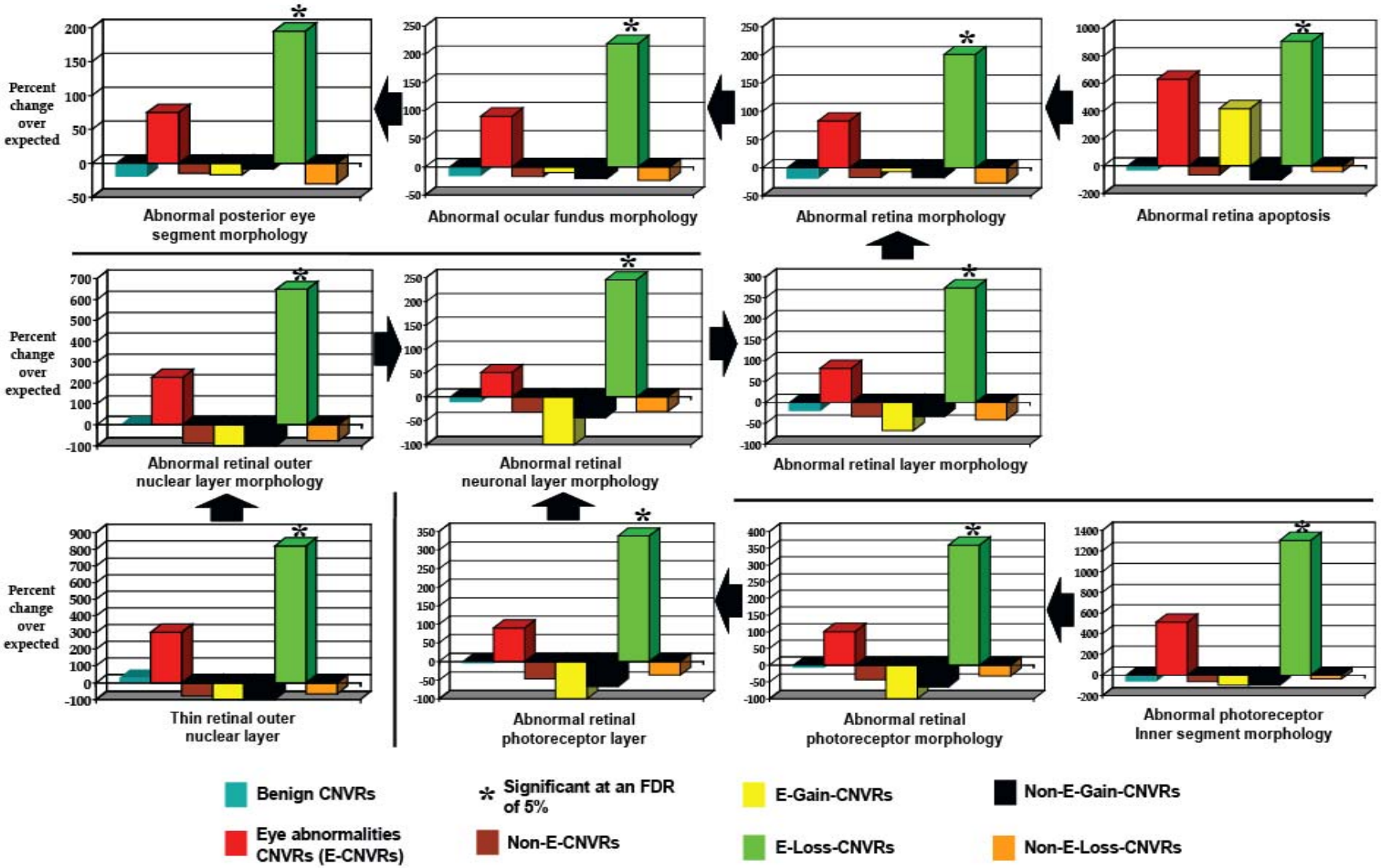
SUPPLEMENTARY FIGURE 1



Supplementary Figure 1: Enrichments of MGI phenotype terms among genes overlapped by CNVRs from DD patients who exhibit eye abnormalities. Eleven specific eye phenotypes are found to be significantly over-represented in *Loss* and/or *Loss minus benign* eye symptom-associated CNVRs. The phenotypes result from the disruption of mouse genes that have been mapped to their unique human orthologue. Columns marked with an asterisk ("*") are significantly enriched (FDR < 5%). The arrows denote the ontological relationships between the phenotypes within the Mammalian Phenotype Ontology; the phenotypic term at the base of the arrow is a child term of the phenotypic term at the head of the arrow.

Supplementary Table 1: Copy Number Variants (CNVs) detected in this study (see Methods). See separate excel file.

Supplementary Table 2: Clinical features presented by patients considered in this study (see Methods). See separate excel file.

Supplementary Table 3: See next page.

Supplementary Table 4: Candidate Gene Details. Additional information is given for each gene that contributes to the enrichments shown in **Figures 1**, **2**, **3** and **4**. Within the Secondary symptom-associated phenotypes, the secondary symptom prefixes the associated phenotype: **Sez** seizures, **Beh** behavioural symptoms, **Eye** eye symptoms. "**Brain-specific**" notes whether the expression level of the gene is higher than 4 times the median expression level across all non-brain tissues (48). "**CNVs**" lists the DD-associated CNVs that overlap the gene (**Table 3**). The CNV format is [Patient ID]_[Chr]_[Start]_[G=Gain/L-Loss]_[patient secondary symptoms], where the patient secondary symptoms are coded **Ur** urinary tract, **BrMa** brain malformations, **ShSt** short stature, **Limb** limb malformations, **Sez** seizures, **Dys** dysmorphia, **Cl** cleft palate/lip, **Beh** behavioural abnormalities

See separate excel file.

Supplementary Table 3: Matching patients secondary clinical features to MGI phenotypic categories. The model phenotypic categories tested for each secondary clinical feature group is indicated with an "X".

	Human secondary clinical features groups					
MGI Phenotypic section	Behavioral	Brain Malformations	Cardiac Defects	Cleft Lip	Cleft Palate	Dysmorphia
MP:0001186 pigmentation						
MP:0002006 tumorigenesis						
MP:0002873 normal						
MP:0003012 no analysis						
MP:0003631 nervous system	X	X				
MP:0005367 renal/urinary system						
MP:0005369 muscle						
MP:0005370 liver/biliary system						
MP:0005371 limbs/digits/tail						
MP:0005372 life span-post-weaning/aging						
MP:0005373 lethality-postnatal						
MP:0005374 lethality-prenatal/perinatal						
MP:0005375 adipose tissue						
MP:0005376 homeostasis/metabolism						
MP:0005377 hearing/vestibular/ear						
MP:0005378 growth/size						
MP:0005379 endocrine/exocrine gland						
MP:0005380 embryogenesis						
MP:0005381 digestive/alimentary						
MP:0005382 craniofacial				X	X	X
MP:0005384 cellular						
MP:0005385 cardiovascular system			X			
MP:0005386 behaviour/neurological	X	X				
MP:0005387 immune system						
MP:0005388 respiratory system						
MP:0005389 reproductive system						
MP:0005390 skeleton						
MP:0005391 vision/eye						
MP:0005392 touch/vibrissae						
MP:0005393 skin/coat/nails						
MP:0005394 taste/olfaction						
MP:0005395 other phenotype						
MP:0005397 hematopoietic						

	Human secondary clinical features groups					
MGI Phenotypic section	Eye abnormality	Genito Urinary	Limb Anomalies	Seizures	Short Stature	SN Hearing loss
MP:0001186 pigmentation						
MP:0002006 tumorigenesis						
MP:0002873 normal						
MP:0003012 no analysis						
MP:0003631 nervous system				X		X
MP:0005367 renal/urinary system		X				
MP:0005369 muscle						
MP:0005370 liver/biliary system						
MP:0005371 limbs/digits/tail			X			
MP:0005372 life span-post-weaning/aging						
MP:0005373 lethality-postnatal						
MP:0005374 lethality-prenatal/perinatal						
MP:0005375 adipose tissue						
MP:0005376 homeostasis/metabolism						
MP:0005377 hearing/vestibular/ear						X
MP:0005378 growth/size					X	
MP:0005379 endocrine/exocrine gland						
MP:0005380 embryogenesis						
MP:0005381 digestive/alimentary						
MP:0005382 craniofacial						
MP:0005384 cellular						
MP:0005385 cardiovascular system						
MP:0005386 behaviour/neurological				X		
MP:0005387 immune system						
MP:0005388 respiratory system						
MP:0005389 reproductive system		X				
MP:0005390 skeleton			X			
MP:0005391 vision/eye	X					
MP:0005392 touch/vibrissae						
MP:0005393 skin/coat/nails						
MP:0005394 taste/olfaction						
MP:0005395 other phenotype						
MP:0005397 hematopoietic system						