**Supplemental Figures**

Figure S1

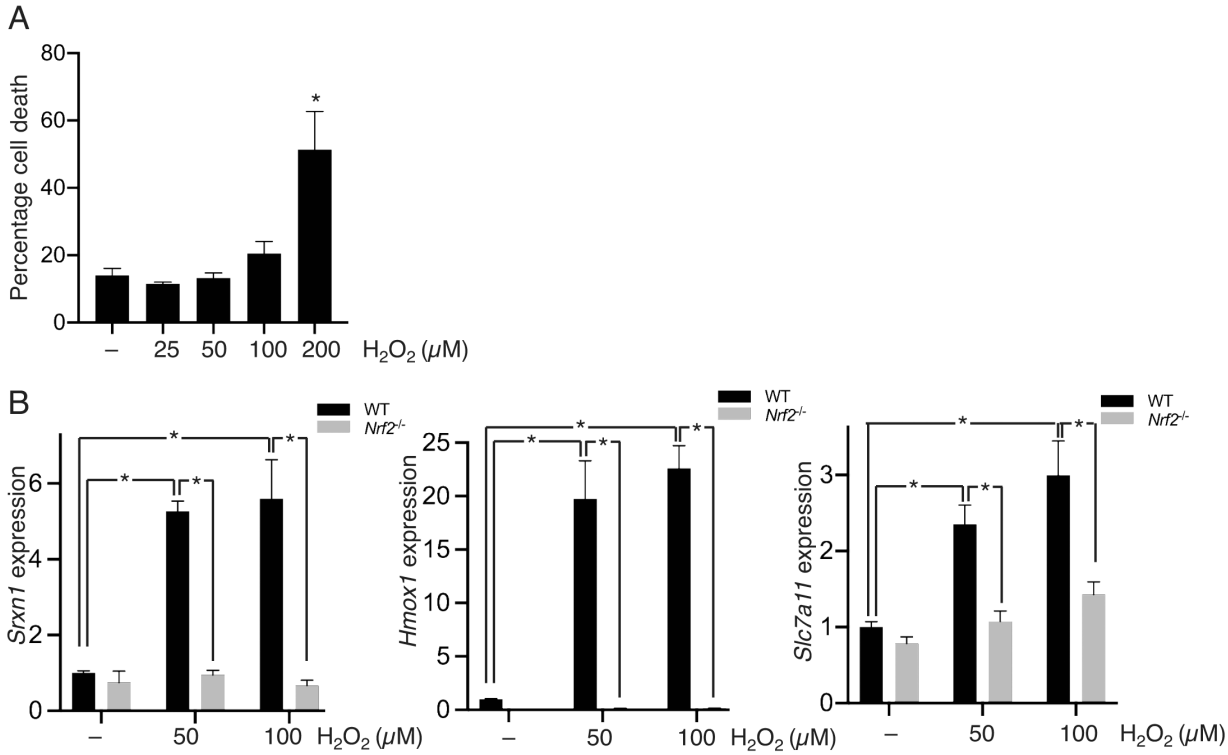


**Figure S1**. **A)** Cell viability in response to a range of $H_2O_2$ doses. To induce oxidative stress a range of $H_2O_2$ doses (25µM-200µM) was utilized and cell viability was evaluated in mixed astrocyte/neuronal cultures by assessing nuclear integrity. **P*<0.05, one-way ANOVA with Dunnett's *post-hoc test*, (n=3-4). **B)** $H_2O_2$ treatments triggers induction of *Srxn1*, *Hmox1* and *Slc7a11* expression which is eliminated by Nrf2-deficiency. Mixed astrocyte/neuronal cultures of the indicated genotypes were treated with the indicated doses of $H_2O_2$ for 6 h, before performing qPCR analysis of gene expression (normalized to Gapdh). Expression levels are expressed relative to WT-control. **P*<0.05, two-way ANOVA with Tukey's *post-hoc* test (n=3-9).

Figure S2

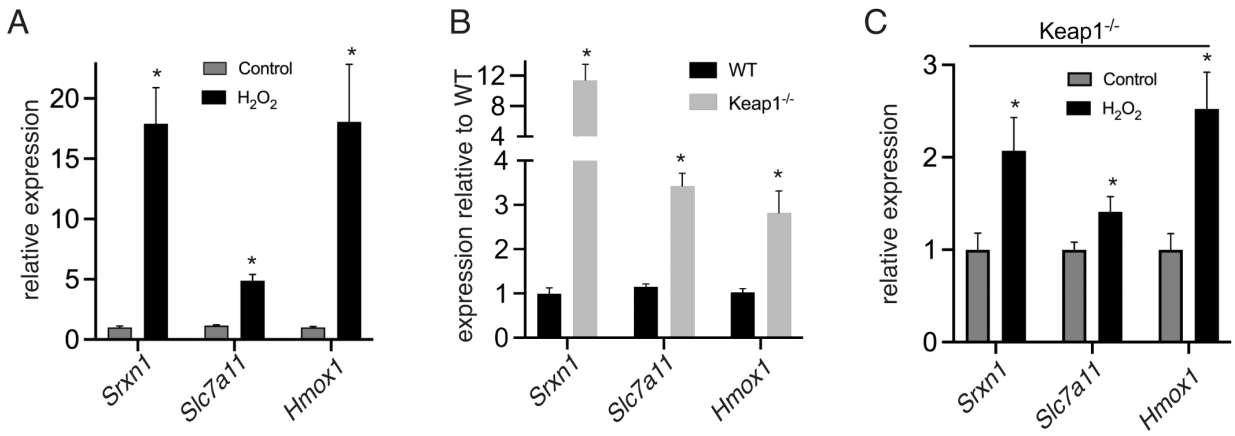


**Figure S2. A)** Mono-cultures of astrocytes were treated ± 100 µM $H_2O_2$ for 8h and the indicated genes analyzed by qPCR. **P*<0.05 (unpaired t-test, n=4). **B)** RNA was extracted from mono-cultures of astrocytes from Keap1 KO mice and WT litter mates, and the indicates genes analysed by qPCR **P*<0.05 (unpaired t-test, n=9-11). C) Keap1 KO astrocyte mono-cultures were treated as in (A)p and the indicated genes analyzed. **P*<0.05 (unpaired t-test, n=9-11).

Figure S3

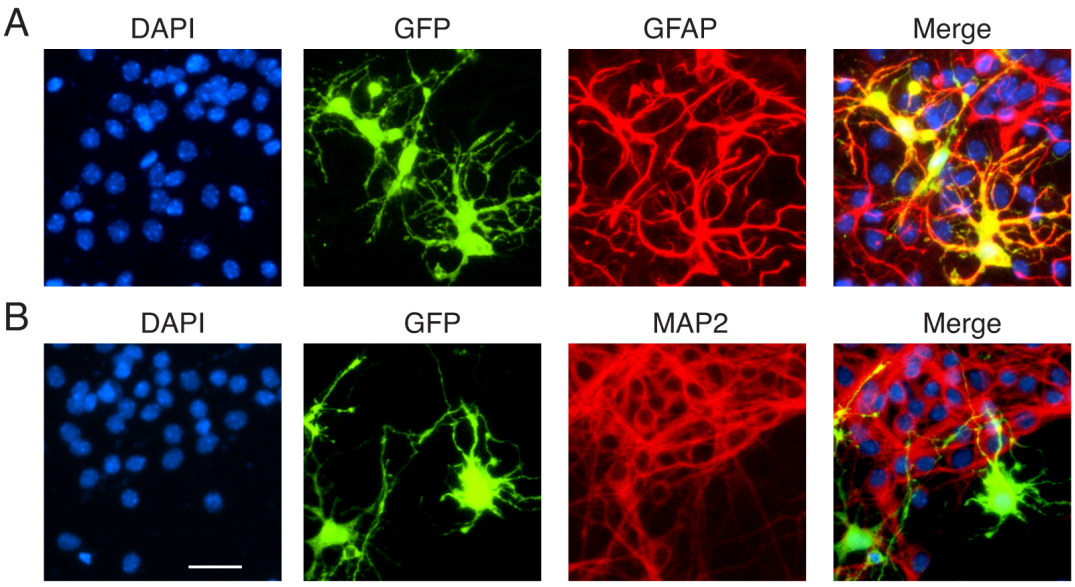


**Figure S3 A,B)** Example images of the approach to target astrocyte transfection within mixed neuronal/astrocyte cultures as described previously (Alabdullah et al., 2019; Marwick and Hardingham, 2017). GFAP is used as an astrocyte marker and MAP2 a neuronal marker Scale bar: 50 µm.

Figure S4

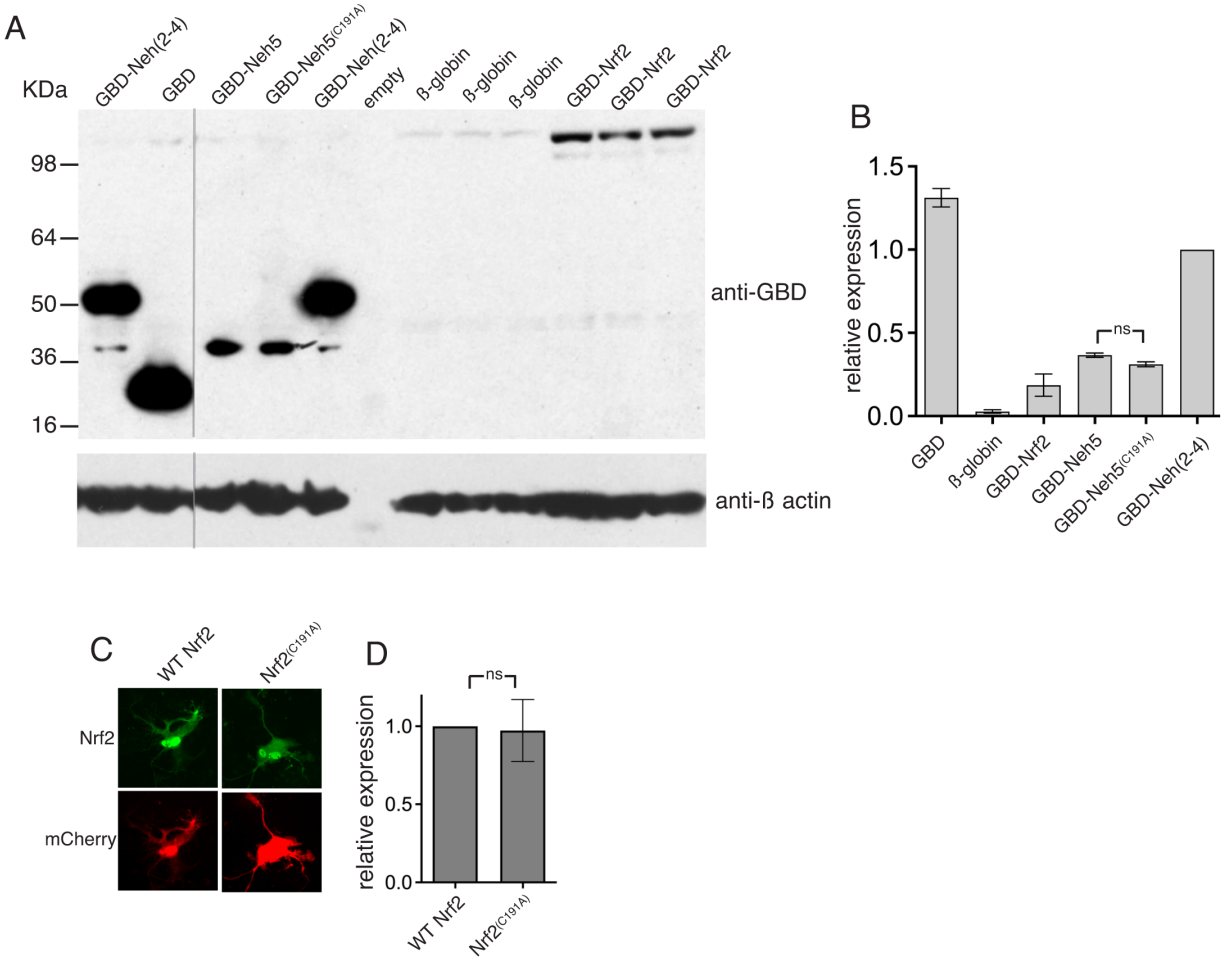


**Figure S4. A,B)** Constructs encoding the GAL4 DNA binding domain (GBD) fused to the indicated domains of Nrf2 were transfected into HEK-293 cells. At 24 h post transfection, protein was harvested and analyzed for GBD expression normalized to a β-actin loading control, (n=5). C,D) Astrocytes were transfected with constructs encoding WT or mutant Nrf2 tagged with GFP, plus a mCherry transfection marker. Levels of ectopically expressed Nrf2 were quantified in 78 (WT) and 73 (mutant) transfected cells using an anti-GFP antibody (n=4).