Liya Xu

University of Southern California
USA

A diagnostic aqueous humor protein signature predicts metastatic potential in uveal melanoma

Abstract:

Purpose: Gene expression profiling (GEP) has been clinically validated for stratifying uveal melanoma (UM) patients into two prognostic classes: class 1 (low metastatic risk) and class 2 (high metastatic risk). However, performing GEP analysis requires an intraocular tumor biopsy, which may be limited by tumor heterogeneity and accessibility of the tumor tissue. As a less invasive alternative, specifically the eye-specific aqueous humor (AH) liquid biopsy, has emerged. Previous research in our lab has identified UM-specific differentially expressed proteins (DEPs) from AH that could be used to differentiate GEP classes. In this study, we aim to verify these results and develop a scoring system using a UM-specific DEP signature for predicting metastatic potential.

Methods: The validation set consisted of thirty treatment-naive UM AH samples collected before plaque brachytherapy. Patients were subgrouped into GEP 1 (n=20) and GEP 2 (n=10) based on their GEP classes. Eighty microliters of AH samples were analyzed using the proximity extension assay-derived multiplexed Olink platform. Protein expression levels from the Olink® Explore 3,072 panel were assessed, and a UM- specific protein signature was compared between the GEP classes. Multiple logistic regression was used to calculate the predicted probability of the observation, and Youden's index was utilized to determine the optimal cut-off value.

Results: Through a stepwise selection, we identified 15 the most significant proteins that could serve as potential biomarkers for GEP 2 UM. The combination of 6 DEPs as a panel demonstrated the best performance in differentiating GEP classes. The area under the curve from a receiver operating characteristic (ROC) curve is 0.935 and under an optimal cut-off, the sensitivity and the specificity for discriminating GEP class 2 is 100% and 80%, respectively. Pathway analysis indicated that these DEPs regulate metastatic-related processes.

Conclusions: This study identified a unique AH UM protein signature that can differentiate between GEP class 1 and class 2 at the diagnostic stage, even when the tumor is too small to biopsy. Further verification will be necessary using a larger UM cohort.

Biography

Liya Xu received her PhD in Neuroscience from University of Southern California 2010. Subsequently, she joined Biomedical Pioneering Innovation Center (BIOPIC) of Peking University to lead the development of one-step next generation sequencing (NGS) based Preimplantation Genetic Diagnosis (PGD) for simultaneous avoidance of monogenic disease and chromosome abnormality. Since 2017, her collaboration with Dr. Jesse Berry has been focusing on developing aqueous humor (AH) as a surrogate tumor biopsy for retinoblastoma (RB). It holds the potential to unlock a new era of precision medicine that will transform the way to detect RB, guide the management and prognosis for RB and lead to alternative treatment regimens that offer a personalized approach to medicine for these children with a greater chance of saving the eye.