Supporting Information

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Fig. S1. Isl1 is expressed in a subset of the *Dlx 5/6* fate-mapped (*Dlx 5/6-CIE; CC-EGFP*) striatal cells at E18.5. (*A*) FoxP1 immunostaining shows that FoxP1 marks all striatal-projection neurons. (*B*; high power in *C*) The majority of *Dlx 5/6* fate-mapped cells express FoxP1. (*D*) Isl1 is expressed in the embryonic striatum. (*E*; high power in *F*) Isl1 is expressed in less than half of *Dlx 5/6* fate-mapped cells.



Fig. S2. *Dlx 5/6* fate-mapped cells contribute to both the striatonigral and striatopallidal pathway. (*A*) *Dlx 5/6* fate-mapped cells are found throughout the telencephalon and diencephalon. The white lines in *A* delineate the approximate levels of the coronal sections in *B–E. Dlx 5/6* fate-mapped cells synapse with both the (*B*) GP and the (*D*) SNr as indicated by the coexpression of Syn with EGFP⁺ *Dlx 5/6* fate-mapped cells. *C* and *E* are high powered images of the boxed area in *B* and *D*, respectively. GP, globus pallidus; Hyp, hypothalamus; OB, olfactory bulb; rTh, reticular thalamic nucleus; SNr, substantia nigra pars reticulata; Stm, striatum; Th, thalamus.



Fig. S3. The telencephalic and ventral forebrain inactivation of *Isl1* leads to a severe reduction of *Isl1* in the developing striatum at E14. Telencephalic inactivation of *Isl1* using the *Foxg1*^{tTa};tetO-cre binary system causes a dramatic loss of Isl1 in the developing striatum as well as the septum and hypothalamus (*B*) compared with controls (*A*). At adult stages, the telencephalic-specific deletion of *Isl1* leads to a loss of Isl1-positive neurons in the striatum but intact expression of Isl1 in the reticular nucleus and zona incerta of the diencephalon of conditional mice (*D*) compared with controls (*C*). The high-power *Insets* in *C* and *D* show Isl1-positive striatal interneurons in control (*C*) and lack thereof in the conditional mutant (*D*). Ventral forebrain inactivation of *Isl1* using the *DIxSI6*-cre leads to a significant reduction of Isl1 in the developing striatum and hypothalamus (*F*) whereas Isl1 is still expressed in the septum (arrows in *F*) compared with controls (*C*). The, reticular thalamus; Th, thalamus; ZI, zona incerta.



Fig. S4. Cholinergic interneurons are specifically reduced in *Is*/1 conditional mutants. Choline acetyltransferase (ChAT) immunostaining shows a marked reduction of cholinergic interneurons in the striatum of *Is*/1 conditional mutants (*B*) compared with controls (*A*). Immunostaining for interneurons expressing either neuropeptide Y (NPY) or parvalbumin (PV) indicates that these populations of interneurons are unaffected in the striatum of *Is*/1 conditional mutants (*D* and *F*) compared with controls (*C* and *E*).



Fig. S5. Expression of Gsx2, Ascl1, and Dlx proteins in the *Isl1* conditional mutant telencephalon at E14.5. Gsx2 expression in control (*A*) and *Isl1* mutant (*D*) LGE and MGE appears indistinguishable. Moreover, Ascl1 and Dlx are expressed similarly in control (*B* and *C*) and *Isl1* mutants (*E* and *F*).



Fig. S6. Colocalization of IsI1 and Ikaros in the LGE SVZ. (A) Although IsI1 is expressed throughout the developing striatal complex, Ikaros is enriched in the dorsolateral region of the developing striatum at E14.5. (B) High-power z-stack from the E14.5 LGE SVZ showing colocalization of IsI1 and Ikaros in many cells. Note that there seem to be only a few Ikaros-only cells and many IsI1-only cells. (C) High-power z-stack from the E18.5 LGE SVZ again showing colocalization of IsI1 and Ikaros; however, at this stage, there seem to be more Ikaros-only cells.



Fig. 57. Helios expression in the *Isl1* conditional mutant striatum. (A) Helios is expressed by cells in the dorsolateral regions of the developing striatum at E18.5. (B) High power of boxed striatal area in A. (C) *Isl1* conditional mutants exhibit a smaller striatum at E18.5; however, the density of Helios cells appears similar to the controls. (D) High power view of boxed area in C.



Fig. 58. Proliferation in the *Isl1* conditional mutant LGE at E14.5. (A) pH3-positive (i.e., M-phase) cells are observed in apical (i.e., VZ) and basal (i.e., SVZ) portions of the control LGE. (B) High power of boxed region in A showing little, if any, colocalization of Isl1 and pH3 in the SVZ. (C) Similar numbers of pH3 cells are observed in the *Isl1* mutant LGE at both apical and basal positions. (D) High power view of the boxed area in C.

DNA C