

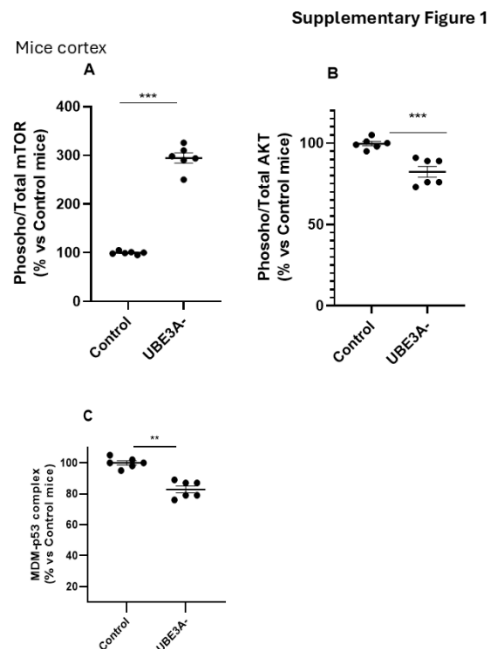
Dysfunction of the autophagy system and MDM2-p53 axis leads to the accumulation of amyloidogenic proteins in Angelman Syndrome models

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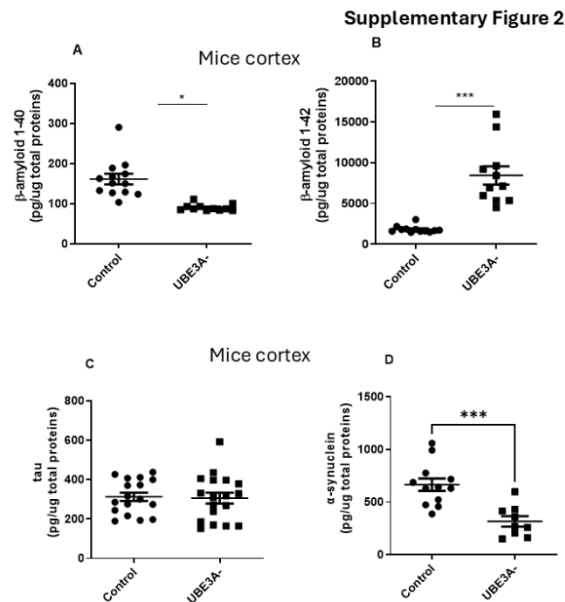
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Supplementary Figure S1. mTOR/AKT pathway and MDM2-p53 axis in the AS mice model. (A-B) Cortex lysates from WT and AS mice were tested with specific antibodies (total mTOR and phospho-mTOR, panel A; total AKT or phospho-AKT, panel B) by immunoezymatic assays, as reported in the Methods section. The data are expressed as ratio between phosphorylated/total mTOR or as ratio between phosphorylated/total AKT and reported in % versus the control samples. Data are mean $\pm$ SEM of **four independent experiments**. Comparisons between WT and AS were performed using an unpaired two-tailed Student's t-test; ** $p < 0.01$, *** $p < 0.001$. (C) Cortex lysates from WT and AS mice were used to detect MDM2-p53 complex by a specific immunoezymatic assay,

as reported in the Methods section. The data are expressed as percentage versus WT samples and are mean $\pm$ SEM of three independent experiments. Comparisons between Control and AS samples were performed using an unpaired two-tailed Student's t-test; ** $p < 0.01$, *** $p < 0.001$.



Supplementary Figure S2. Misfolded proteins levels in the AS mice model. Tissue lysates obtained from cortices of WT and UB3A⁻ animals used to detect β -amyloid1-40 (A), β -amyloid1-42 (B), tau (C) and α -synuclein (D) by specific immunoezymatic assays, as reported in the Methods section. The data are expressed as pg/ μ g total proteins (mean $\pm$ SEM). Comparisons between Control and UB3A⁻ were performed using an unpaired two-tailed Student's t-test. The following symbols were used to indicate significance: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$ vs Control.