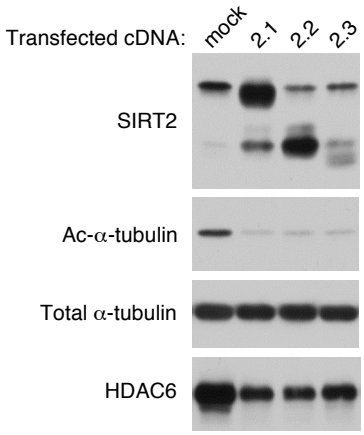
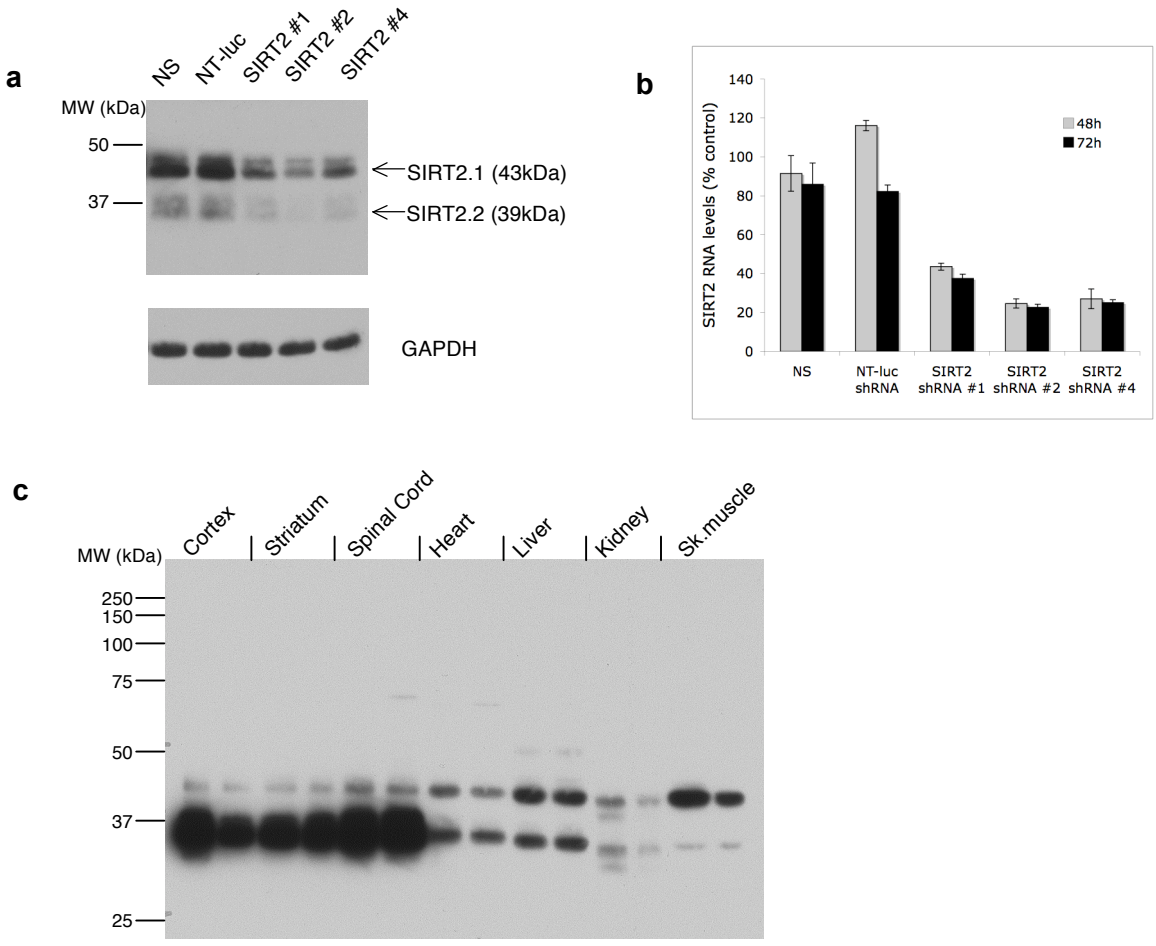
Maxwell Supplementary Fig 1



Supplementary Figure 1. Reduced tubulin acetylation in SIRT2-transfected N2a cells does not result from increased HDAC6 levels. Immunoblots show reductions in both acetylated α-tubulin and HDAC6 levels in transfected cells.

Maxwell Supplementary Fig 2



Supplementary Figure 2. Validation of SIRT2 antbodies. a. Immunoblot showing reduced SIRT2 protein levels in shRNA transfected N2a cells, harvested at 72 h. β-actin is shown to indicate sample loading. Doublet bands visible for each isoform represent phosphorlyated (upper) and unphosphorylated (lower) forms. **b.** qPCR (TaqMan) analysis shows reduced SIRT2 RNA levels in N2a cells transfected in parallel with those analyzed in (**a**), harvested at 48 and 72 h. Mouse β-actin was used as the internal control for the TaqMan assays; n = 3, error bars indicate 95% CI. Results are expressed as percent of mock-transfected control. **a, b:** NS: no shRNA; NT-luc: shRNA targeting luciferase. **c.** Uncropped version of blot shown in Fig 2A of the printed manuscript, probed with antibodies validated in **a**.

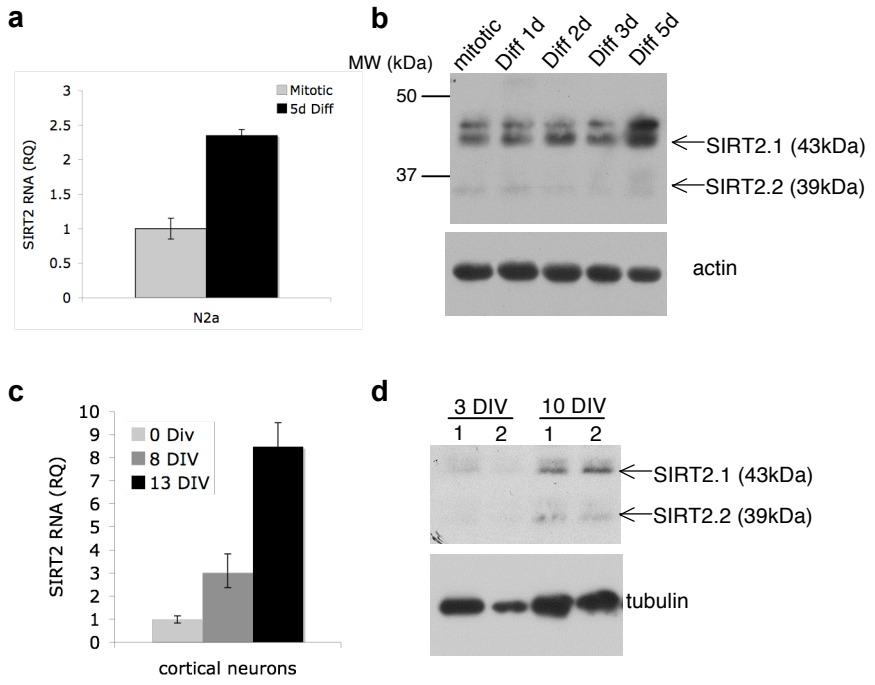
Maxwell Supplementary Table 1

Supplementary Table 1. Required case information for human brain tissues analyzed.

Sample #	Brain ID	Sex	Age	PMI	Race	NPDX
1	435	F	72	<12	W	Control
2	611	M	86	23	W	Control
3	741	M	97	7	W	Control
4	803	M	51	16	W	Control
5	911	M	60	24	W	Control

PMI: postmortem interval; NPDX: neuropathological diagnosis

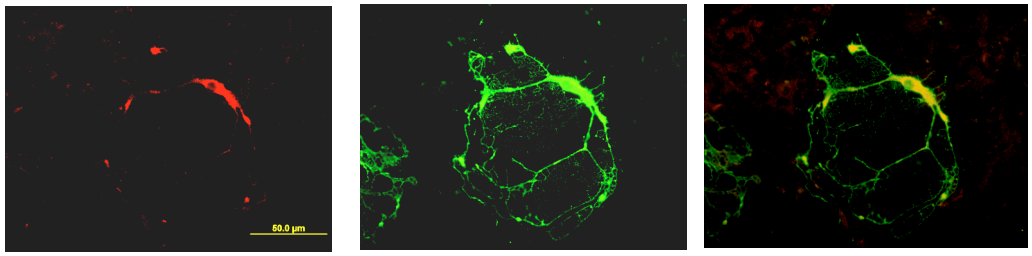
Maxwell Supplementary Fig 3



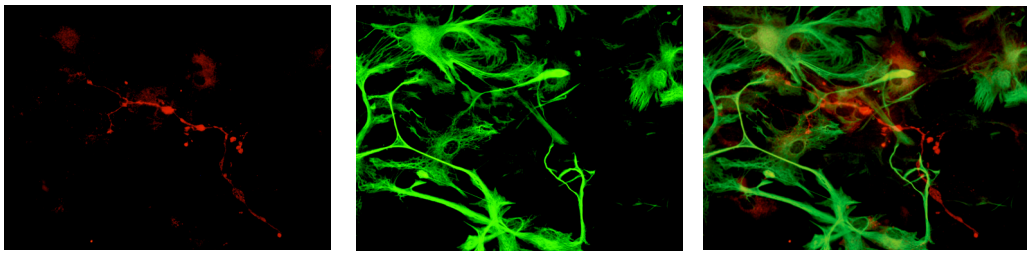
Supplementary Figure 3. SIRT2 expression is enhanced in differentiated N2a cells and is a marker of mature neurons. a. qPCR (TaqMan) analysis of SIRT2 RNA levels in N2a cells under normal growth conditions (mitotic) or after 5 days in differentiation medium. Mouse β-actin was used as the internal control for the TaqMan assays; n = 3, error bars indicate 95% CI. **b.** Immunoblot showing SIRT2 protein levels in N2a cells, harvested under normal growth conditions (mitotic) or after indicated number of days in differentiation medium. Actin is shown to indicate sample loading. Arrows indicate the two protein isoforms detected in N2a cells. Doublet bands visible for each isoform represent phosphorlyated (upper) and unphosphorylated (lower) forms. **c.** qPCR (TaqMan) analysis of SIRT2 RNA levels in cultured primary cortical neurons harvested at 0, 8, or 13 days *in vitro* (DIV). Mouse β-actin was used as the internal control for the TaqMan assays; n = 3, error bars indicate 95% CI. **d.** Immunoblot showing SIRT2 protein levels in primary cortical neurons harvested after 3 or 10 DIV. Results shown are from two independent cultures, plated in multiwell dishes and harvested at indicated timepoints.

Maxwell Supplementary Fig 4

a

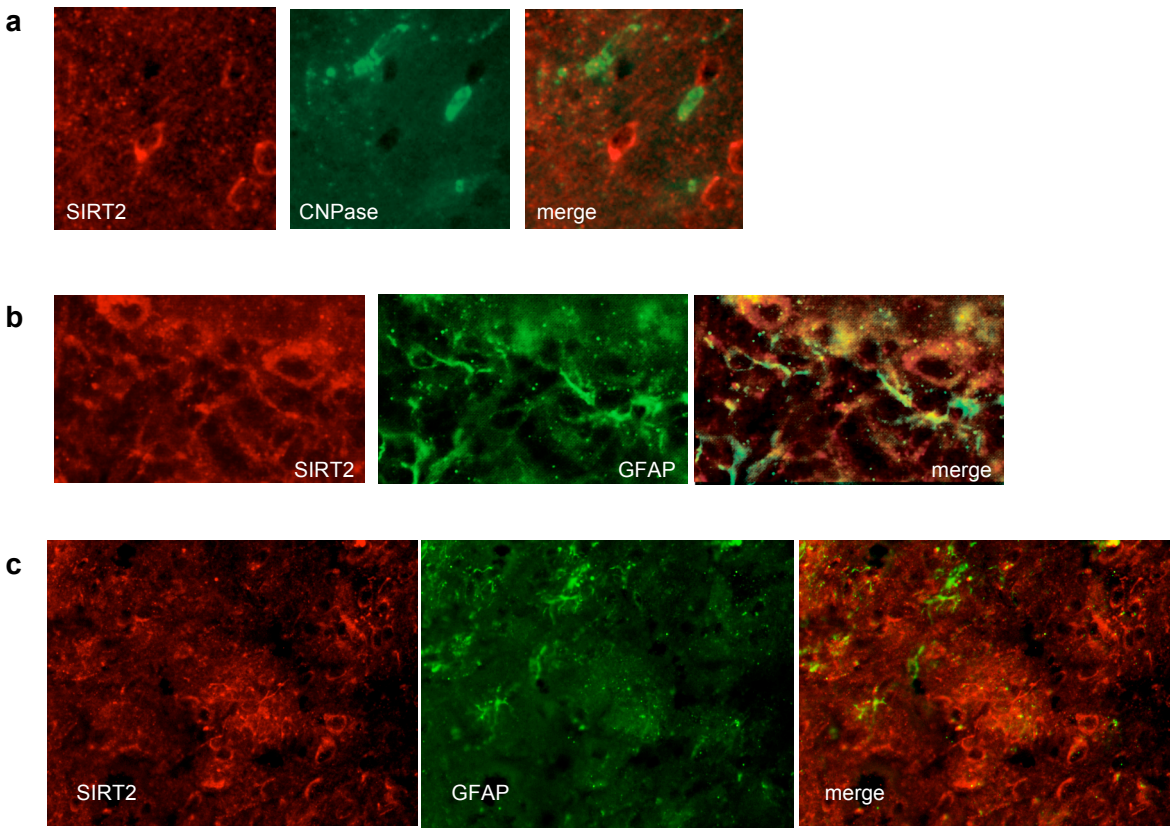


b



Supplementary Figure 4. SIRT2 expression in primary mixed cortical cultures. a. SIRT2 (red) and the oligodendroglial marker CNPase (green) staining overlap in primary mixed cortical cultures. **b.** SIRT2 (red) antibodies do not label GFAP-expressing (green) astroglial cells in primary mixed cortical cultures.

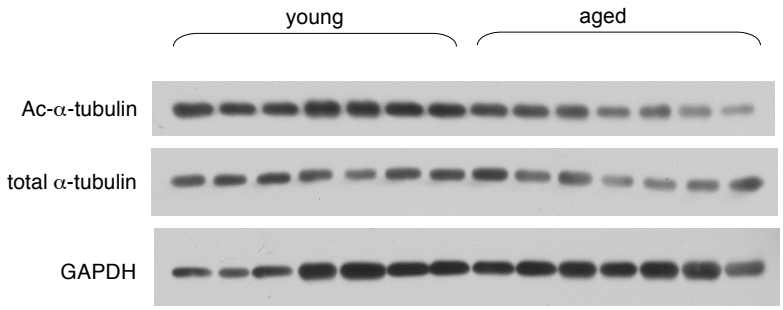
Maxwell Supplementary Fig 5



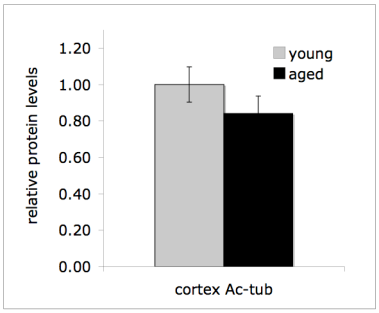
Supplementary Figure 5. SIRT2 (red) antibodies do not label CNPase- (**a**) or GFAP- (**b, c**) expressing (green) cell bodies in the adult mouse brain. **a, b.** Single color and merged images of the insets shown in Figures 3C (**a**) and 3D (**b**) of the printed manuscript. **c.** SIRT2 and GFAP antibodies stain distinct cell populations in the striatum.

Maxwell Supplementary Fig 6

a



b



Supplementary Figure 6. Acetylated α-tubulin levels show a modest decrease in cortices of aged mice. a. Representative immunoblot showing acetylated α-tubulin in cortices of young (4-5 month) and aged (18-22 month) mice. Total α-tubulin is shown for comparison; GAPDH indicates sample loading. **b**. Quantification of acetylated α-tubulin from blots as in **a** shows a trend toward decreased levels in aged animals (from 1.0 ± 0.09 to 0.84 ± 0.1) that is not statistically significant (P = 0.17). Results are shown as percentages relative to young animals. N = 10 animals per group; error bars indicate standard deviation. Two-tailed *P* values were calculated using the student's *t*-test with α = 0.05.