

Cellular Communication Network Factor 2 (CCN2) is essential for visual function

The retina is the innermost, light-sensitive tissue layer of the eye found in most vertebrates and some mollusks. During retinal development, multipotent retinal progenitor cells (RPCs) give rise to successive and overlapping waves of postmitotic neurons and Müller glia. There is mounting evidence that dynamic remodeling of the extracellular matrix (ECM) is a key factor in retinogenesis, and multiple ECM proteins have been identified as necessary for proper development. The ECM protein Cellular Communication Network Factor 2 (CCN2) is a context-dependent mediator of angiogenesis, cytoskeletal remodeling, ECM stiffness, cell motility, proliferation, apoptosis, and adhesion. Recent work using a germline-deleted CCN2 knockout mouse model indicates CCN2 is also a critical regulator of embryonic retinal development, and further suggests retinogenesis is mediated by a reciprocal Yes-associated protein (YAP)-CCN2 regulatory axis. However, as germline deletion of CCN2 results in perinatal lethality, the role of CCN2 in the postnatal retina remains uninvestigated. To test the hypothesis that CCN2 is required for postnatal retinal development and visual function, CCN2 was deleted specifically in early RPCs and postnatal retinas were characterized by molecular, cellular, and functional assays. CCN2-deficient RPCs produced all major retinal cell types, with no alterations of retinal architecture compared to controls. However, CCN2 deficiency resulted in selective loss of YAP expression by Müller glia, which previous studies have associated with disruption of retinal homeostasis and visual function. Indeed, CCN2 deficiency caused an age-dependent disruption of visual function as measured by electroretinography. These findings support a critical role for CCN2 in visual function and implicate disrupted YAP-CCN2 regulation in Müller glia as a potential mechanism.