

Lens development and differentiation are strictly regulated processes. Various disturbances of these processes can lead to vision-limiting pathologies. The vertebrate lens is composed of epithelial cells and terminally differentiated fiber cells. Differentiation of fiber cells is connected with expression of fiber cell specific proteins (such as crystallins), cell cycle exit, and finally with the degradation of cell nucleus and organelles.

Wnt/ β -catenin signaling plays important roles during early eye development as well as later during the lens differentiation. To investigate the consequences of constitutive activation of Wnt/ β -catenin signaling in lens fiber cells transgenic mouse strain, called CLEF, was created. Constitutive activation of Wnt/ β -catenin signaling in fiber cells of CLEF mouse is achieved by transgenic protein CLEF that contains C-terminal activation domain of β -catenin fused to the amino terminus of full-length protein Lef1. The expression of CLEF transgene is under the control of α A-crystallin promoter. As a result of constitutive activation of Wnt/ β -catenin signaling in fiber cells, adult CLEF mice develop cataracts and microphthalmia, and the morphology of adult mutant lenses is disrupted. Transgenic CLEF mRNA is expressed starting from E13.5 and by E16.5 transgenic CLEF protein is detected. To provide an understanding of molecular changes, microarray analysis of postnatal day two CLEF and wt lenses was performed. Microarray and qRT-PCR analyses revealed upregulated expression of gene encoding connexin *Gjb5*. However, based on luciferase reporter assay, putative regulatory region of *Gjb5* is not directly regulated by Wnt/ β -catenin signaling. The amount of major fiber cell proteins γ -crystallins is reduced in adult cataractous CLEF lenses. mRNA expression of some γ -crystallins seems to be downregulated as well. CLEF lenses are characterized by abnormal expression of transcription factors cMaf, Sox1 and Pax6 in the central part of the lens at E16.5. Cell cycle regulators Cyclin D1, Cyclin D2 and cyclin-dependent kinase inhibitor p27^{KIP1} are also abnormally expressed in the central part of CLEF lens at E16.5. These data indicate that the constitutive activation of Wnt/ β -catenin signaling in fiber cells results in abnormal and delayed differentiation of fiber cells that spread from transitional zone to the central part of the lens.