

**Supplementary Table 1: Characteristics of transgenic mice used in this study.**

**Supplementary Table 2: Demographic information for postmortem human samples of cerebellar cortex used in this study.**

**Supplementary Table 3: Liver profile of Q84/Q84 transgenic mice and littermate controls used in the MRS study.**

**Supplementary Figure 1: Cerebellar neurochemical levels are altered in homozygous Q84/Q84 mice. A)** Neurochemical profiles of female Q84/Q84 mice (N=5, black bars) and wt littermates (N=7, white bars). **B)** Neurochemical profiles of male Q84/Q84 mice (N=7, black bars) and wt littermates (N=4, white bars). Bars represent average neurochemical concentration  $\pm$  SEM. Comparison between mouse genotypes was performed using Student's t-test and statistical significance is indicated as: \* $P$ <0.05, \*\* $P$ <0.01, and \*\*\* $P$ <0.001.

**Supplementary Figure 2: Cerebellar neurochemical levels are altered in hemizygous Q135 mice. A)** Neurochemical profiles of female Q135 mice (N=3, black bars) and wt littermates (N=5, white bars). **B)** Neurochemical profiles of male Q135 mice (N=4, black bars) and wt littermates (N=2, white bars). Bars represent average neurochemical concentration  $\pm$  SEM. Comparison between mouse genotypes was performed using Student's t-test and statistical significance is indicated as: \* $P$ <0.05, \*\* $P$ <0.01, and \*\*\* $P$ <0.001.

**Supplementary Figure 3: myo-Ins, tCho, and tNAA are commonly decreased in Q84/Q84 and Q135 mice compared to controls.** Boxplot graphs representing the distribution of cerebellar levels of myo-Ins, t-Cho, and tNAA in Q84/Q84 (N=12, dark grey boxes), Q135 (N=7,

light grey boxes) and respective wt littermates (N=11; N=7, white boxes). Median for each group is represented as a black horizontal line inside the box, outliers are shown as circles and extreme outliers are displayed as asterisks. Comparison between mouse genotypes was performed using Student's t-test and statistical significance is indicated by the specific *P* value.

**Supplementary Figure 4: End-stage Q84/Q84 and aged Q135 mice show thinning of the molecular layer thickness with no signs of Purkinje cell loss. A)** Graphs showing the average of four molecular layer thickness measurements ( $\pm$ SEM) in the primary fissure of the SCA3 transgenic mice and respective controls (N=4 animals per group). **B)** Counts of Purkinje cells per area of the depth of the primary fissure folium (N=4 mice per group). Comparison between mouse genotypes was performed using Student's t-test and statistical significance is indicated as: \**P*<0.05.

**Supplementary Figure 5: Correlation of neurochemical concentrations with levels of MBP and NFL in Q84/Q84 and Q135 mouse cerebella.** Plots showing Pearson correlations of levels of MBP with myo-Ins (**A,C**), NFL with tNAA (**B**), and MBP with tCho (**D**) in Q84/Q84 (black circles), Q135 (grey circles), and their respective wt littermate mice (white circles).