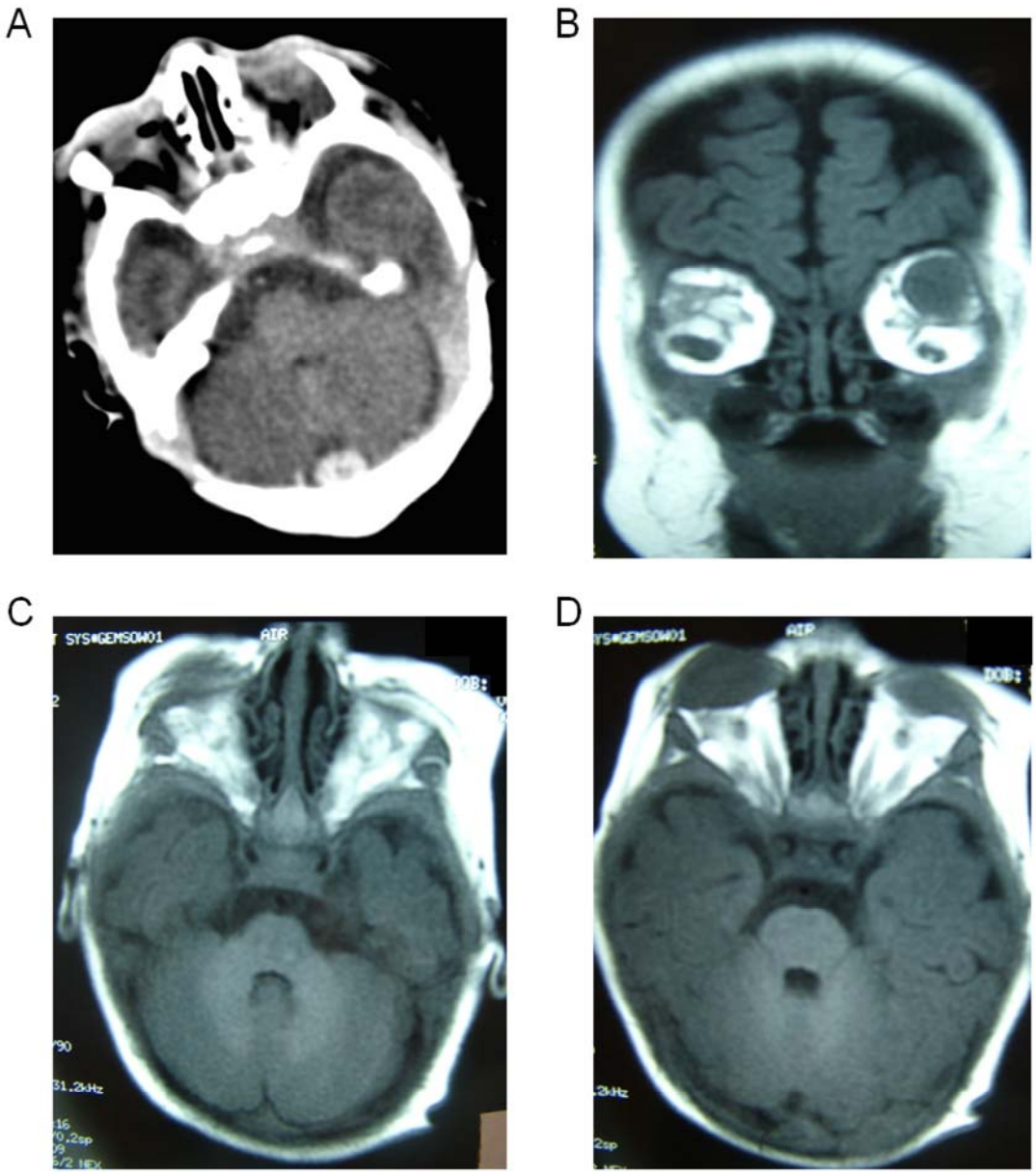
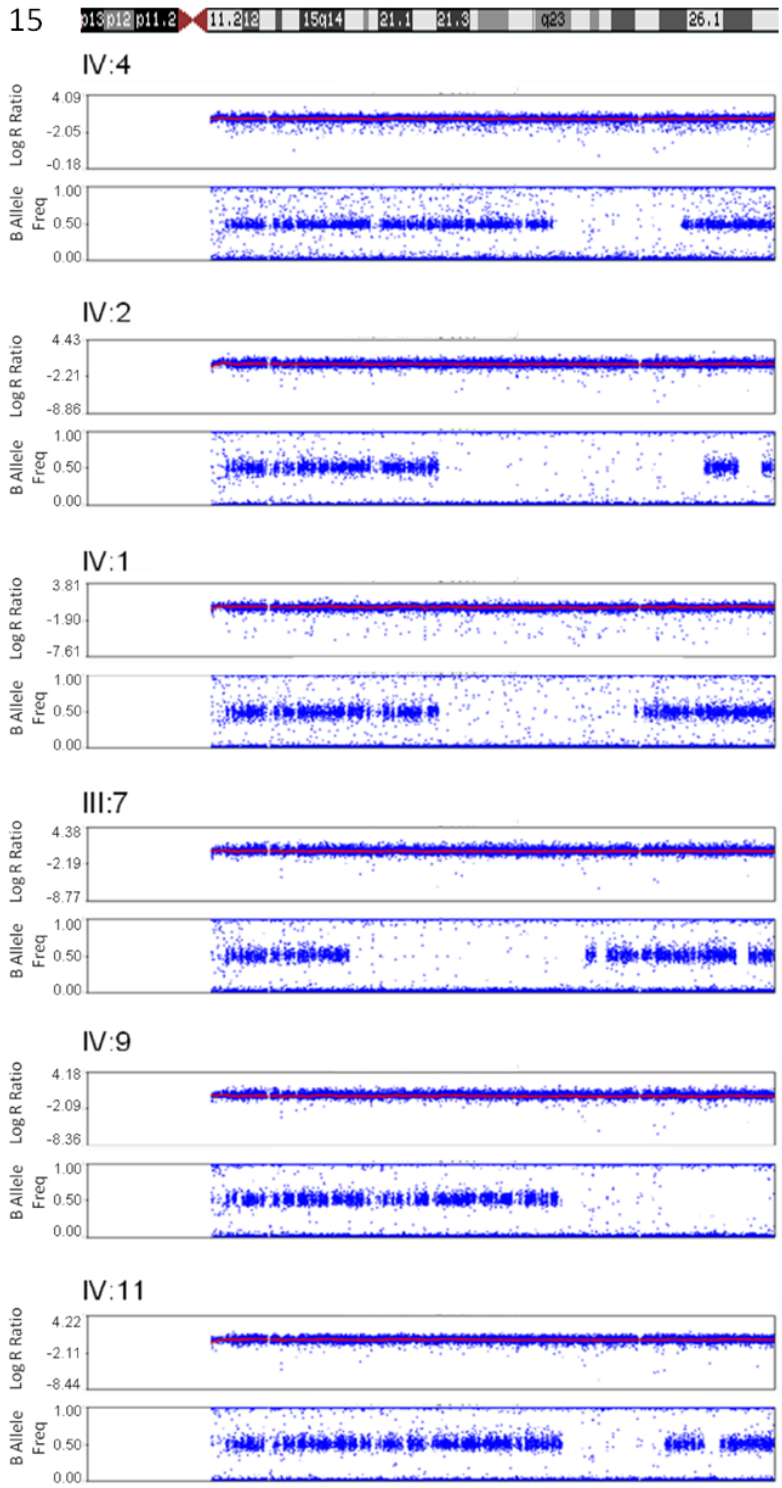


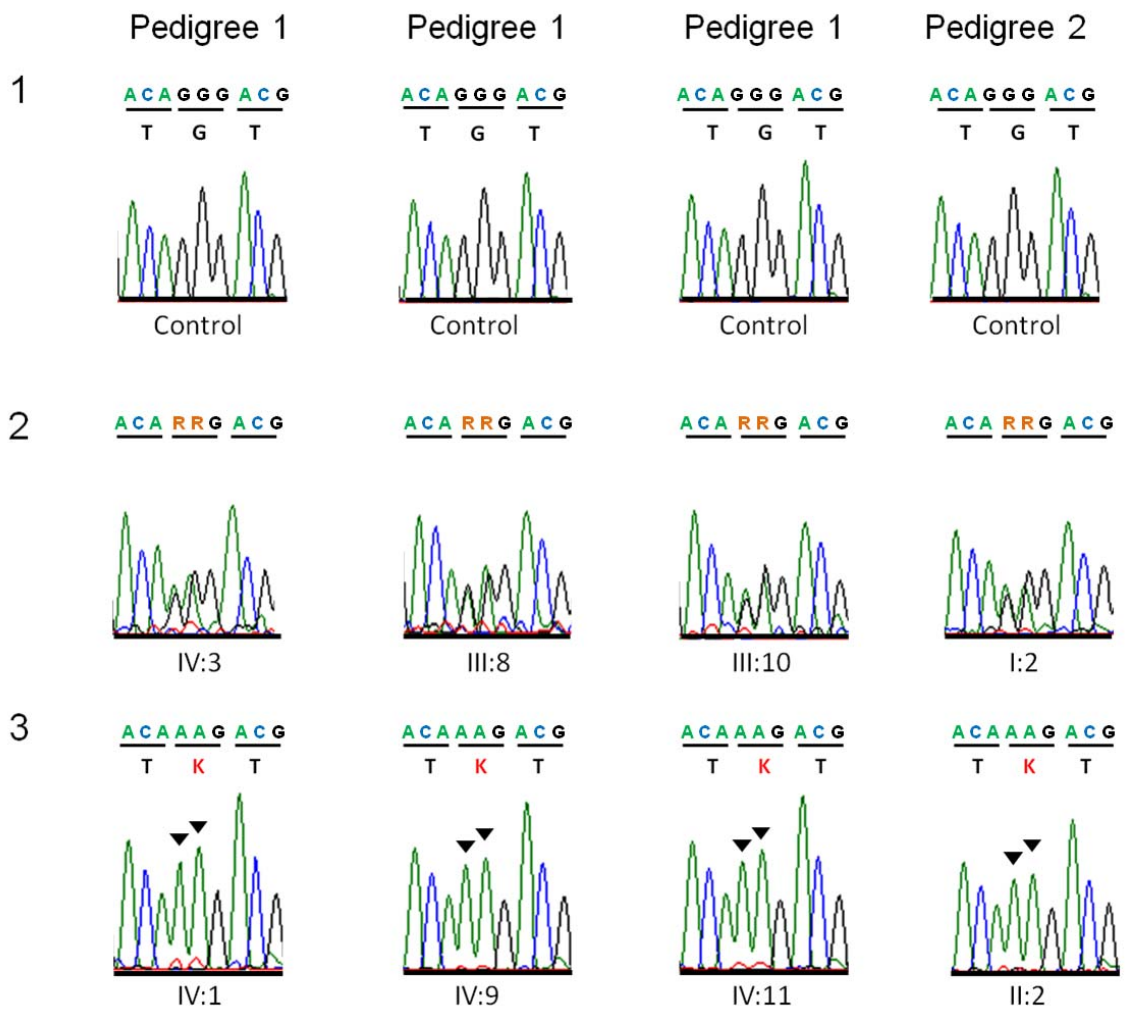
Supp. Figure S1. CT scan and magnetic resonance images of the affected individual from pedigree 2 (A) and pedigree 3 (B-D). The CT scan of the affected individual from pedigree 2 was performed when he was one day old. The patient with Matthew-Wood syndrome (pedigree 3) underwent an MRI at 4 months of age. **A:** An axial non-contrast CT of the brain demonstrates that the left globe is present but small. There is some soft tissue present on the right although there is no obvious globe on this side. The extra-ocular muscles are seen on both sides. **B:** A T1 weighted coronal image shows the presence of a cyst in the upper left orbit which could either be a lacrimal or dermoid cyst. **C:** A T1 coronal image shows normal brain parenchyma and absence of the globes bilaterally. **D:** A T1 weighted coronal

image shows small rounded symmetrical foci of decreased signal at the proximal most end of each optic nerve in the expected position of the head of the optic nerve. The brain parenchyma appears normal. The intra-cranial and intra-orbital optic nerves are present bilaterally. There is evidence of two fluid filled semi-lunar structures directly underneath the eyelids. This has the same signal as the cyst in the left upper orbit and is possible evidence of lacrimal fluid collecting under the eyelids.



Supp. Figure S2. Log R ratio and B allele frequency for each of the six MCOPCB patients across chromosome 15. Runs of homozygosity (ROH) are detected by a loss of heterozygosity in the B allele frequency but no change in the Log R ratio.

Supp. Figure S3. Conservation analysis of *STRA6* residue 304. Conservation of the *STRA6* residue 304 was assessed using PhastCons conservation track (28-way) available in the UCSC genome browser. Residue 304 is located within the red rectangle.



Supp. Figure S4. Validation of STRA6 p.G304K by Sanger sequence analysis. Panels 1, 2 and 3 represent sequence data for the controls, parents and probands respectively. The controls are unaffected members of the Traveller population. The vertical columns denote the different pedigrees. Sequences for one of the affected probands from each family are shown in panel 3. The inverted triangles indicate the two DNA bases that are mutated in residue 304 of *STRA6* in the probands (G to A on the forward strand at both positions).

Supp. Table S1. *A priori* reduction of variants to prioritise putative disease-causing mutations in 3 MCOPCB patients

Criteria	IV:1	IV:2	IV:9	Average
Number of variants	3,965	3,310	3,813	3,696
Number of novel mutations not in dbSNP129	2,649	1,859	2,271	2,260
Number of novel coding mutations	152	130	160	147
Number of novel coding mutations that are homozygous	6	6	6	6
Number of novel homozygous coding mutations that are non-synonymous	2	2	2	2

To identify the disease mutation the number of variants was reduced *a priori* by, **i)** restricting the evaluation to single nucleotide variations, splice variants and indels only, **ii)** excluding SNPs with a frequency >1% in the dbSNP129 data base of normal controls, **iii)** evaluating only novel coding mutations in RefSeq genes, **iv)** limiting the search to homozygous mutations and **v)** prioritising homozygous mutations that result in non-synonymous substitutions. The total reduction of variants is ~1,848-fold (99.9%).

Supp. Table S2. Previously reported SNPs that segregate with the MCOPCB phenotype

Position	Gene	Type	SNP ID	IV:1	IV:2	IV:9	IV:5	IV:10	Substitution
71383876	*NEO1*	3' utr	rs1878941	CC	CC	CC	CT	CT	-
71399521	*HCN4*	3' utr	rs11631286	CC	CC	CC	CT	CT	-
71399886	*HCN4*	3' utr	rs549377	TT	TT	TT	CT	CT	-
72260792	*STRA6*	Exon	rs736118	TT	TT	TT	CT	CC	M527I

Within the candidate loci at 15q24, we identified 4 SNPs (reported in dbSNP129 with a frequency >1%) that were homozygous in the three MCOPCB patients (IV:1, IV:2 and IV:9) and differed to the two unaffected relatives (IV:5 and IV:10). The genomic positions refer to build hg18.

Supp. Table S3. Additional variants identified during sequence analysis of *STRA6* in the MWS patient

Exon	Position	Type	SNP ID	MWS patient	Substitution
14	72263393	Intronic	-	CC	-
17	72260792	Exon	rs736118	TT	M527I

Sequence analysis of the entire *STRA6* gene identified two additional variants in the patient with MWS (pedigree 3). The intronic variant is 10bp from the splice site of exon 14 and is not predicted to affect the splicing process. Similar to the MCOPCB patients, the patient with MWS is homozygous for M527I, which is present in the general population at a frequency of 7%. The M527I variant is not highly conserved and is not predicted to be damaging.