METABOLIC CONSEQUENCES OF MULLER CELL DYSFUNCTION

Purpose:
The link between Müller glial dysfunctionand retinal neuronal injury remains poorly under-stood. This study aimed to characterize changes inretinal metabolic pathways after selective disruptionof Müller cells in a transgenic model.

Method:
Affymatrix microarray was performed onwhole retina samples 1 week, 1 month and 3 monthsafter induced Müller cell ablation. Data were analysedwith limma and qRT-PCR was used for array valida-tion. Isolation of patches of Müller cell ablation wasachieved by laser capture microdissection (LCM) andqRT-PCR was conducted on pathway related genes.Immunofluorescence microscopy was used to validatereslts.

Results:
Neuroprotective and apoptosis-related geneswere upregulated 1 week after Müller cell ablation,angiogenesis, tight junction and metabolic-pathwayrelated genes were downregulated later. Furtheranalysis of glycolytic and mTOR pathways with tissueobtained by LCM revealed significant downregulationof genes related to these pathways in patches of Müllercell loss compared with controls. Immunofluorescentstudies revealed that the dowregulation of glycolyticpathway proteins mainly occurred in the photore-ceptor segments, although Enolase1 was lost alongwith Muller cell bodies in the inner nuclear layer.

Conclusion:
We found reduction of transcriptionand expression of proteins involved in key metabolicpathways in areas where Müller cells had been ablated.This study provides new insights into the relationshipbetween Müller cell dysfunction and retinal diseases.Metabolomic studies are warranted to profile alterationsin levels of key metabolites after Muller cell ablation.