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Identification of periostin-binding proteins to develop therapy against fibrovascular proliferation

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Purpose: Proliferative vitreoretinal diseases such as age-related macular degeneration, diabetic retinopathy are a leading cause of decreased vision and blindness in developed countries. In these diseases, fibro(vascular) membrane (FVM) formation above and beneath the retina plays an important role. We performed genome-wide gene expression profiling of human FVMs and found significant upregulation of periostin. Subsequent analyses indicated that periostin is a pivotal molecule for FVM formation and a promising therapeutic target for these proliferative vitreoretinal diseases. Periostin has been demonstrated to bind to many proteins such as tenascin-C. Interestingly, we have shown that tenascin-C also significantly inhibited retinal and choroidal FVM formation. These results led us to hypothesize that targeting periostin-binding proteins may be effective way to thoroughly inhibit the FVM formation. The purpose of this study is to comprehensively determine the proteins that bind to periostin using mass spectrometry.

Methods: A Flag-tagged human periostin is recombinantly expressed in human retinal pigment epithelial (RPE) cells, and periostin-complexes are isolated by affinity purification. Complexes are then analyzed by mass spectrometry, and protein-periostin interactions are validated by co-immunoprecipitation.

Results: We expect to extract novel periostin-binding proteins including matricellular proteins and enzymes.

Conclusions： By targeting these periostin-binding proteins, we plan to develop comprehensive molecular-targeting therapy to further inhibit choroidal and retinal fibrovascular proliferation.

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