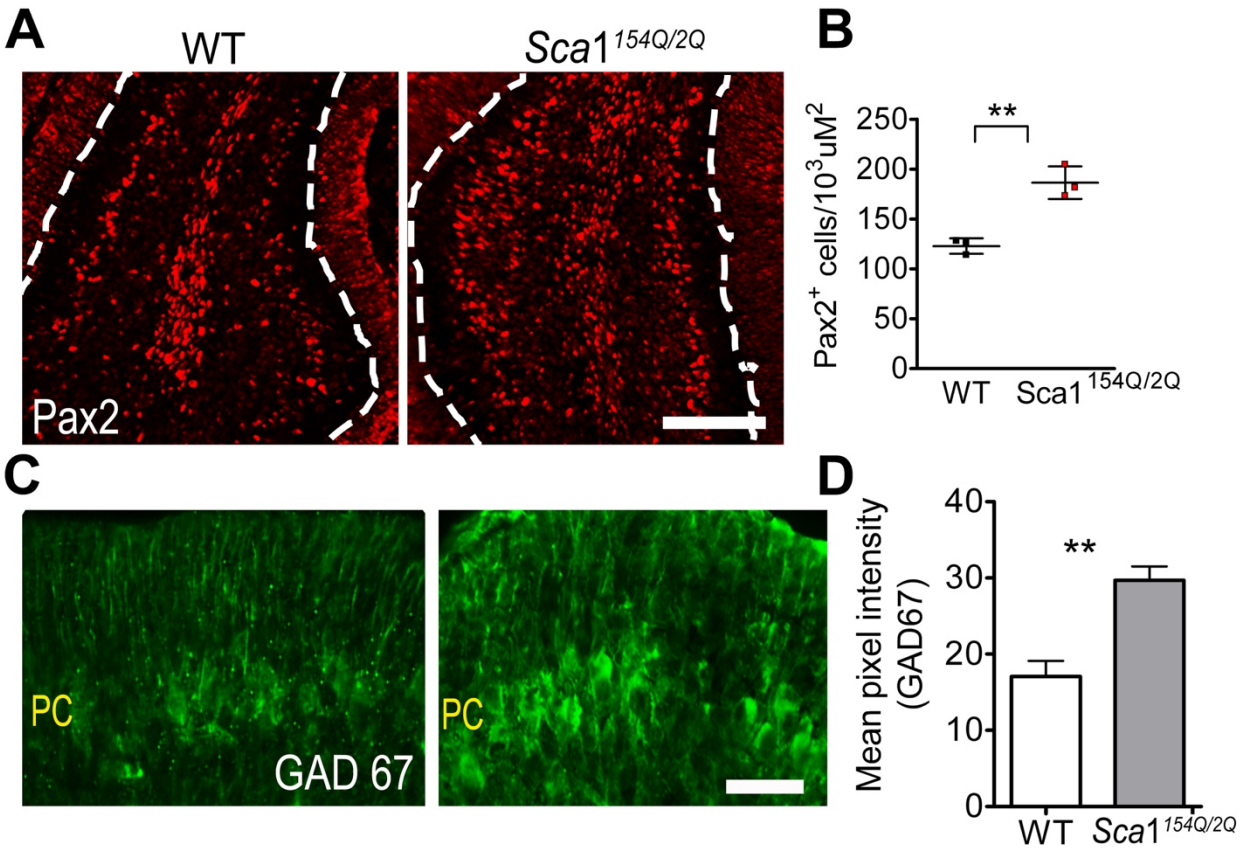
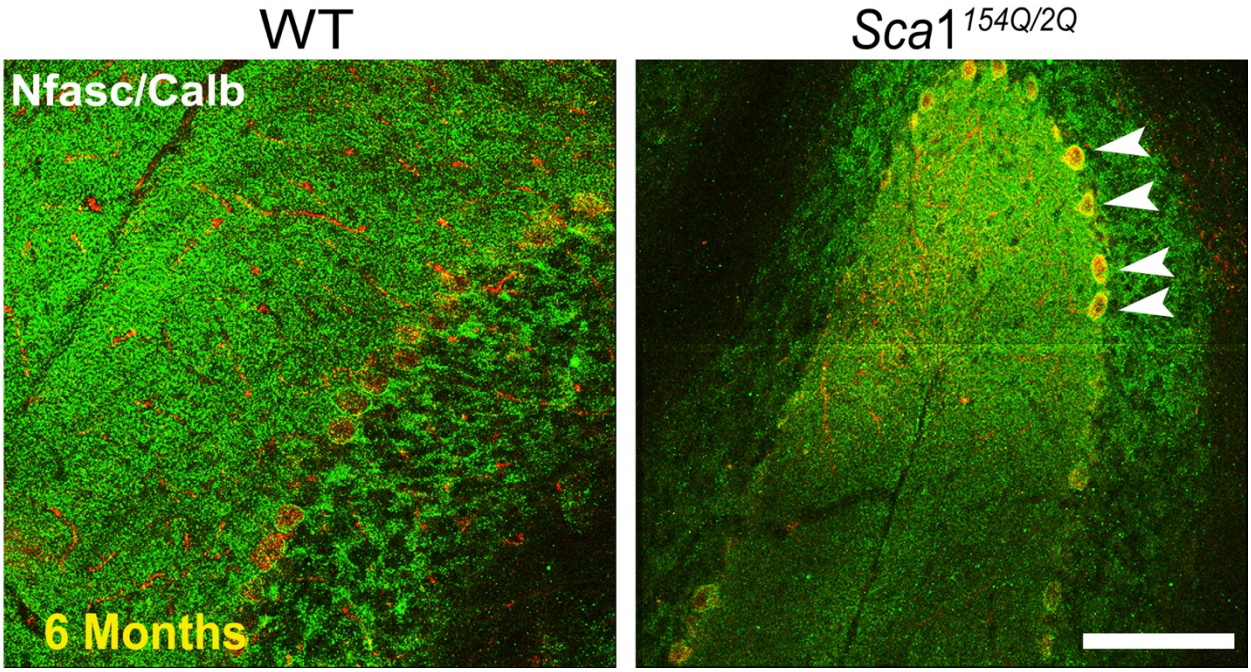
## SUPPLEMENTARY FIGURES AND LEGNEDS

### Supplementary Figure 1



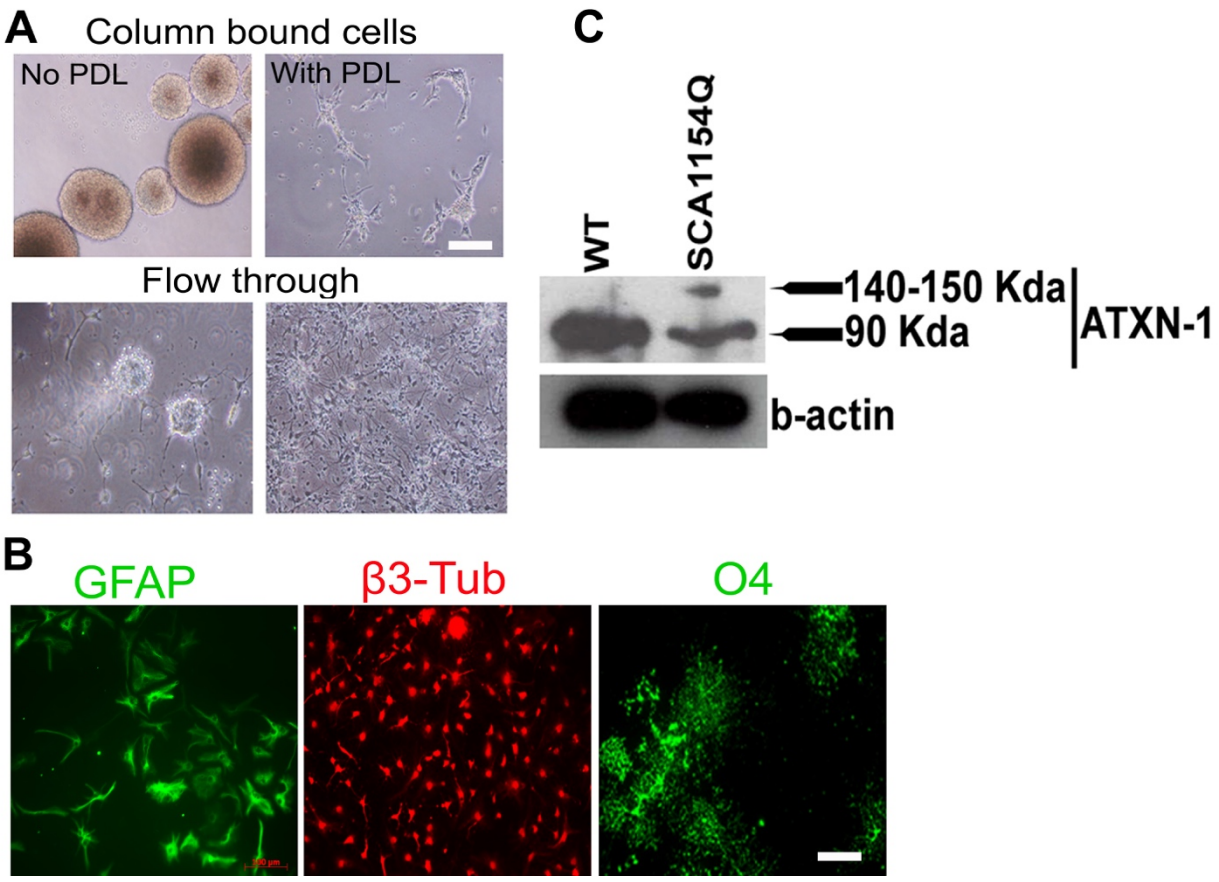

**Supplementary Figure 1. SCA1 mice have more GABAergic progenitors than wild-type mice.** (**A** and **B**) Increased Pax2 and (**C** and **D**) GAD67 staining in SCA1 mice compared to wild type littermates (P7). The area we counted for Pax2 cells is indicated by the dashed white line. Scale bar: 100μm; n=3 pairs of mice. **P < 0.01, Two-tailed unpaired student t-test.

## Supplementary Figure 2



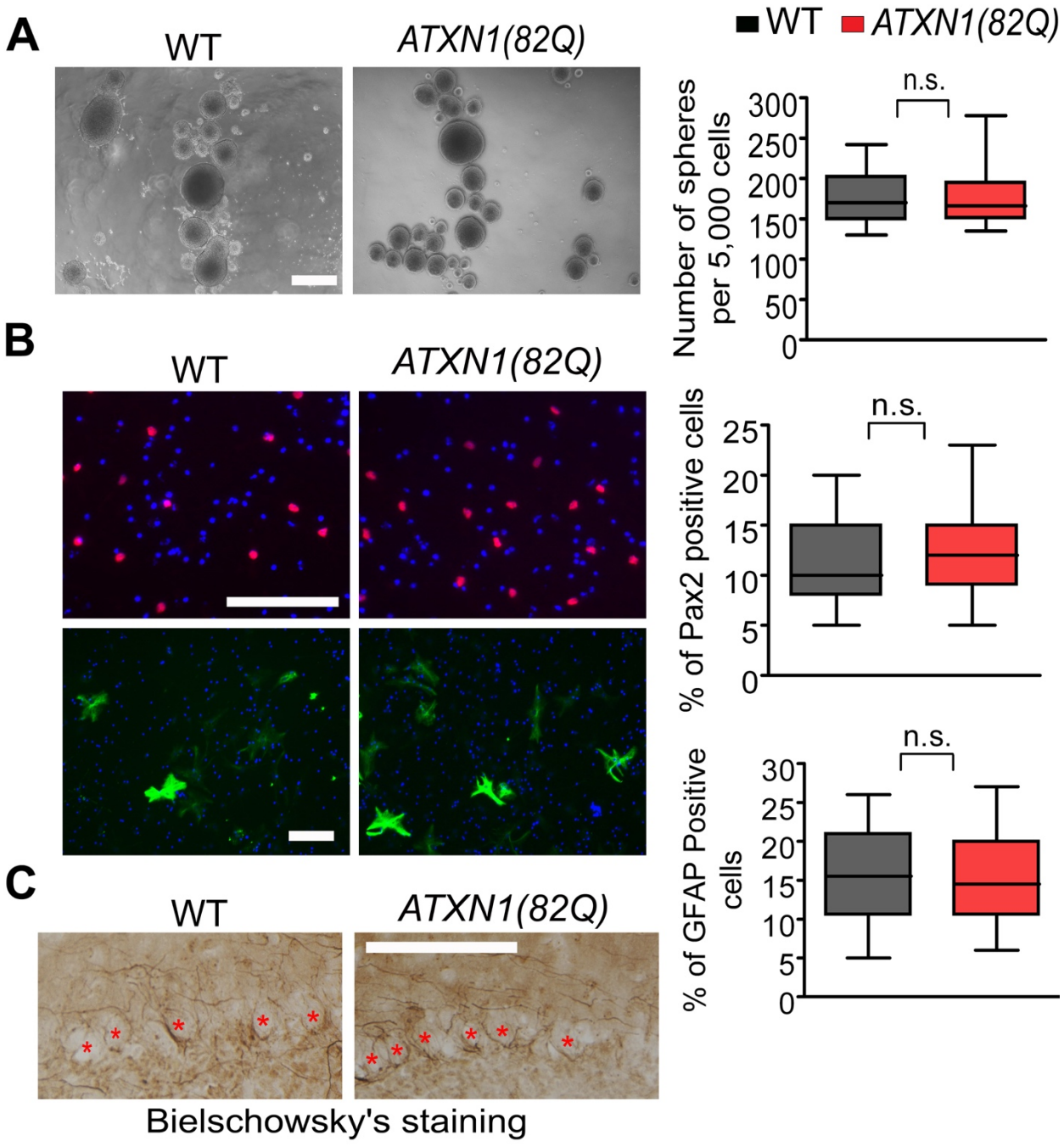

**Supplementary Figure 2. Upregulation of Nfasc in 6-month-old SCA1 mice.** Immunostaining of 6-month-old cerebella with Nfasc (green) and calbindin (red) showed an upregulation of Nfasc in SCA1 mice (visualized as yellow circumferential staining around PCs (arrowhead). 100μm; n=3 pairs of mice.

## Supplementary Figure 3




**Supplementary Figure 3. Cerebellar stem cell isolation, neurosphere formation and differentiation.** (**A**) *Top panel:* Stem cells separated using Prominin-1 antibodies linked to magnetic beads form floating neurospheres. Neurospheres form in the absence of Poly-D-lysine (PDL) (since with PDL they attach and differentiate). *Bottom:* Cells that are unbound to the column (flow through), which are primarily granular neurons, are unable to form neurospheres. (**B**) Differentiated cultures derived from neurospheres were stained with glial (GFAP), neuronal (Beta 3 tubulin) and oligodendrocyte (O4) markers. Four independent experiments were performed. (**C**) Western blot from wil- type and SCA1 neurosphere protein extracts showing the expression of wild-type and mutant ATXN1. See complete unedited blots in the supplemental material. Scale bar: 100μm.

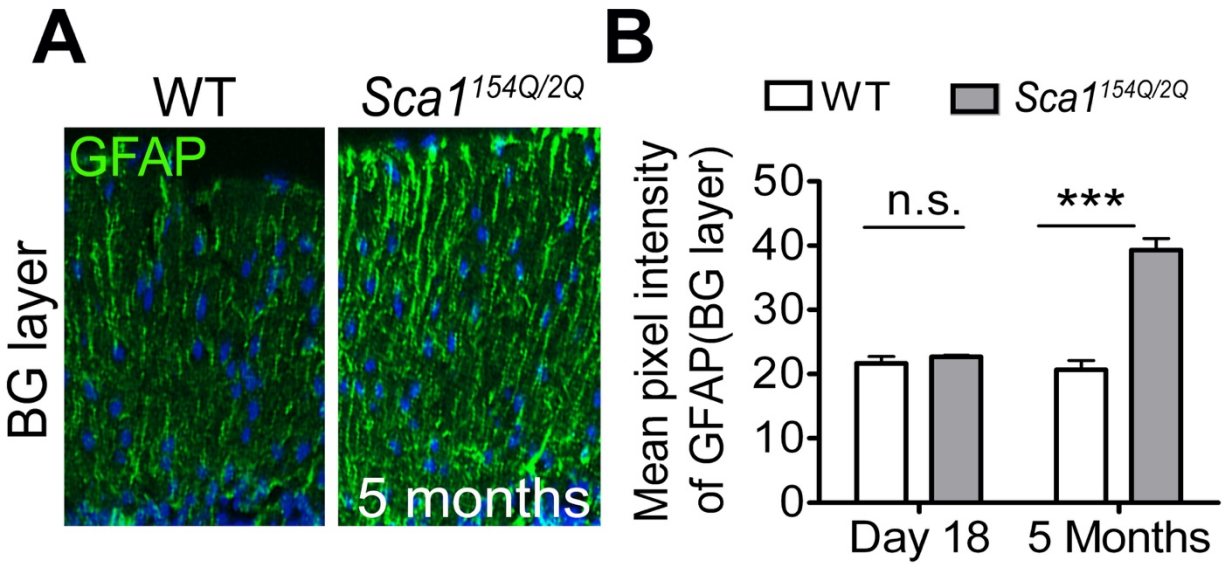
## Supplementary Figure 4




**Supplementary Figure 4. SCA1 transgenic mice (Purkinje cell-specific expression of ataxin-1) mice show no cerebellar/basket cell phenotype.** (**A**) Neurospheres derived from isolated prominin-1 stem cells of *ATXN1(82Q)* mice showed similar proliferative capacity as wild-type

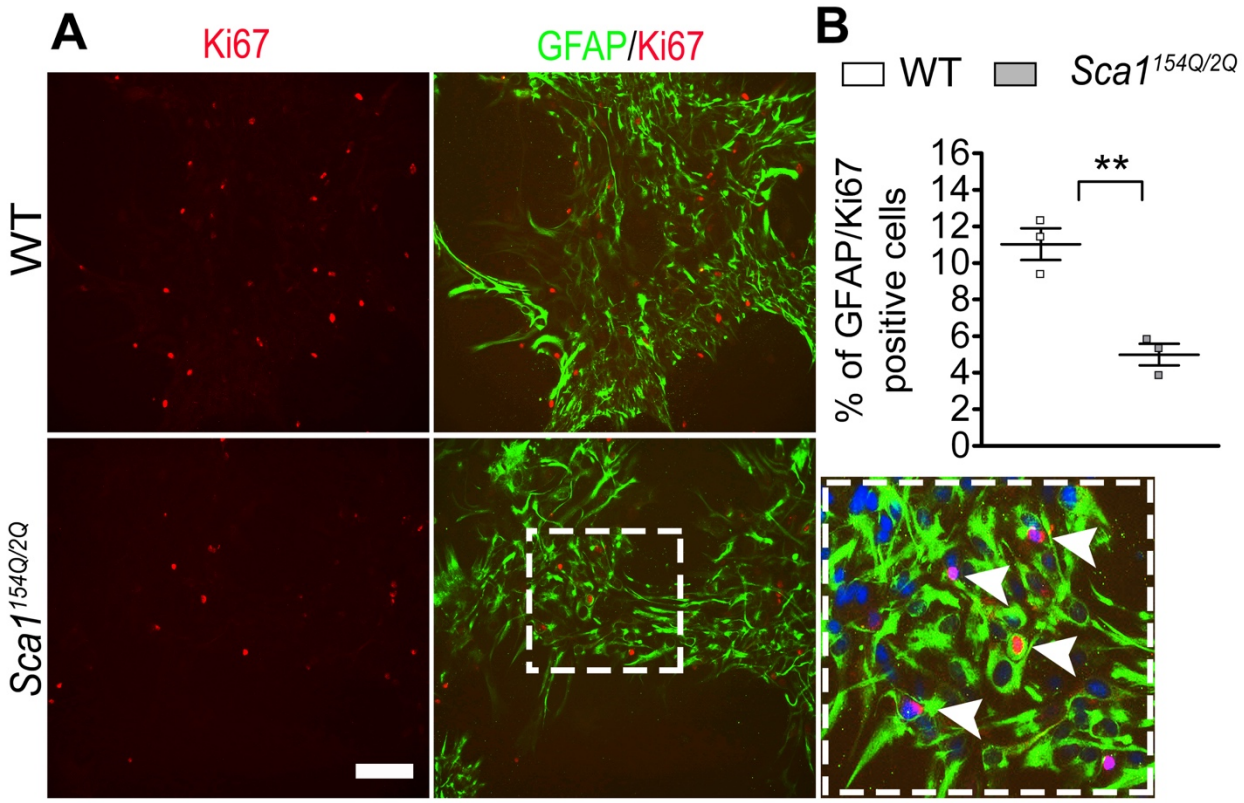
stem cells. Scale bar: 100μm; n=3 pairs of mice. (**B**) Differentiated cerebellar stem cells stained for GABAergic (Pax2; scale bar 50μm) and glial markers (GFAP; scale bar 100μm). Both *ATXN1(82Q)* stem cells and wild-type stem cells yielded the same number of Pax2- and GFAP-positive cells. Scale bar 50μm; n=3 pairs of mice. (**C**) Representative images of Bielschowsky's silver stained cerebella from SCA1 and wild-type mice. *ATXN1(82Q)* and wild-type cerebellum showed normal densities of basket cell axonal processes around PC soma (Asterisk represent PC soma). n.s.= no significance; two-tailed unpaired student t-test.

## Supplementary Figure 5



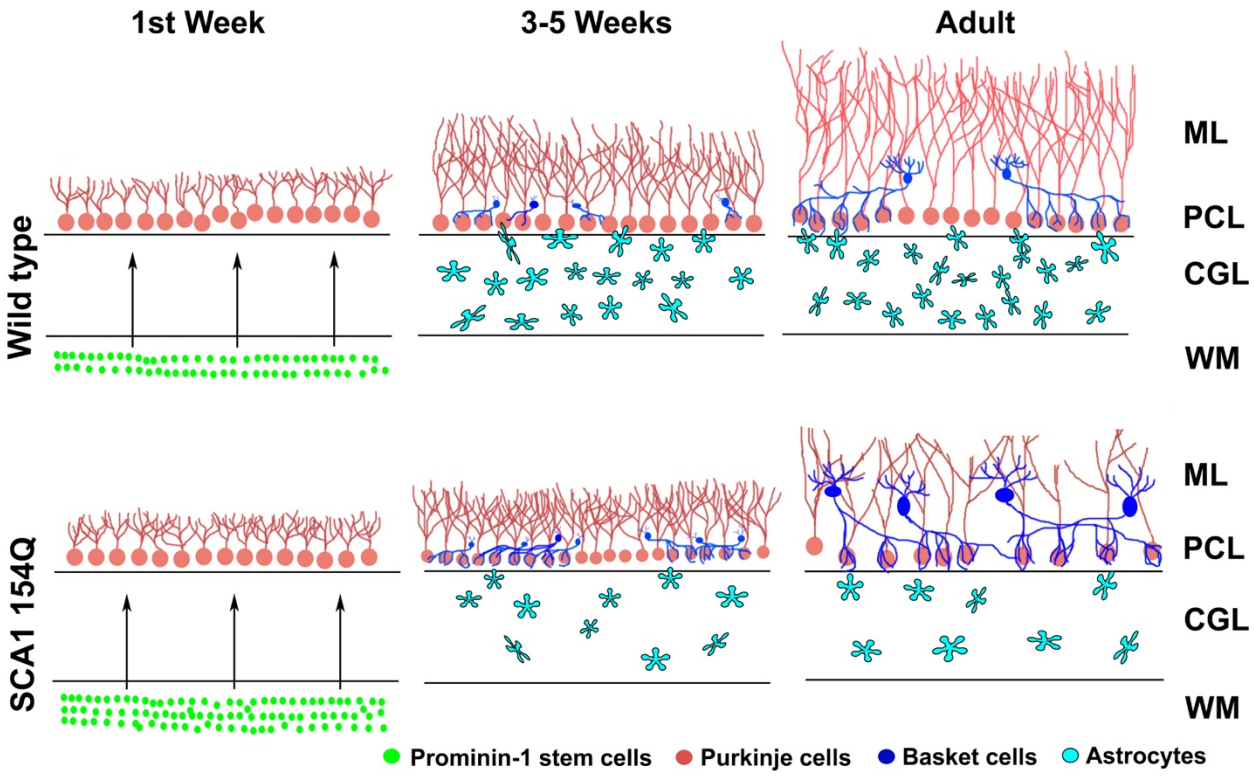

**Supplementary Figure 5. SCA1 mice show reactive Bergmann glia**. (**A** and **B**) GFAP staining of Bergmann glia in the molecular layer revealed an age-dependent increase of the staining intensity in SCA1 mice as compared to wild-type controls; n=3 pairs of mice. ***P < 0.001, n.s.= no significance; two-tailed unpaired student t-test.

## Supplementary Figure 6




**Supplementary Figure 6. Reduced proliferation of isolated astrocytes from *Sca1*$^{154Q/2Q}$ mice cerebella**. (**A** and **B**) Astrocytes isolated from SCA1 cerebella (P4) co-stained with proliferative marker Ki67 (red) and GFAP (green) showed lower proliferative capacity than wild-type controls. n=3 independent experiments. **P < 0.01; two-tailed unpaired student t-test.

## Supplementary Figure 7



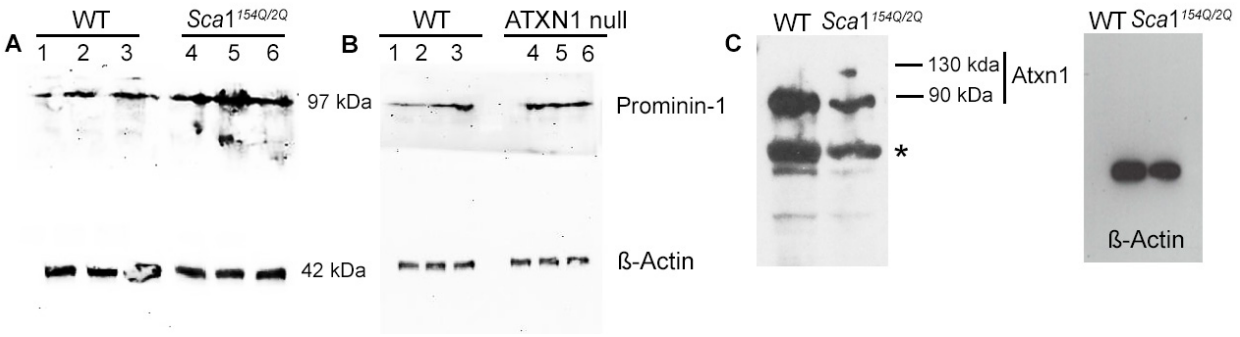

**Supplementary Figure 7. Postnatal dysregulation of cerebellar stem cells in *Sca1*$^{154Q/2Q}$.** During the first week of life, there was abnormally high proliferation of prominin-1 cerebellar stem cells (green) in SCA1 mice. These mutant stem cells migrate into the molecular layer. By 3-5 weeks, this larger-than-normal population of stem cells preferentially differentiated into GABAergic interneurons (blue) rather than the velate astrocyte lineage (green). This phenotype persisted into adulthood (6 months). (ML: molecular layer, PCL: Purkinje cell layer, CGL: Cerebellar granular layer, WM: White matter).

## Supplementary Table 1

| Age of Onset | Age at Death | CAG Repeats |
|---|---|---|
| Early-onset patients | | |
| 30 | 47 | 28/47 (M) |
| 20-22 | 54 | 35/50 (M) |
| 27 | 48 | 31/51 (M) |
| 26 | 36 | 34/49 (F) |
| 28 | 47 | 32/50 (F) |
| 33 | 63 | 33/41 (F) |
| Late-onset patients | | |
| 50 | 64 | 30/44 (M) |
| 50 | 61 | 34/46 (M) |
| 52 | 65 | 31/42 (M) |
| 41 | 73 | 33/41 (F) |
| 45 | 66 | 31/46 (F) |
| 55 | 80 | 29/38 (F) |

**Supplementary Table 1:** The age of onset, age at death, and the CAG repeat length for the 12 SCA1 patients used in this study.

# Supplementary Figure 8




**Supplementary Figure 8:** Full length Western blot images

(**A**) Full length western blot image of Figure 1C (**B**) Full length western blot image of Figure 1G.

(**C**) Full length western blot image of supplementary figure 3C (Asterisk, nonspecific band).