Regulation of *PXDN* In Eye Development and *PXDN* Gene Variant Screening Within aSouth African Cohort of Patients Presenting with Anterior Segment Dysgenesis.

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Peroxidasin (*PXDN*) is an extracellular matrix-associated haem-containing peroxidase predominantly expressed in the vasculature and eye[1]. Whilst *PXDN* functions have yet to be fully elucidated, PXDN crosslinks collagen IV through sulfilimine bond formation in the presence of hypohalous acids[2]. Aberrant PXDN expression has been associated with kidney fibrosis, heart failure, atherosclerosis, and with relevance to this study, various pathologies of the eye where it likely provides structural support via basement membrane synthesis in the cornea and lens during eye development, as well as protect thelens, trabecular meshwork and cornea against oxidative damage[1,3]. Furthermore, *PXDN* mutations associate with anterior segment dysgenesis (ASD), congenital cataracts and corneal opacity[1,2,4]. To further understand the role of *PXDN* in the eye, we aimed to identify the transcriptional regulators of *PXDN* with relevance to the eye and performed next generation sequencing (NGS) in South African patients exhibiting the aforementioned eye disorders to screen for pathogenic variants in *PXDN* and other ASD genes. Protein expression of key regulators of eye development, namely PITX2, FOXC1 and PAX6, and *PXDN*, in response to Fibroblast Growth Factor-2 were quantified by western blotting and localisation visualised using immunofluorescence confocal microscopy; and chromatin immunoprecipitation-PCR and luciferase assays were employed to detect transcription factor-*PXDN* promoter interactions. Expression data established that *PXDN* and the potential regulators FOXC1, PAX6 and PITX2 were induced by FGF2 at varying timepoints. ChIP-PCR results showed that FOXC1, PAX6 and PITX2 interact with various regions of the *PXDN* gene promoter, with luciferase reporter assay currently underway. Our NGS analysis has identified disease causing variants in PAX6 and GJA8 genes in a South African ASD cohort. In support of the involvement of *PXDN* in the structures of the eye, our findings further support the integral role of *PXDN* in eye development.

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