Research Highlight

Fibrillin Microfibrils Keep the Cornea in Shape

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Although the lion's share of the credits for a healthy cornea, from transparency to biomechanical strength, goes to fibrillar collagens, the less touted elastic microfibrils get a closer look in this issue. Microfibrils (~10–12 nm in diameter) in the extracellular matrix are composed of fibrillin polymers associated with elastin, other glycoproteins, and growth factors to provide a dynamic signaling platform for cells.[1] Mutations in the fibrillin (*FBN*) glycoproteins, encoded by *FBN1, FBN2*, and *FBN3*, are associated with multiple connective tissue disorders, the most notable being *FBN1* causing Marfan syndrome (MFS),[2] in which microfibril ultrastructures were examined in the skin and aorta. Recent studies combine high-resolution electron and immunofluorescent microscopy with three-dimensional reconstruction to gain new insights into the cornea. Thus, microfibrils carry an elastin core in the sclera, extending into elastin-free microfibrils in the cornea, possibly to balance elasticity with rigidity.[3] White et al.,[4] in this issue, report a functional correlation between the geometry of the cornea and ultrastructure changes in microfibrils in a mouse model of MFS carrying a dominant negative mutation in *Fbn1*. They used optical coherence tomography to measure corneal thickness and curvature, and serial block face scanning electron microscopy for microfibril ultrastructure. Their study yields three startling new findings. First, the MFS mice show decreased thickness and increased curvature of the cornea, whereas microfibrils are disorganized and their density in the central stroma is reduced. Second, collagen-associated stromal proteoglycan filaments appear to connect to elastic fibers, suggesting their interactions with fibrillin. Third, interfibrillar spacing of collagen fibrils in the MFS mouse is increased while their diameter is decreased—a known link to corneal functional loss. This study makes a compelling case for further molecular dissection of fibrillin functions; from microfibril structure to growth factor–mediated cell signaling that ultimately affects collagen architecture and corneal functions in MFS.

References

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