP) profile can accurately identify low- and high-risk metastatic risk tumors by direct tumor biopsy. The vitreous in UM eyes contain secreted proteins some which may be key biomarkers. In this study, we seek to identify proteomic signatures in UM vitreous that correlate with GEP signatures.

Methods:
Case-control study. Liquid vitreous biopsies were collected from two groups: eyes from control subjects (n = 3) undergoing pars plana vitrectomy to remove an epiretinal membrane (ERM), and eyes from test subjects (n = 8) with UM. Vitreous samples were obtained via 27 gauge pars plana vitrectomy in 7 eyes. GEP Class and PRAME designation was performed on tumor biopsy specimens. Vitreous analyzed using a quantitative multiplex ELISA array that concurrently measured the levels of 1,000 proteins. Protein expression changes were evaluated by principal component analysis, 1-way ANOVA (significant p-value <0.05), hierarchical clustering, and pathway analysis to identify candidate protein biomarkers and pathways from the training dataset.

Results:
Mean age of UM patients was 53.9 years. The UM tumors had no ciliary body involvement and mean thickness was 6.6mm. GEP designation was Class 1A (3 eyes), Class 1B (2 eyes), Class 2 (3 eyes) while PRAME expression was positive in 4 (50%) tumors. A total of 62 significantly elevated proteins were detected in the multiplex ELISA, compared to controls. Principle component analysis identified protein signatures separation between vitreous from UM from controls (p = <0.001). Similarly, protein signatures were able to separate UM tumors by both GEP class and PRAME status.

Conclusions:
Vitreous proteomic signatures can uniquely categorize UM by both GEP and PRAME status. Further insights into these candidate proteins that will serve as biomarkers and possible therapeutic targets for UM.