A clinical and molecular characterisation of *CRB1*-associated maculopathy – Supplementary Data

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Supplementary Table 1. Published cases of bi-allelic variants in *CRB1* associated with a macular dystrophy phenotype.

Published Case	Diagnosis (observations)	Allele 1	Allele 2
Tsang *et al.*[7]	Macular Dystrophy (unusual 5-year progression of macular atrophy).	c.4142C>T, p.(Pro1381Leu)	c.3991C>T, p.(Arg1331Cys)
Wolfson *et al.* [8]	Maculopathy with cystoid macular oedema.	c.2506C>A, p.(Pro836Thr)	c.2506C>A, p.(Pro836Thr)
Shah *et al.* [9]	Isolated maculopathy	c.493_501del9, p.(Ile167_Gly169del)	c.584G>T, p.(Cys195Phe)
Vincent *et al.* [10] Family A Family B	Familial Foveal Retinoschisis	 c.2483G>A, p.(Cys948Tyr) c.498_506del, p.(Ile167_Gly169del)	 c.367G>T, p.(Gly123Cys) c.2290C>T, p.(Arg764Cys)
Sanchez-Alcudia *et al.* [27]	"Macular and RPE atrophy" (CF aged 70)	c.498_506del, p.(Ile167_Gly169del)	c.2483G>A, p.(Cys948Tyr)
Zhao *et al.* [38]	Macular telangiectasia type 2	c.1685_1698delinsCAAGATGG; p.(Asn562_Gly566delinsThrArgTrp)	c.1685_1698delinsCAAGATGG; p.(Asn562_Gly566delinsThrArgTrp)

Supplementary Table 2: Comparison of phenotypes associated with different combinations of *CRB1* variants.

Phenotype (1+2)	Allele 1 [gnomAD frequency]	Allele 2 [gnomAD frequency]	Allele 3 (null/"severe missense") [gnomAD freq]	Phenotype (2+3)	Allele 2 hom phenotype
Macular dystrophy (Sup. Table 1)	p.(Ile167_Gly169del) [173/277040]	p.(Ile167_Gly169del) [173/277040]	p.(Cys383Serfs*66) [not seen] p.(Cys896Ter) [8/277170] p.(Cys948Tyr) [56/276322]	"EORD"[26] "EORD" / MD[26] milder EORD (patient III.6)[27]	"EORD" (ie. not LCA)[42] Macular dystrophy (this study)
		p.(Ser478ProfsTer24) [not seen]	-		unknown
		p.(Pro1381Thr) [not seen]	p.(Gly850Ser) [6/276848]	LCA[6]	unknown
		p.(Cys896Ter) [8/277170]	p.(Cys896Ter) [8/277170]	LCA[43]	LCA[43]
		p.(Arg764Cys) [22/276628]	p.(Ser403Ter) [not seen] p.(Gly827Ter) [not seen] p.(Cys948Tyr) [56/276322] p.(Glu995Ter) [not seen]	LCA[4, 11]	unknown
		p.(Cys195Phe) [4/277056]			unknown
	p.(Gly123Cys) [not seen]	p.(Cys948Tyr) [56/276322]	p.(Ile205Aspfs*13) [8/245706] p.(Arg526Ter) [9/277150]	LCA[26] LCA[105]	LCA[6]
	p.(Arg1331Cys) [5/246184]	p.(Pro1381Thr) [not seen]	p.(Gly850Ser) [6/276848]	LCA[105]	unknown
		p.(Pro836Thr) [not seen]	p.(Cys243Ter) [not seen]	EORP	Foveal schisis plus full field cone abnormalities Early onset RP [13]
		p.(Ser740Phe) [not seen]	-		Functional data suggests similar to p.Pro836Thr hom – macular and mild cone abnormalities[8, 13]