

Figure S1. Degree distribution of proteins in the ataxia network based on Y2H interactions.

Degree of a protein is the number of proteins it interacts within the ataxia network.

Figure S2. Calbindin (green) and TRIM23 (red) are shown for wild-type and knock-in samples at 10 weeks. The TRIM23 channel has been scaled 3X in both samples using ImageJ. Scaling demonstrates that the low expression of TRIM23 is not due to cell loss.

Figure S3. Immunostaining in wild-type and *Ataxin-7*^{266Q/+} mouse retinæ at a single timepoint, 10 weeks. Panels show GRN, RAD23A, immunostaining in the ganglion cell layer is not different between the wild-type and knock-in retina. TRIM54 is in the INL and GCL in wild-type and knock-in retina. SIAH1 is in the outer segments, ONL and OPL and is substantially the same between genotypes, though staining seems slightly brighter in wild-type tissue. CARD10 expression lost from the outer segments in knock-in retinæ though this can likely be attributed to photoreceptor degeneration rather than altered protein expression.

Table S1. Summary of each bait used in the Y2H screen. The amino acid range, polyglutamine length and isoform are given as appropriate. The transformation efficiency, number of colonies and the resultant number of different prey proteins are also given for each bait.

Table S2. Binary Y2H protein-protein interactions for CACNA1A and ataxin-7. Also indicated are the pairs tested by GST-AP and the result of the recapitulation. For CACNA1A the isoform tested by GST-AP and results are listed.

Table S3. Summary of network properties of the updated ataxia network from this study compared with the previously published Y2H-only ataxia network and the expanded (literature curated and Y2H) interaction network.

Table S4. Comorbidity studies. A. All ICD-9 codes with a significant increase in the ataxia patients. B. ICD-9 codes that are significantly enriched in the ataxia patient population and represented by known causative proteins in the ataxia interactome.

Table S5. Binary protein-protein interactions and corresponding disease associations.

Table S6. Macular degeneration and additional ICD-9 codes that have overlapping or similar clinical manifestations have increased relative risk in ataxia patients.





