Online Methods

Human Subjects. The study protocol was approved by the Yale Human Investigation Committee. Institutional review board approvals for genetic studies, along with written consent from all study subjects, were obtained at the participating institutions (Supplementary Notes).

MRI Sequences. MRI examinations presented were performed with a 3T scanner (Trio, Siemens, Erlangen).

Illumina Genotyping. Whole-genome genotyping of the samples was performed on the Illumina Platform with Illumina Human 370K Duo or 610K Quad Beadchips using the manufacturer`s protocol (Illumina, SanDiego, CA, USA). The image data were normalized and the genotypes were called using Illumina`s data analysis software (Bead Studio, Illumina). Linkage analysis was performed using Allegro v2.0 software (DeCode Genetics, Inc., Iceland).

Sanger Sequencing. The exons and exon-intron boundaries of *WDR62* were determined using the UCSC Genome Browser (http://genome.ucsc.edu), unique primers were designed using Sequencher 4.8 (Gene Codes, Ann Arbor, MI, USA) and synthesized by Invitrogen (Carlsbad, CA, USA). The fragments were amplified, purified and direct re-sequencing was performed using ABI`s 9800 Fast Thermocyclers. The amplicons were analyzed on 3730xL DNA Analyzer (Applied Biosystems Inc., Foster City, CA, USA).

Targeted Sequence Capture. Genomic DNA of sample NG 26-1 was captured on a NimbleGen 2.1M human exome array (based on the April 30th, 2008 build of the CCDS database) with modifications to the manufacturer`s protocol [9]. The pre- and post- capture libraries were compared by quantitative PCR for the determination of the relative fold enrichment of the targeted sequences.

Exome Sequencing. Single-read cluster generation was performed on the Cluster Station (Illumina, San Diego, CA, USA). The captured, purified, and clonally amplified library targeting the exome from patient NG 26-1 was sequenced on Genome Analyzer IIx. Two lanes of single-read sequencing at a read length of 74 base pairs was performed following the manufacturer`s protocol. Image analysis and base calling was performed by Illumina pipeline version 1.5 with default parameters which is installed on Yale's High Performance Computing Cluster.

Exome Sequence Analysis. The sequence reads obtained were aligned to the human genome (hg18) using Maq[19]and BWA[20] software. The percent alignment of the reads to both the reference genome as

well as the targeted region, exome, was calculated using perl scripts[9]. Similarly, perl scripts were used for the detection of mismatch frequencies and error positions. SAMtools [21] was used for the detection of single nucleotide variations on the reads aligned with Maq. The indels were detected on the reads aligned with BWA for its ability to allow for gaps during the alignment. Shared homozygous segments of the affected individuals were detected using Plink software version 1.06[12], and the variants were filtered for shared homozygosity. The variants were annotated for novelty with comparison to both dbSNP (build 130) and nine personal genome databases and previous exome sequencing experiments performed by our human genomics groups.

Functional Annotation. Published microarray datasets of E9.5, E11.5 and E13.5 mouse brain tissue (GSE8091) were downloaded from the GEO data base (http://www.ncbi.nlm.nih.gov/projects/geo/query/acc.cgi)[18] and processed using R Statistical Program (Affy package) [22]. Genes that correlated highly with *Wdr62* (Bonferroni corrected $P < 0.01$) were functionally annotated using DAVID Tools (http://david.abcc.ncifcrf.gov/)[23].

Animals. Experiments were carried out in accordance with protocols approved by the Institutional Animal Care and Use Committee at Yale University School of Medicine.

In situ hybridization. Sections and whole-mount embryos were processed for non-radioactive in situ hybridization as described previously with minor modifications[24]. An RNA probe complementary to mouse Wdr62 (bases 3,525 to 4,480 of the mouse *Wdr62* cDNA, NM_146186) was prepared and labeled with digoxigenin-11-UTP. Embryos and tissue sections were analyzed using a Zeiss Stemi dissecting microscope or a Zeiss AxioImager fitted with a Zeiss AxioCam MRc5 digital camera. Images were captured using AxioVision AC software (Zeiss) and assembled using Adobe Photoshop.

Immunostaining and confocal imaging. Embryonic day (E) 15.5 embryos were obtained from timed-pregnant CD-1 mice (Charles River). For timed pregnancies, midday of the day of vaginal plug discovery was considered embryonic (E) day 0.5. Dissected brains were fixed by immersion in 4% PFA for 16hr at 4°C and sectioned at 70μm using a vibratome (Leica VT1000S). Human fetal brains at 19 and 20 weeks of gestation were obtained under the guidelines approved by the Yale Institutional Review Board (protocol #: 0605001466) from the Human Fetal Tissue Repository at the Albert Einstein College of Medicine (CCI #: 1993-042), fixed by immersion in 4% PFA for 36hr, cryoprotected and frozen, and cryosectioned at 60μm. For mouse sections, an unconjugated donkey anti-mouse IgG Fab fragment (Jackson Immuno Research Laboratories, 1:200) was added to block endogenous mouse IgG. Primary antibodies were

diluted in blocking solution at the following concentrations; mouse anti-WDR62 (Sigma-Aldrich), 1:400; rabbit anti-SOX2 (Millipore), 1:500; rabbit anti-TBR2 (Abcam), 1:500; chicken anti-GFP (Abcam), 1: 1500; rat anti-alpha-tubulin (Abcam), 1:500; rabbit anti-gamma-tubulin (Sigma), 1:250 and standard methods were followed. Confocal images were collected using laser-scanning microscope (Zeiss LSM 510). For diaminobenzidine (DAB) staining, brain sections were incubated with biotinylated secondary antibodies and processed using the ABC and DAB kits (Vector Laboratories). Images were acquired using a digital scanner (Aperio).

Cell culture. For neural progenitor cultures, dorsal telencephalon was dissected from E12.5 mouse embryos and enzymatically dissociated and resuspended as previously described[25]. For cell lines, Neuro2a, HeLa, and HEK-293FT cells plated glass cover slips coated with poly-L-ornithine (15ug/ml) at $5x10^5$cells/cm^2 in 24-well plates. Sixteen hrs after plating, the cells were fixed by immersion in 4% PFA for 15 minutes at room temperature and processed for immunostaining.

Subcellular fractionation and Western blotting. Dorsal telencephalon was dissected from E14.5 mouse embryos and fractionated using the CelLytic nuclear extraction kit (Sigma). The manufacturer's protocol was followed with the exception that cell lysis was achieved by addition of 0.5% Triton X-100. Immunoblotting was done with primary antibodies diluted at the following concentrations: rabbit anti-WDR62 (Novus), 1:1000; rat anti-alpha-tubulin (Abcam), 1:5000.

In utero electroporation. CAG-Gfp plasmid DNA was transfected into VZ progenitors of E13.5 embryos by in utero electroporation as previously described [26]. At E15.5, the embryos were harvested and fixed for immunostaining.

22. Irizarry, R.A. et al. Summaries of Affymetrix GeneChip probe level data. *Nucleic Acids Res* **31**, e15 (2003).
23. Huang da, W., Sherman, B.T. & Lempicki, R.A. Systematic and integrative analysis of large gene lists using DAVID bioinformatics resources. *Nat Protoc* **4**, 44-57 (2009).
24. Stillman, A.A. et al. Developmentally regulated and evolutionarily conserved expression of SLITRK1 in brain circuits implicated in Tourette syndrome. *J Comp Neurol* **513**, 21-37 (2009).
25. Abelson, J.F. et al. Sequence variants in SLITRK1 are associated with Tourette's syndrome. *Science* **310**, 317-20 (2005).
26. Kwan, K.Y. et al. SOX5 postmitotically regulates migration, postmigratory differentiation, and projections of subplate and deep-layer neocortical neurons. *Proc Natl Acad Sci U S A* **105**, 16021-6 (2008).