Peptides of the variable IgG domain as potential biomarker candidates in primary open-angle glaucoma (POAG)

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Autoantibody profiling has gained increasing interest in the research field of glaucoma promising the detection of highly specific and sensitive marker candidates for future diagnostic purposes. Recent studies demonstrated that immune responses are characterized by the expression of congruent or similar complementarity determining regions (CDR) in different individuals and could be used as molecular targets in biomarker discovery. Main objective of this study was to characterize glaucoma-specific peptides from the variable region of sera-derived immunoglobulins using liquid chromatography--mass spectrometry (LC-MS)-based quantitative proteomics. IgG was purified from sera of 13 primary open-angle glaucoma patients (POAG) and 15 controls (CTRL) and subsequently digested into Fab and Fc by papain.

Fab was further purified, tryptic digested and measured by LC-MS/MS. Discovery proteomics revealed in total 75 peptides of the variable IgG domain showing significant glaucoma-related level changes ($P < 0.05$; log2 fold change $\geq 0.5$): 6 peptides were high abundant in POAG sera, whereas 69 peptides were low abundant in comparison to CTRL group. Via accurate inclusion mass screening strategy 28 IgG V domain peptides were further validated showing significantly decreased expression levels in POAG sera.

Amongst others 5 CDR1, 2 CDR2 and 1 CDR3 sequences. In addition, we observed significant shifts in the variable heavy chain family distribution and disturbed $\kappa/\lambda$ ratios in POAG patients in contrast to CTRL. These findings strongly indicate that glaucoma is accompanied by systemic effects on antibody production and B cell maturation possibly offering new prospects for future diagnostic or therapy purposes.

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