Supplementary Figures, Table, and Movie

Figure S1 Distribution of ALDH1A1, calbindin, and TH-positive neurons in the SNpc and VTA of 2-month-old nTg mice

Representative images show ALDH1A1 (green), calbindin (red), and TH (blue) staining in the SNpc and VTA of 2-month-old control mice. The dash line marks the boundary between SNpc and VTA. DM: dorsomedial, VL: ventrolateral. Scale bar: 100μm

Figure S2 Distribution of Aldh family genes in the brain of P56 nTg mice

(**A**) *In situ* hybridization of *Th*, *Aldh1a1, Aldh1l1, Adh2* in coronal sections of postnatal day 56 （P56）male C56/BL6 mice (Allen Brain Atlas, http://www.brain-map.org/).

(**B**) *In situ* hybridization of *Th*, *Aldh1a1, Aldh1a2, Aldh1a3, Aldh1b1, Aldh3a2, Aldh3b1, Aldh3b2, Aldh4a1, Aldh5a1, Aldh6a1, Aldh7a1, Aldh8a1,* and *Aldh18a1* in sagittal sections of P56 male C56/BL6 mice (Allen Brain Atlas, http://www.brain-map.org/).

Figure S3 Distribution of ALDH1A1-positive and negative DA neurons in human SNpc

(**A-B**) 3D reconstruction of DA neurons in human SNpc shows the distribution of ALDH1A1 and NM-double positive ($ALDH1A1^+/NM^+$, yellow) as well as ALDH1A1-negative but NM-positive ($ALDH1A1^-/NM^+$, red) neurons remaining in the SNpc of control (Ctrl, **A**) and PD (**B**) human brains.

Fig. S4 Reduction of ALDH1A1 staining in DA neurons at the SNpc of patients with sporadic PD

Representative bright-field images show ALDH1A1 staining (purple) in the VM, PL and VL of control and severe PD SNpc. DA neurons were marked by the presence of NM (brown) in the soma. The small panels highlight the soma (left) and neurites (right) in the boxed areas of the large panels. Scale bar: 100μm (large panel); 10μm (small panel).

Fig. S5 Expression of transgenic α-synuclein in cultured cortical neurons

Western blot analyses show expression of transgenic α-synuclein in cultured cortical neurons derived from P0 CaMKII-tTA/tetO-A53T pups. The C20 α-synuclein antibody recognizes both human and mouse α-synuclein, while the syn211 antibody recognizes only human α-synuclein. The presence of DOX suppresses the expression of transgenic α-synuclein. The expression of actin was used as the loading control.

Table S1. List of control and PD cases.

Movie. 3D reconstructions of DA neurons in the midbrain of 18-month-old nTg (movie 1) and A53T (movie 2) mice.

Figure S1

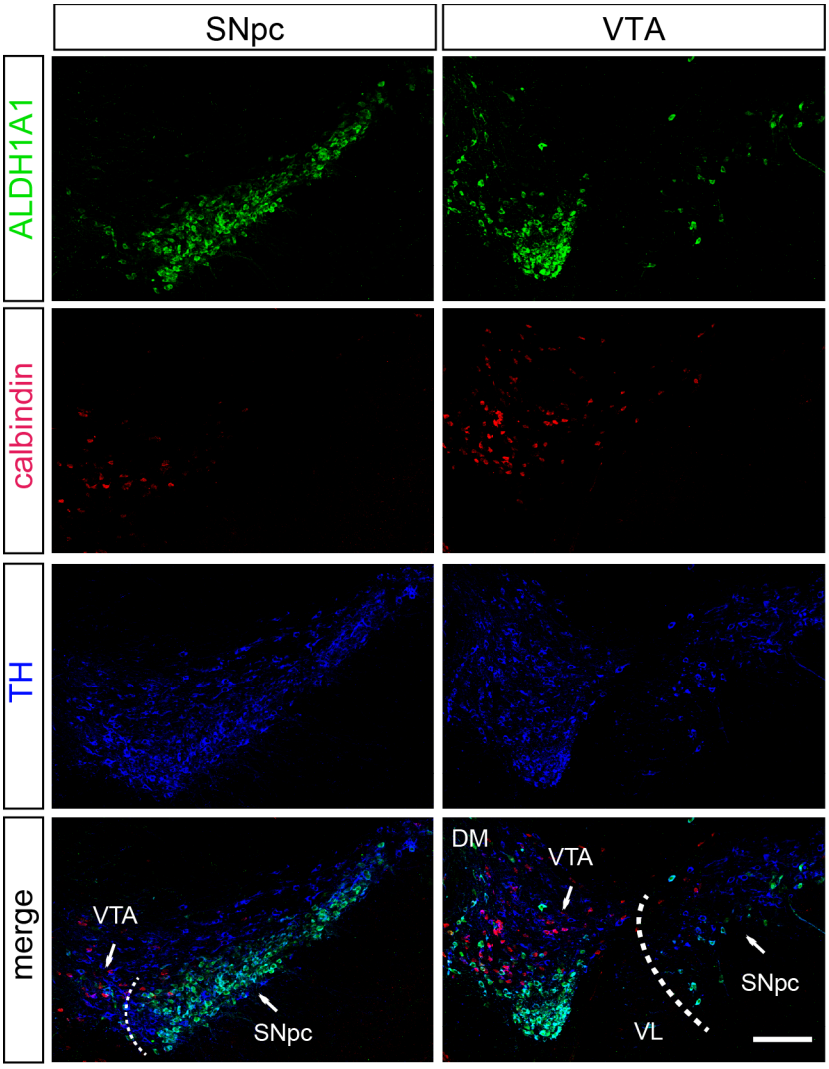

Figure S2

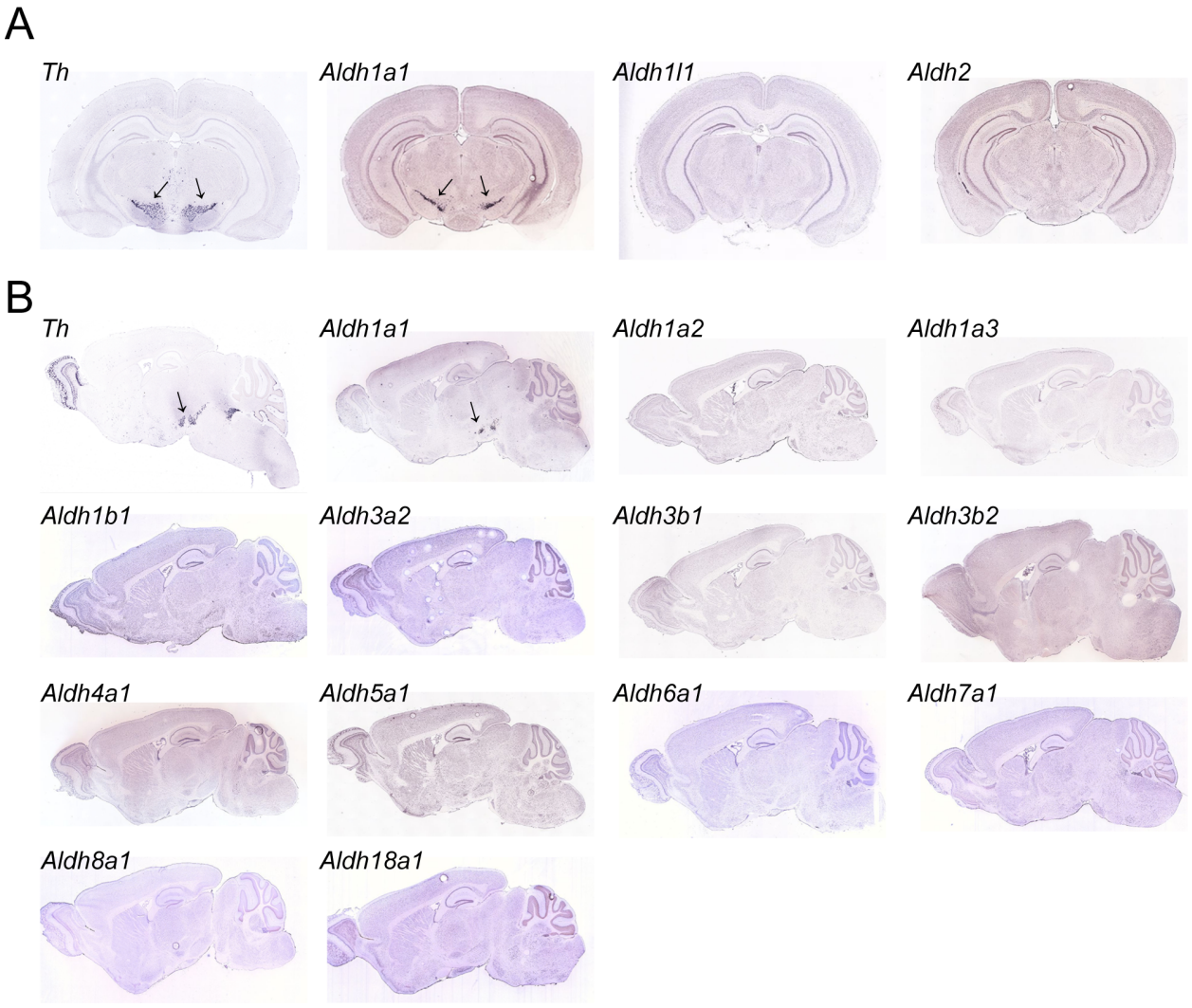
A
Th
Aldh1a1
Aldh1l1
Aldh2
B
Th
Aldh1a1
Aldh1a2
Aldh1a3
Aldh1b1
Aldh3a2
Aldh3b1
Aldh3b2
Aldh4a1
Aldh5a1
Aldh6a1
Aldh7a1
Aldh8a1
Aldh18a1

Figure S3

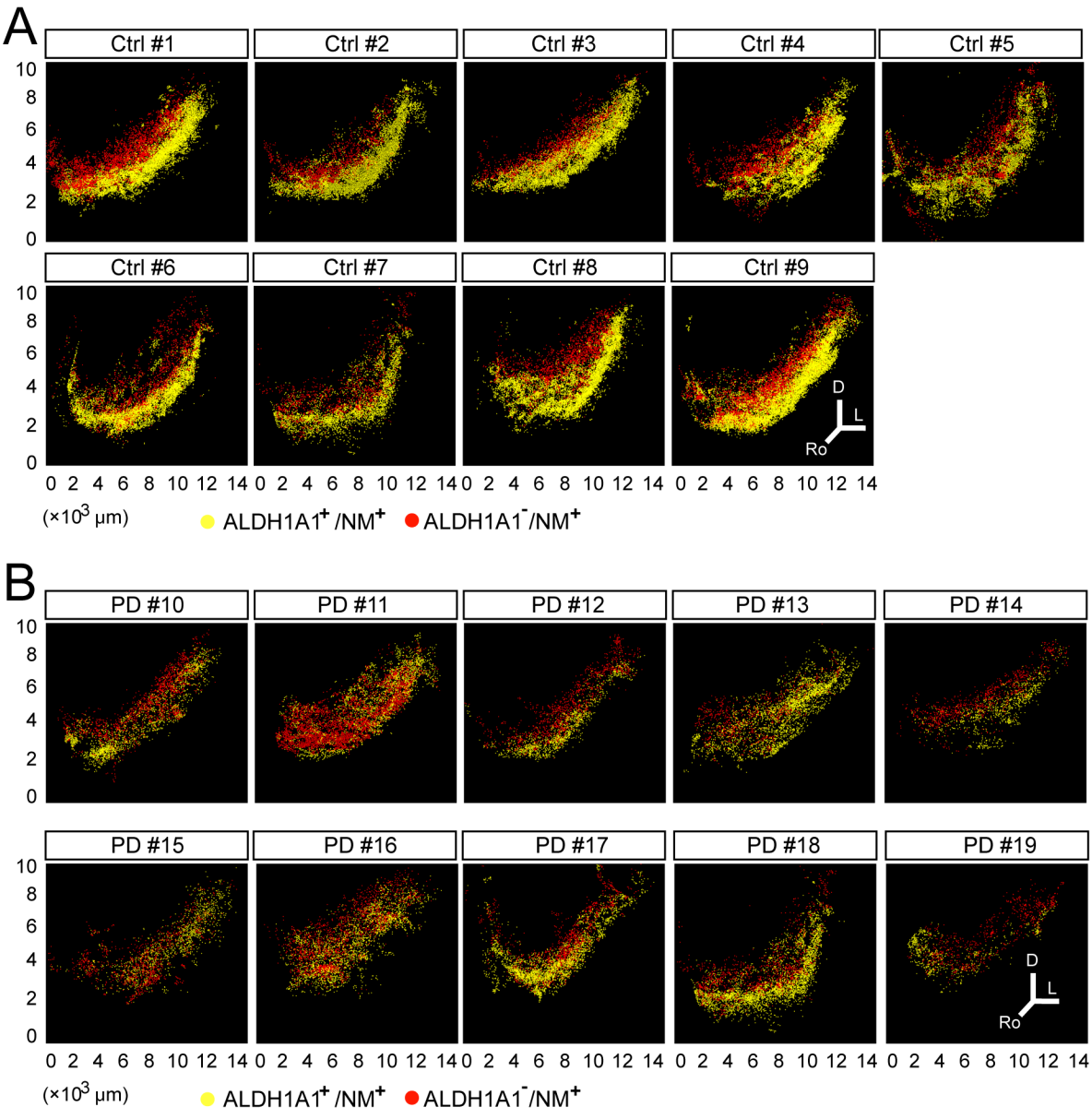
A
Ctrl #1
Ctrl #2
Ctrl #3
Ctrl #4
Ctrl #5
Ctrl #6
Ctrl #7
Ctrl #8
Ctrl #9
D
L
Ro
0 2 4 6 8 10 12 14
(×10³ μm)
ALDH1A1⁺/NM⁺
ALDH1A1⁻/NM⁺
B
PD #10
PD #11
PD #12
PD #13
PD #14
PD #15
PD #16
PD #17
PD #18
PD #19
D
L
Ro
0 2 4 6 8 10 12 14
(×10³ μm)
ALDH1A1⁺/NM⁺
ALDH1A1⁻/NM⁺

Figure S4

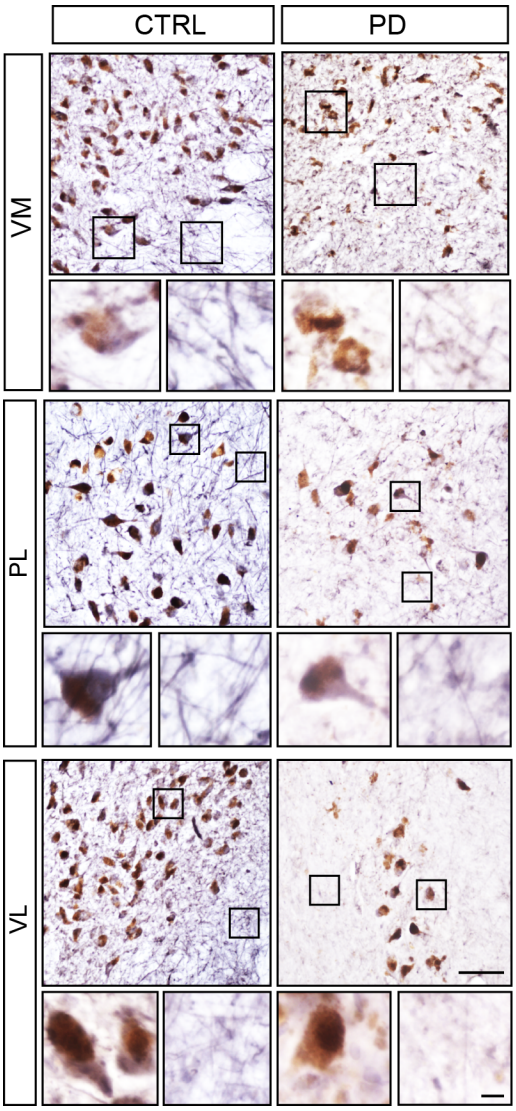

Figure S5

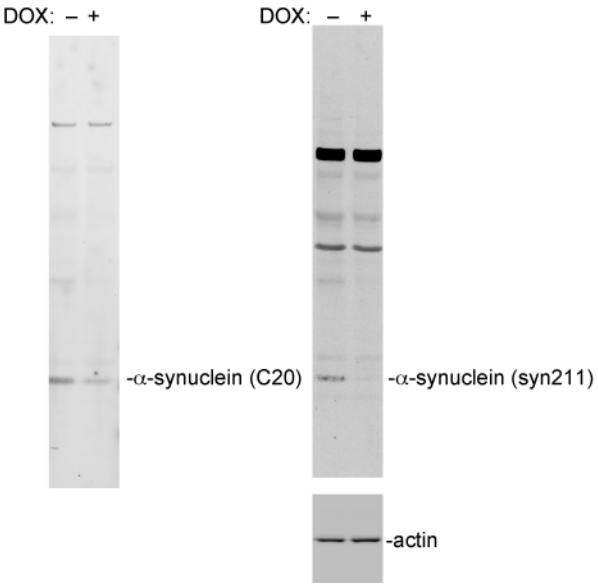

Table S1: Human brain information

Case	Diagnosis	Age	Sex	Duration	Braak	Neuropathologic Stage	Depigmentation	SNpc LB	UPDRS	Hoehn&Yahr	Source
#1	Control	81	M	0	III	No Lewy bodies	Normal	0	6.5	N/A	BSHRI
#2	Control	80	M	0	I	No Lewy bodies	Normal	0	3	N/A	BSHRI
#3	Control	86	M	0	II	No Lewy bodies	Normal	0	2	N/A	BSHRI
#4	Control	89	M	0	II	No Lewy bodies	Normal	0	7	N/A	BSHRI
#5	Control	78	M	0	N/A	No Lewy bodies	Normal	0	N/A	N/A	JHUMS
#6	Control	76	M	0	N/A	No Lewy bodies	Normal	0	N/A	N/A	JHUMS
#7	Control	86	M	0	N/A	No Lewy bodies	Normal	0	NA	N/A	JHUMS
#8	Control	87	F	0	III	No Lewy bodies	Normal	0	1	N/A	BSHRI
#9	Control	73	F	0	I	No Lewy bodies	Normal	0	N/A	N/A	BSHRI
Case	**Diagnosis**	**Age**	**Sex**	**Duration**	**Braak**	**Neuropathologic Stage**	**Depigmentation**	**SNpc LB**	**UPDRS**	**Hoehn&Yahr**	**Source**
#10	PD	90	M	15	II	Brainstem Predominant	Moderate	1	N/A	N/A	BSHRI
#11	PD	89	M	1	III	Brainstem Predominant	Mild	0	0	N/A	BSHRI
#12	PD	71	M	10	III-IV	Limbic	Moderate	N/A	N/A	5	JHUMS
#13	PD	80	F	11	III	Brainstem/Limbic	Moderate	3	N/A	N/A	BSHRI
#14	PD	78	F	16	III	Neocortical	Severe	3	N/A	N/A	BSHRI
#15	PD	79	F	20	IV	Neocortical	Severe	3	24	N/A	BSHRI
#16	PD	77	F	21	II	Brainstem Predominant	Moderate	3	N/A	N/A	BSHRI
#17	PD	73	F	7	II	Brainstem Predominant	Mild	N/A	N/A	2	JHUMS
#18	PD	85	F	13	V-VI	Neocortical	Severe	N/A	N/A	4	JHUMS
#19	PD	73	F	18	III-IV	Limbic	Severe	N/A	N/A	4	JHUMS

Duration(Yrs): Disease duration in years

UPDRS: time elapsed (months) from last UPDRS until death

Braak: Braak tangle stage score

Neuropathologic Stage: Lewy body progression through 10 brain regions

SNpc LB: the Lewy pathology density score for SNpc for that case

N/A: data not availalble

BSHRI: Banner Sun Health Research Institute

JHUMS: the Johns Hopkins University School of Medicine