Glaucoma phenotypic spectrum in patients with *PITX2* and *FOXC1* mutations includes primary open angle glaucoma and primary congenital glaucoma

Purpose: Anterior Segment Dysgenesis (ASD) is a heterogeneous group of disorders characterised by ocular abnormalities affecting the iris, cornea and the drainage angle, and can be associated with extraocular features. Half of the patients develop secondary glaucoma. The purpose of this study was to evaluate the spectrum of glaucoma in individuals with mutations in the *PITX2* and *FOXC1* genes, associated with ASD.

Methods: Participants were recruited through the Australian and New Zealand Registry of Advanced Glaucoma. The *PITX2* and *FOXC1* genes were screened using direct DNA sequencing and Multiplex Ligation Probe Amplification (MLPA) for genetic variants and copy number variations respectively.

Results: 33 individuals from 17 families were included: 14 had *PITX2* and 19 had *FOXC1* mutations. Among individuals with *PITX2* mutations, 64% (9/14) had glaucoma with a median age at diagnosis of 20 years. Two individuals did not have ocular features of ASD: one had primary open-angle glaucoma (POAG) and the other had ocular hypertension. Glaucoma was present in 63% (12/19) of individuals with *FOXC1* mutations (median age at diagnosis 13 years), including 6 who had been diagnosed with congenital glaucoma. Six individuals did not have ocular features of ASD including 3 who had been diagnosed with POAG and 3 with primary congenital glaucoma (PCG).

Conclusion: Our results show that 64% of individuals with *PITX2* and *FOXC1* mutations had glaucoma. These two genes show strong clinical variability with 24% individuals not displaying the classic ocular features of ASD and being diagnosed with POAG or PCG.