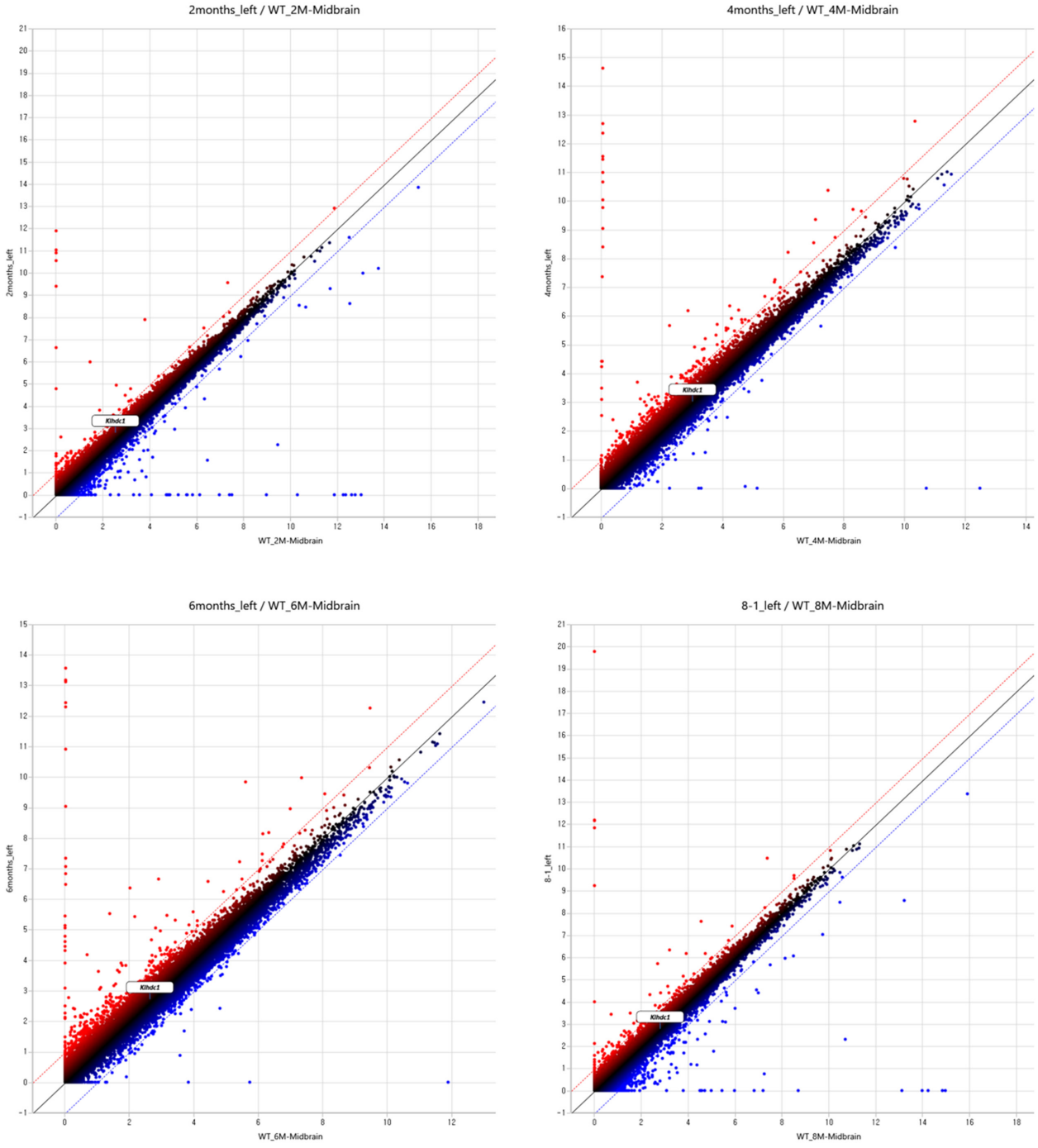
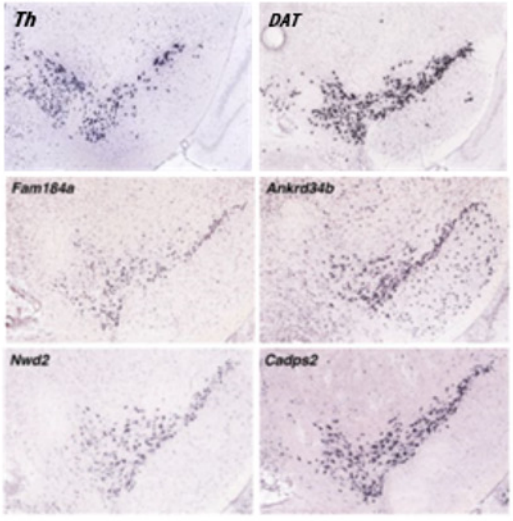


Supplementary Fig. S1. Scatter plot of normalized read counts generated by RNA-Seq in SNpc of WT versus A53T mice from 2 to 8 months of age. Up-regulated genes are colored in red, and down-regulated genes are colored in blue. Up and down 2 fold threshold line was shown as a thin diagonal red and blue line, respectively. Each data point represents a single gene, and *klhdc1* placement indicates its mean respective expression level in comparison between WT vs A53T mice.

A

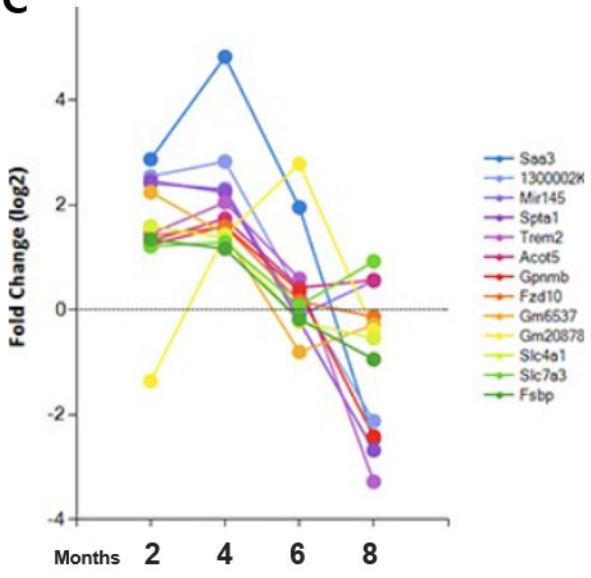
Expression of various marker genes confirms successful isolation of dopaminergic neurons		
Gene name	**Fold change** (8M/2M)	
	Left (TG)	**Right (Viral Injection of FAF1)**
Th, tyrosine hydroxylase	**0.231**	**0.240**
Slc6a3, neurotransmitter transporter, DAT	**0.089**	**0.145**
Drd1, dopamine receptor D1	0.620	0.902
Drd2, dopamine receptor D2	0.937	0.824
Drd3, dopamine receptor D3	0.686	0.638
Drd4, dopamine receptor D4	4.955	0.479
Drd5, dopamine receptor D5	1.345	1.283
Fam184a, family with sequence similarity 184, member A	0.821	0.937
Ankrd34b, ankyrin repeat domain 34B	0.758	0.922
Nwd2, NACHT and WD repeat domain containing 2	0.630	0.947
Cadps2, Ca2+-dependent activator protein for secretion 2	0.497	0.559
FAF1, Fas associated factor 1	**Fold change** (R/L)	
2 months	2.1	
8 months	1.96	

B

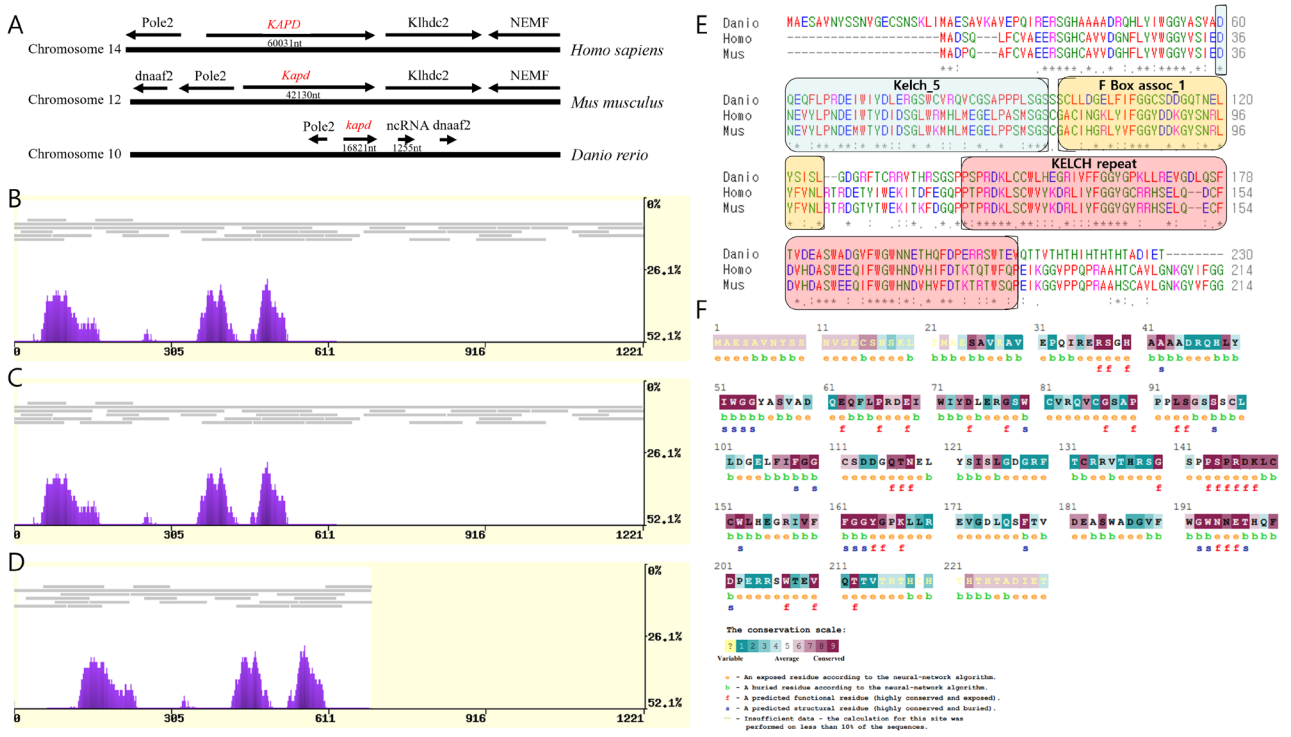


Allen Brain Atlas (https://mouse.brain-map.org/search/index)

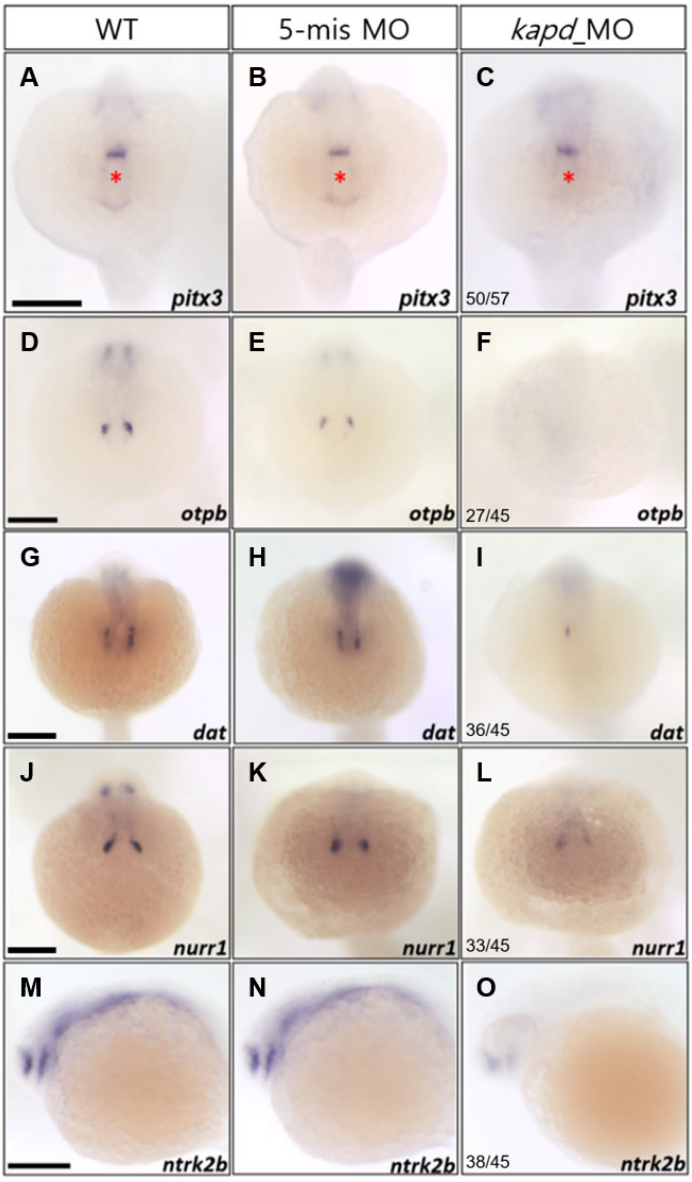
C



Supplementary Fig. S2. Transcriptomic analysis of dopaminergic neurons in 2- to 8-month-old transgenic mice (A53T) in comparison with the wild type. (A) A total of 23,284 genes were tested and plotted for each sample. Red indicates up-regulation at a particular position, whereas blue indicates down-regulation. The level of FAF1 transcript was used as an anatomical reference for this analysis. (B) Markers of SN DA neurons confirmed the quality of the transcriptomic profiles. (C) DEGs with significant fold changes confirmed the purity of the isolated dopaminergic neurons.



Supplementary Fig. S3. Genomic organization of vertebrate *KAPD* loci and comparison of the zebrafish *kapd* sequence with those of other vertebrates. (A) Map locations are based on zebrafish genome sequence provided by NCBI Gene (https://www.ncbi.nlm.nih.gov/gene). eShadow analysis was performed on *kapd* coding sequences. Conservation plot is shown with reference to the base organism as (B) *Homo sapiens* (1.2 kb), (C) *Mus musculus* (1.2 kb), or (D) *Danio rerio* (0.69 kb) using a 50 bp sliding window for the conservation profile (purple peaks). Y-axis corresponds to percent identity; x-axis corresponds to size in base pairs. (E) Deduced amino acid sequence of the zebrafish *kapd* aligned with those of *Homo sapiens* and *Mus musculus*. Residues marked with colored boxes are conserved among Kelch proteins. (F) Sequence conservations analysis of protein sequence was performed using ConSurf (https://consurf.tau.ac.il).



Supplementary Fig. S4. Knockdown of *kapd* down-regulates expression of *pitx3*, *otpb*, *dat*, *nurr1*, and *ntrk2b* in zebrafish embryos at 24 hpf. (A-O) WISH analysis of *kapd* in mature DA neurons using markers *pitx3*, *otpb*, *dat*, and *nurr1* at 24 hpf. Shown are WT embryos (A, D, G, J, and M), embryos injected with 5-mismatch MO as a control (B, E, H, K, and N), and embryos injected with *kapd* MO (C, F, I, L, and O). *kapd* morphants exhibited no significant change in *pitx3* expression patterns at 18 hpf (C). *kapd* morphants exhibited reduced expression of *otpb* (F), and the level of *dat* transcripts was significantly reduced in the ventral diencephalic region (I). Knockdown of *kapd* caused a remarkable reduction of *nurr1* transcripts in the diencephalon, which abuts the preoptic area, at 24 hpf (J-L). (M-O) Embryos were examined for the expression of the marker *ntrk2b*, which encodes a tyrosine kinase receptor, at 24 hpf. Injection of *kapd* MO decreased the size of the diencephalon and dorsal telencephalon expression domains relative to those of WT (M) and 5-mismatch MO control (N) at 24 hpf (O). (A-O) Scale bars = 250 μm.