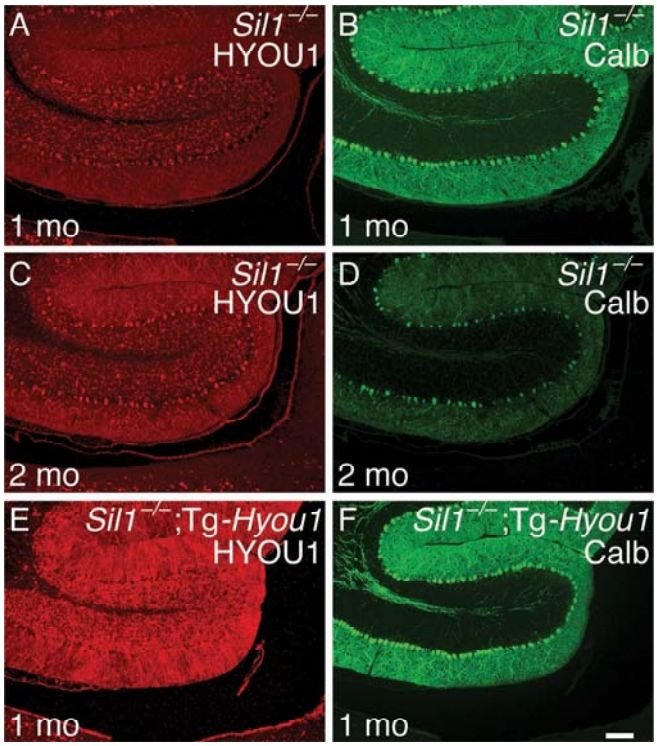
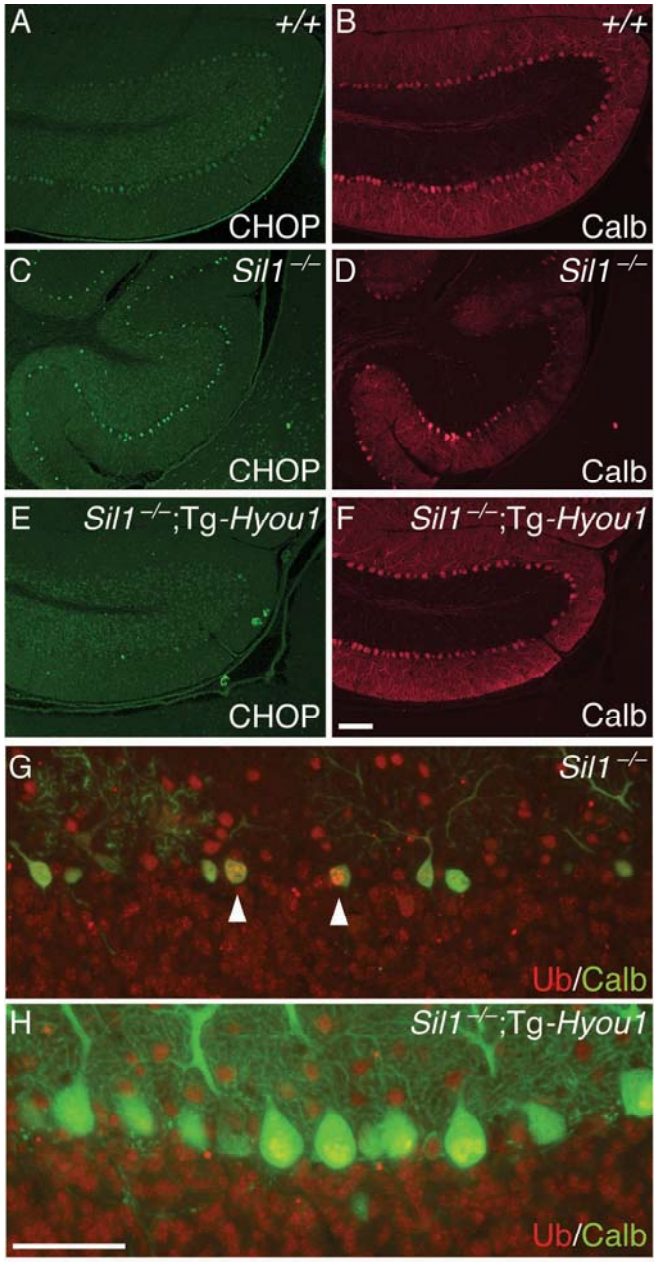
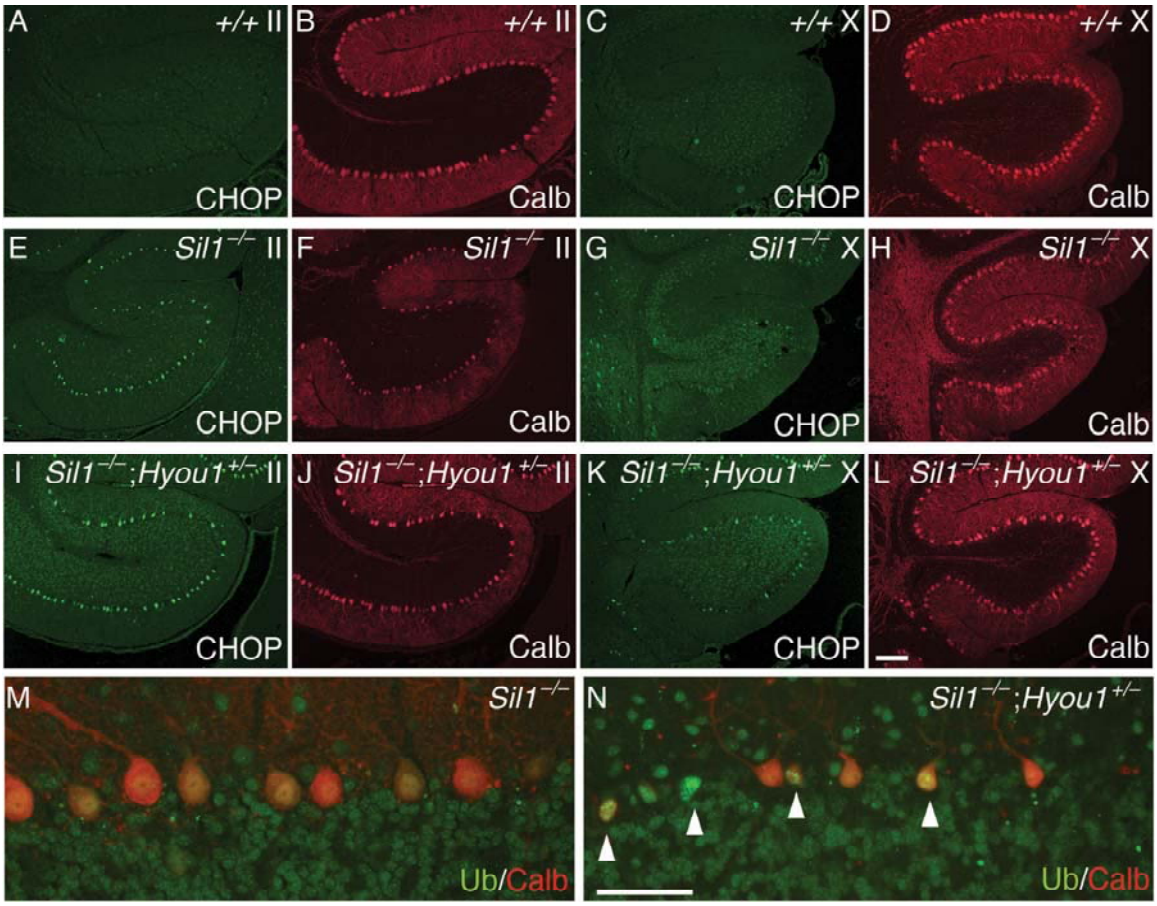
Supplementary data



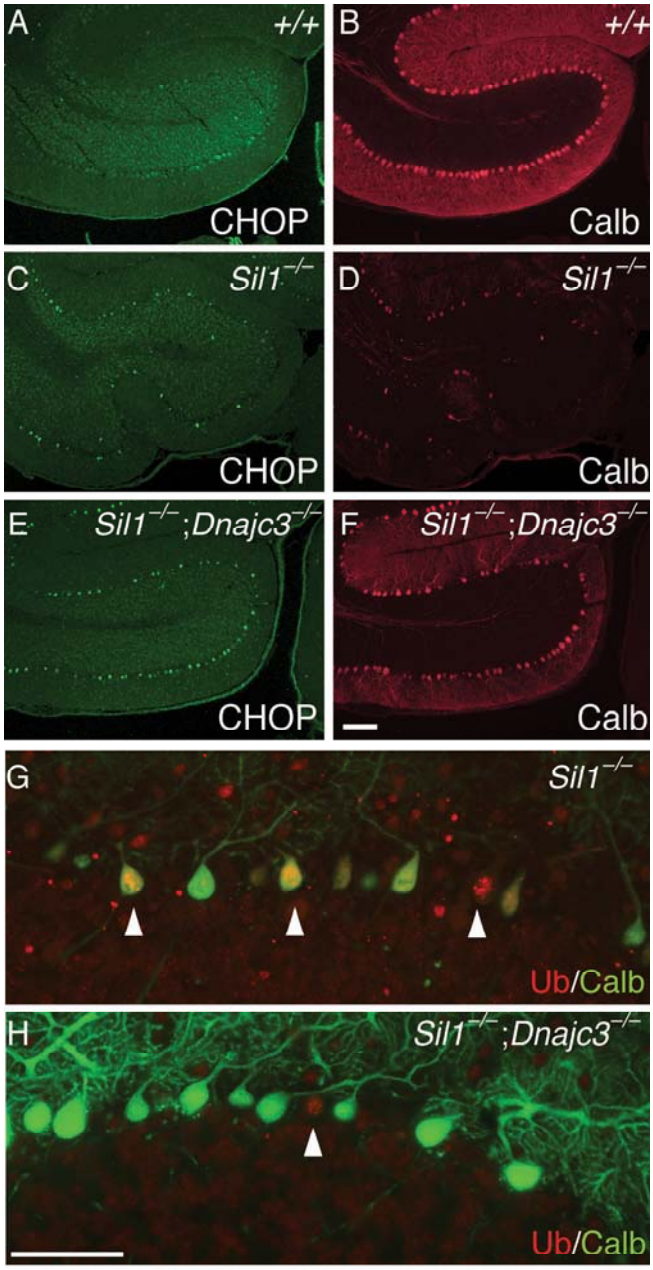
Supplementary figure 1. A *Hyou1* transgene confers constitutively elevated cerebellar expression. Cerebellar sections from 1-month-old (A, B), 2-month-old (C, D) *Sil1*$^{-/-}$ and 1-month-old *Sil1*$^{-/-}$; Tg-*Hyou1* (E, F) mice were immunostained with antibodies to HYOU1 (A, C, E) and calbindin-D28 (Calb; B, D, F). Images of lobule II are shown. Camera exposure times are equal for images of the same channel. Scale bar=100 µm.



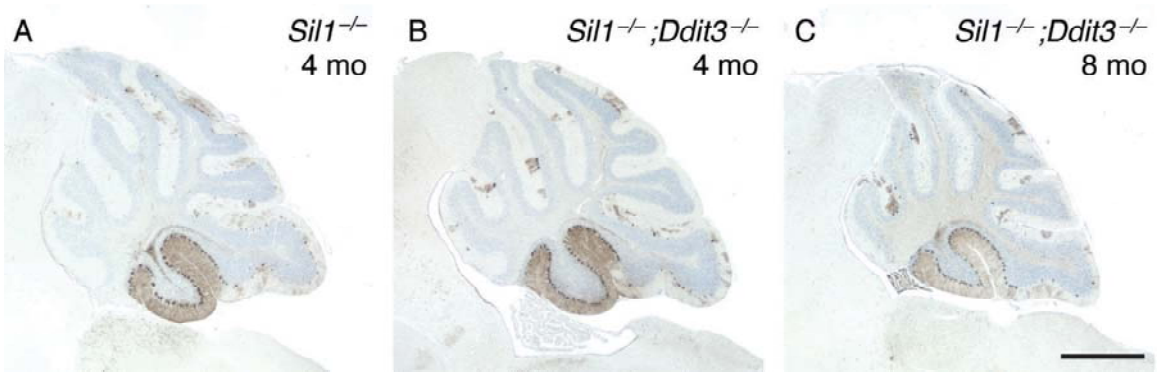
Supplementary figure 2. Cerebellar overexpression of HYOU1 in cerebella prevents ER stress caused by loss of SIL1 function. A-F. Activation of CHOP is suppressed by expression of *Hyou1* transgene in the *Sil1*$^{-/-}$ cerebellum. Cerebellar sections from 2-month-old wild type (A, B), *Sil1*$^{-/-}$ (C, D), and *Sil1*$^{-/-}$; Tg-*ORP150* (E, F) mice were incubated with antibodies against CHOP (A, C, E) and calbindin-D28 (B, D, F), respectively. Images of lobule II are shown. Camera exposure times are equal for images of the same channel. Scale bar: 100 µm. **G-H.** Overexpression of HYOU1 suppresses formation of protein inclusions caused by *Sil1* deficiency. Cerebellar sections from 3-month-old *Sil1*$^{-/-}$ (G) and *Sil1*$^{-/-}$; Tg-*Hyou1* (H) mice were immunostained with antibodies against ubiquitin (Ub; red) and calbindin-D28 (Calb; green). Merged images are shown. Note the ubiquitin-positive protein inclusions (G; arrowheads) in *Sil1*$^{-/-}$ Purkinje cells. Inclusions were not observed in *Sil1*$^{-/-}$; Tg-*Hyou1* neurons (H). Scale bar: 50 µm.



Supplementary figure 3. Reduced *Hyou1* expression aggravates ER stress caused by loss of SIL1 function. **A-L.** CHOP upregulation in lobule II or lobule X of 2-month-old wild type (+/+; A-D), 2-month-old *Sil1*$^{-/-}$ (E-H), and 1-month-old (I-L) *Sil1*$^{-/-}$; *Hyou1*$^{+/-}$ cerebella. Sections were immunostained with antibodies against BiP and calbindin-D28 (Calb). Camera exposure times are equal for images of the same channel. Scale bar: 100 µm. **M-N.** Reduced *Hyou1* expression accelerates formation of protein inclusions caused by *Sil1* deficiency. Cerebellar sections from 2-month-old *Sil1*$^{-/-}$ (M) and *Sil1*$^{-/-}$; *Hyou1*$^{+/-}$ (N) mice were immunostained with antibodies to ubiquitin (Ub; green) and calbindin-D28 (Calb; red). Merged images are shown. Note the presence of ubiquitin-positive protein inclusions (N; arrowheads) in *Sil1*$^{-/-}$; *Hyou1*$^{+/-}$ Purkinje cells at this age. Inclusions were not observed in Purkinje cells of age-matched *Sil1*$^{-/-}$ mice (M). Scale bar: 50 µm.



Supplementary figure 4. Depletion of DNAJC3 activity does not suppress CHOP upregulation caused by *Sil1* deficiency. A-F. Expression of CHOP in cerebellar Purkinje cells of 3-month-old wild type (A, B), *Sil1*$^{-/-}$ (C, D) and *Sil1*$^{-/-}$; *Dnajc3*$^{-/-}$ (E, F) mice. Sections were stained with antibodies against CHOP (A, C, E) and calbindin-D28 (Calb; B, D, F). Images of lobule II are shown. Scale bar: 100 µm. **G-H.** Loss of DNAJC3 function suppresses formation of protein inclusions caused by *Sil1*-deficiency. Cerebellar sections from 3-month-old *Sil1*$^{-/-}$ (G) and *Sil1*$^{-/-}$; *Dnajc3*$^{-/-}$ (H) mice were immunostained with antibodies to ubiquitin (Ub; red) and calbindin-D28 (Calb; green). Merged images are shown. Note the presence of ubiquitin-positive protein inclusions in (G; arrowheads) *Sil1*$^{-/-}$ Purkinje cells. Fewer inclusions (H; arrowhead) are observed in *Sil1*$^{-/-}$; *Dnajc3*$^{-/-}$ Purkinje cells. Scale bar: 50 µm.



Supplementary figure 5. Deletion of *Chop* does not alter Purkinje cell degeneration caused by ER stress. Cerebella from 4-month-old *Sil1*$^{-/-}$ (A) and 4- or 8-month old *Sil1*$^{-/-}$ *Dnajc3*$^{-/-}$ (C, D) mice were immunostained with antibodies to calbindin D-28. Scale bar: 100 µm.