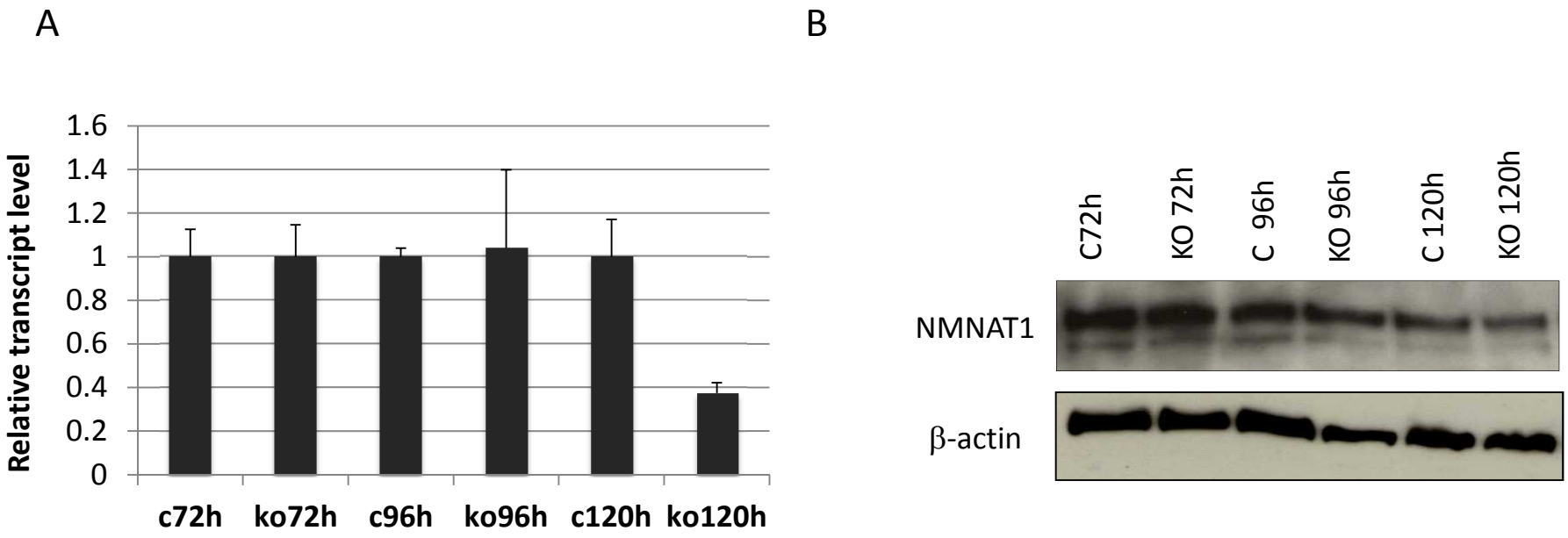


Fig.1 Nmnat1 ko in cortical cells showed a very stable protein despite a decrease in the mRNA level. Relative transcript level of NMNAT1 (A) and NMNAT1 protein level (B) upon transfection of CRE vector in cortical cells from NMNAT1 $_{flox/flox}$ mouse at different time points. This is representative of three individual experiments.

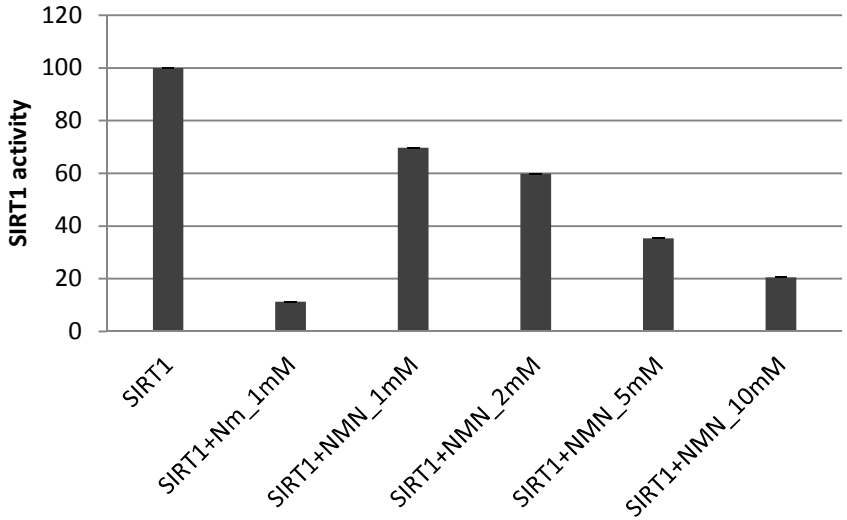


Fig.2 SIRT1 activity is inhibited by NMN. SIRT1 activity in the presence of Nm, its physiological inhibitor, and NMN at different concentrations. Error bars indicates standard deviations of three independent experiments.

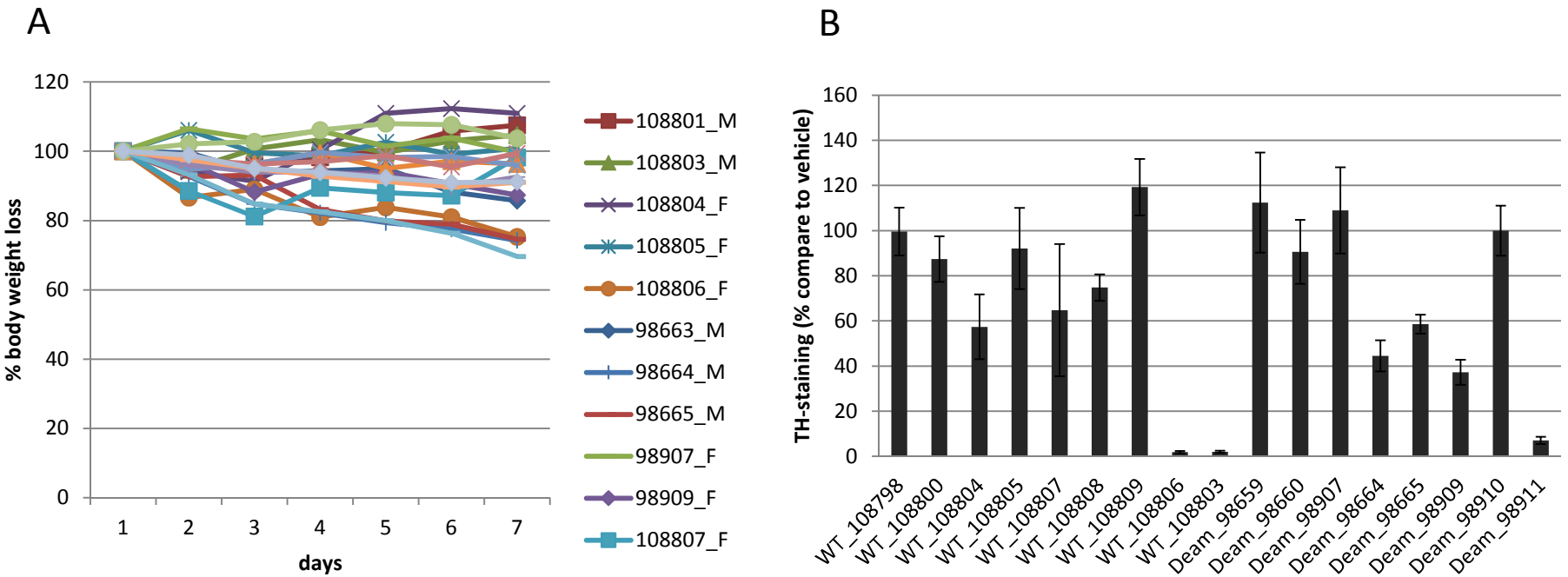


Fig. 3 Deamidase mice do not show protection from 6-HAD induced dopaminergic neurons degeneration. Mice body weight during the first week after the surgery (A). Tyrosine hydroxylase immunostaining of the striatum area. The intensity of the tyrosine hydroxylase signal of the right side of the brain where 6-HDA was injected is normalized to the one of the left side of the brain, where the vehicle was injected. Error bars represent 5 brain slides for each mouse (B).

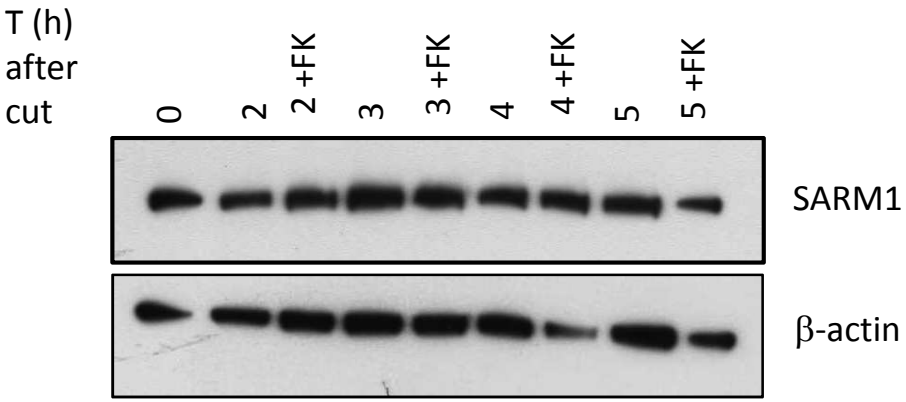


Fig.4 SARM1 is not cleaved after axon cut. SARM1 protein level in axons upon cut at different time points with and without the addition of the drug FK866, which protects the axon after cut.

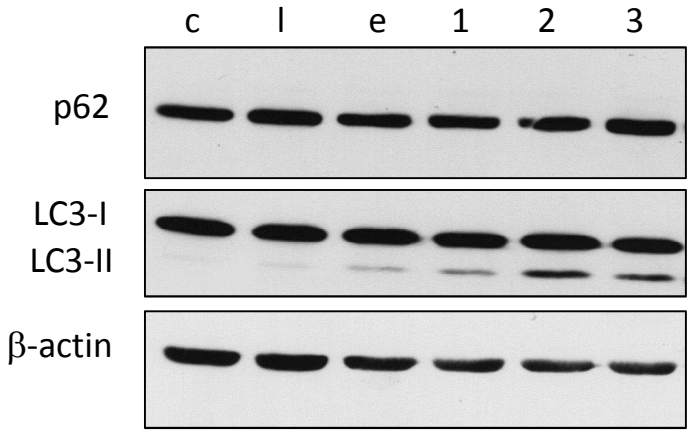


Fig.5 NMNAT2 and, to some degree, NMNAT3 induce autophagy. p62 and LC3, two markers of the autophagic flux, were detected in Neuro2a cells transfected for 48hours. C:cells; l:lipofectamine only; e:empty vector; 1:NMNAT1-flag; 2:NMNAT2-flag; 3:NMNAT3-flag

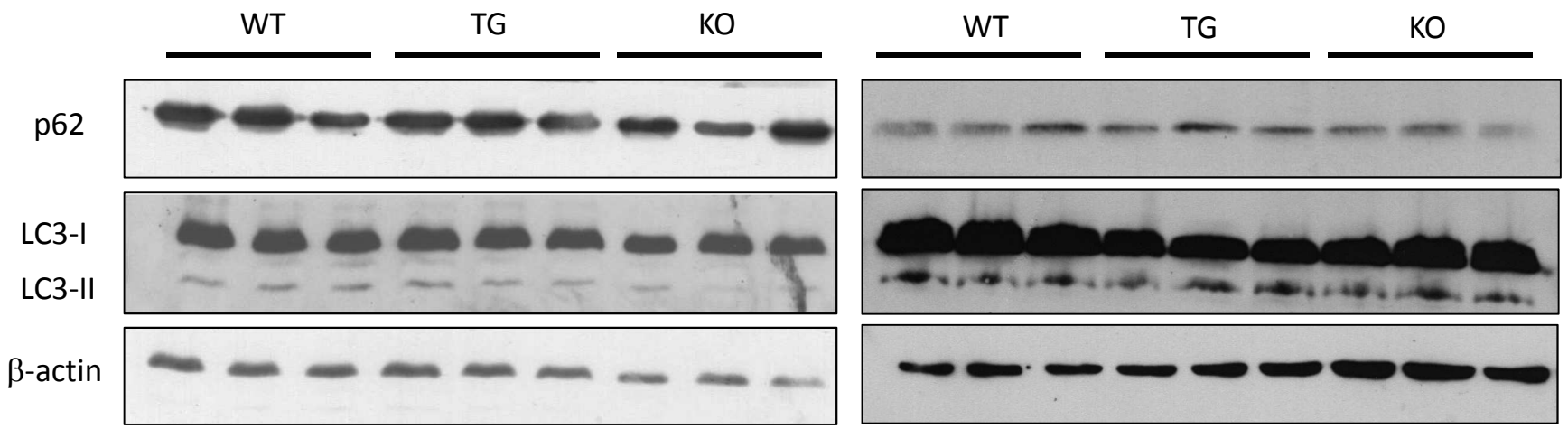
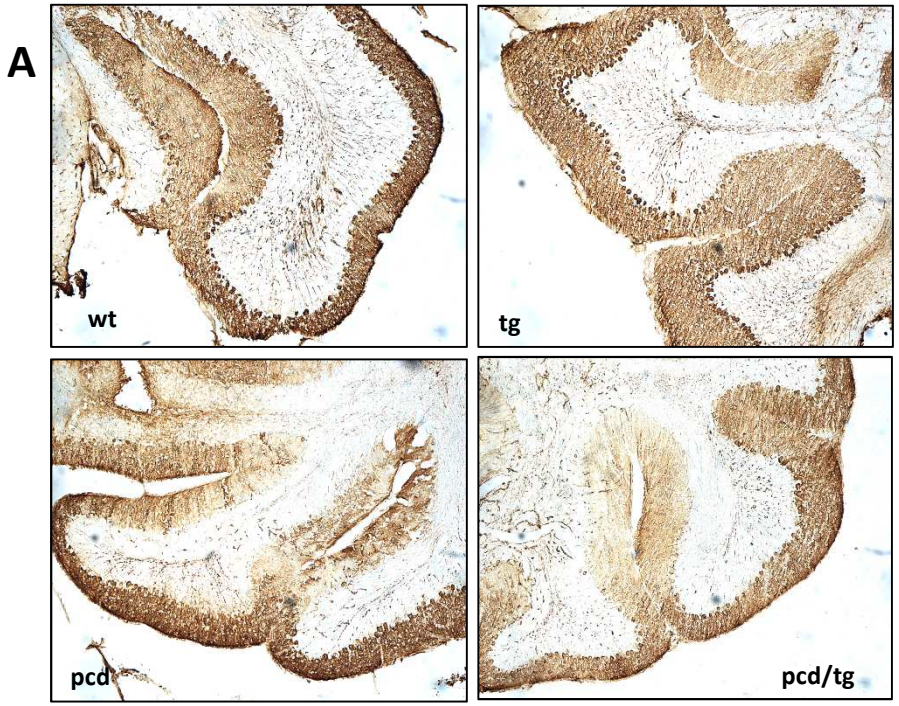
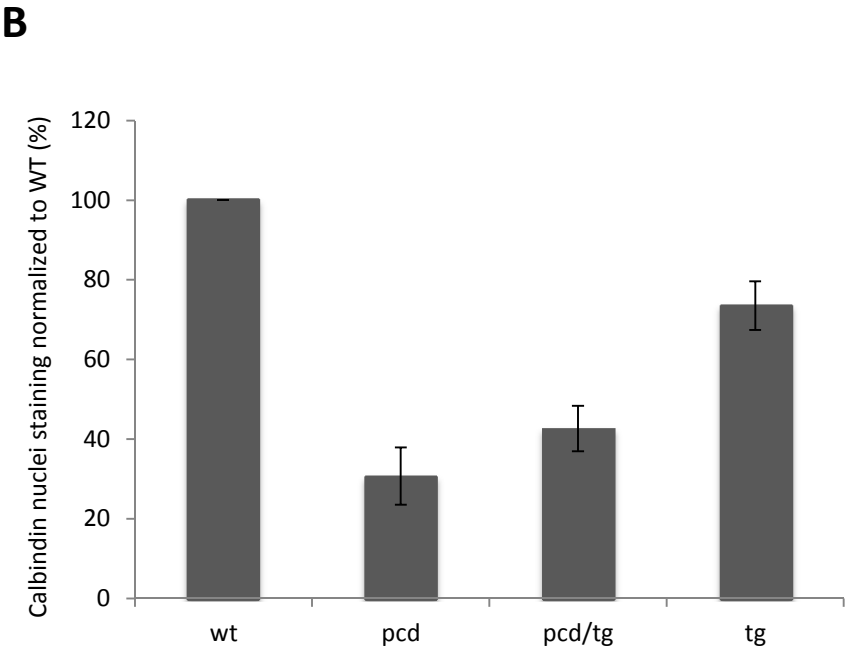


Fig.6 In brain and muscle the overexpression of NMNAT1 does not modulate autophagy. p62 and LC3, autophagic markers, were detected in the homogenate of grastocnemius (left panel) and brain (right panel). WT: wild type; TG: nmnat1tg (overexpressing nmnat1); KO: heterozygotes knock-out for nmnat1.





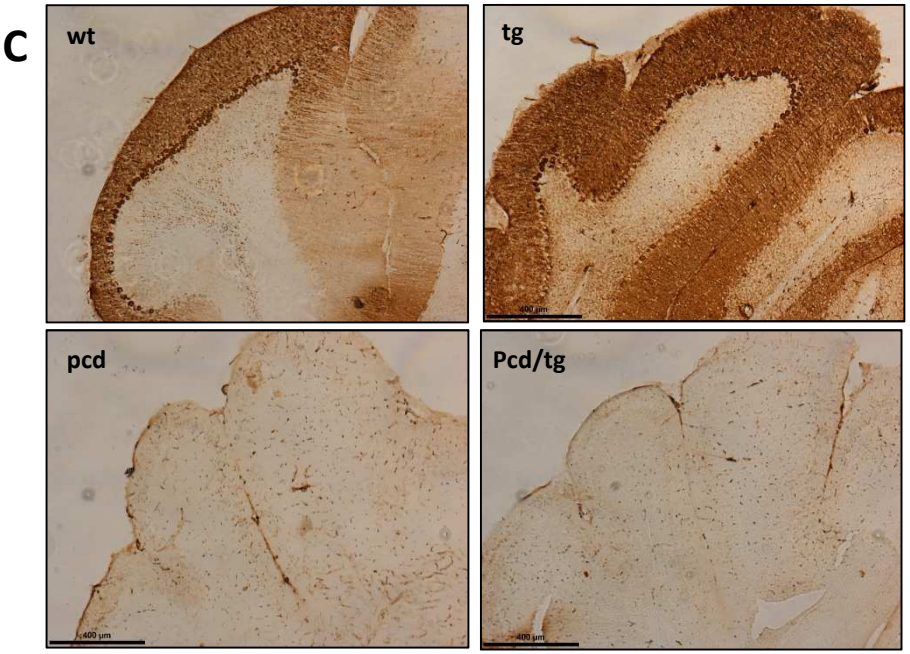


Fig.7 The overexpression of NMNAT1 in vivo delayed purkinje cells degeneration in the pcd5j background early after birth. Representative slides of cerebellum stained for calbindin, from the 4 different genotypes at 20 days (A) and 60 days (C). At 60 days the purkinje cells degeneration is profound and no difference was observed between the pcd and the pcd/tg. B: count of calbindin positive cells in both sides of the brain from all the cerebellum loops. Standard deviation refers to 4 slides for each genotype.