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Identification of two new candidate genes OAF and PVRL1 for Peters anomaly and ectopia lentis

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Peters anomaly (PA) is a congenital defect of the anterior chamber of the eye. The aim of this study is identification of molecular alterations responsible for a syndromic form of Peters anomaly (PA), identified in an individual with an apparently balanced chromosome translocation t(11;18)(q23.3;q11.2)dn. Disruption of the human orthologue of the *Drosophila oaf* gene (*OAF*) by the 11q23.3 breakpoint results in reduced expression level of this transcriptional regulator. Additionally, expression of the cell adhesion protein *PVRL1*, a paralogue of *PVRL3* associated with congenital ocular defects, situated 500 kb upstream from 11q23.3 breakpoint is significantly increased. The 18q11.12 breakpoint is within the intergenic region between *CTAGE1* and *RBBP8*. Genomic imbalance that could contribute to the observed phenotype was excluded. Finally, analysis of mouse lens expression datasets suggests that *OAF* expression is significantly enriched in the lens from early stages of development through adulthood, whereas *PVRL1* is lens-enriched until E12.5 and then down-regulated. Our findings that mouse lens epithelium, that remains abnormally connected to the overlying cornea in PA, normally exhibits high *OAF* expression and low *PVRL1* expression, in contrast to the propositus who exhibits low *OAF* and high *PVRL1* expression offers further support that these are the molecular alterations responsible for this phenotype. Interaction data for *PVRL1* further supports this model. This two gene misregulation model may justify the absence of reported isolated mutations within these genes in unrelated PA patients. In conclusion, these findings suggest that disruption of *OAF* and misregulation of *PVRL1* likely contributes to the observed ocular phenotype.