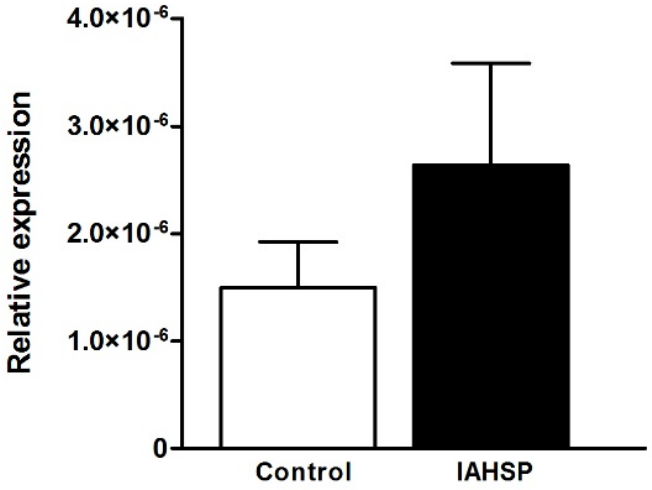
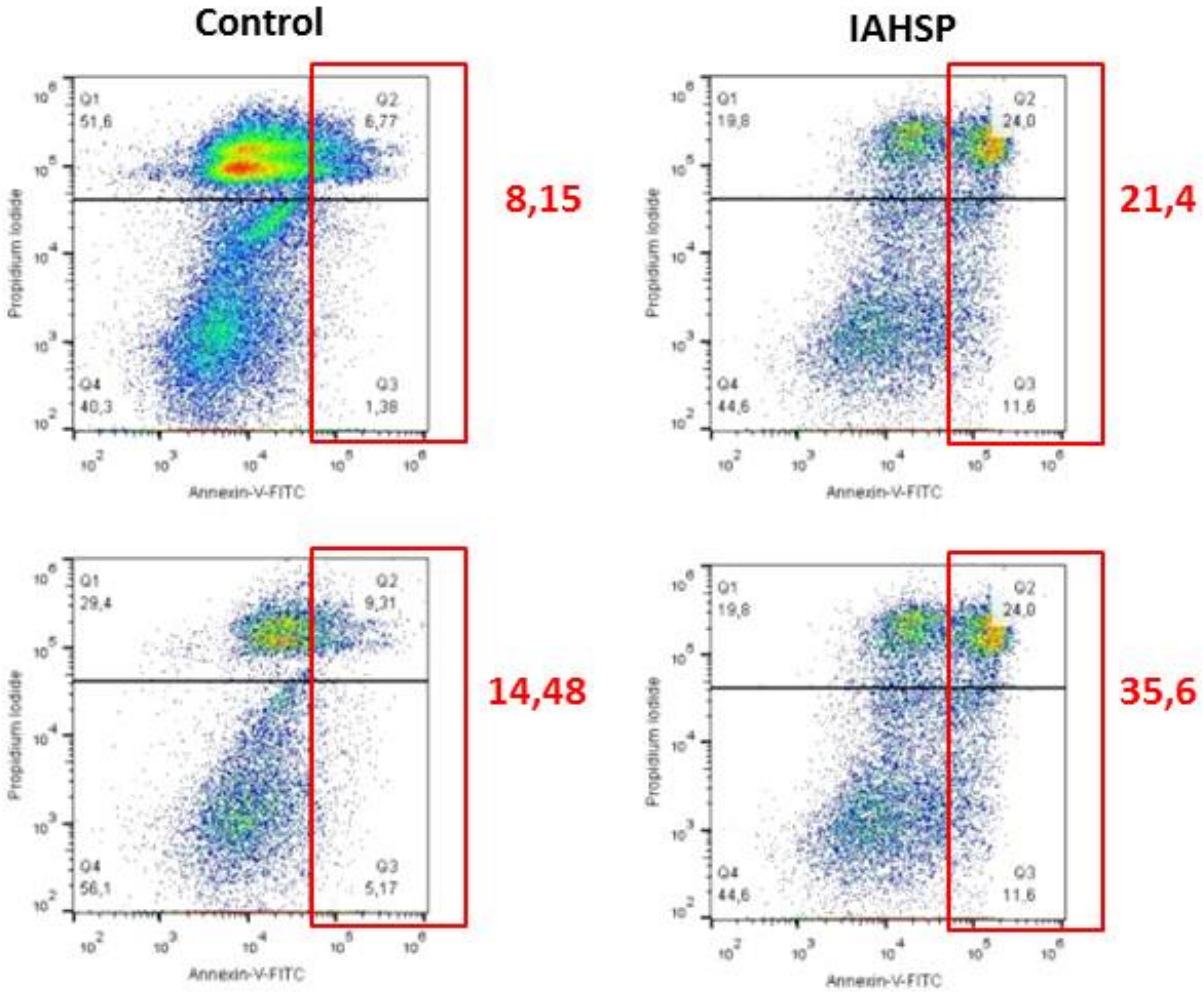


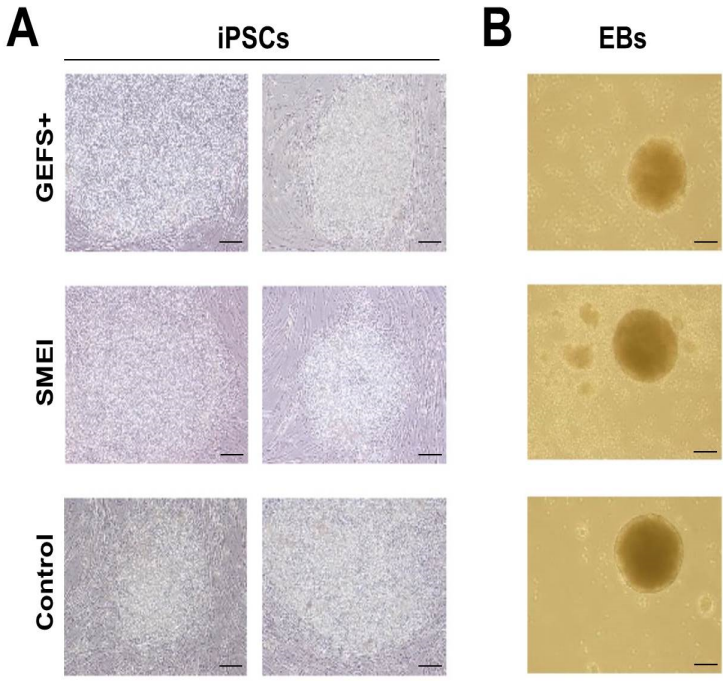
Supplemental Figure 1. Expression levels of Bcl2 in control and IAHSP iPSCs

Real time-PCR analysis of Bcl2 expression in control (white bar) and IAHSP (black bar) iPSCs (n = 3 colonies per group). Transcriptional levels of the target gene were expressed as relative values (2-ΔCt) normalized with 18s



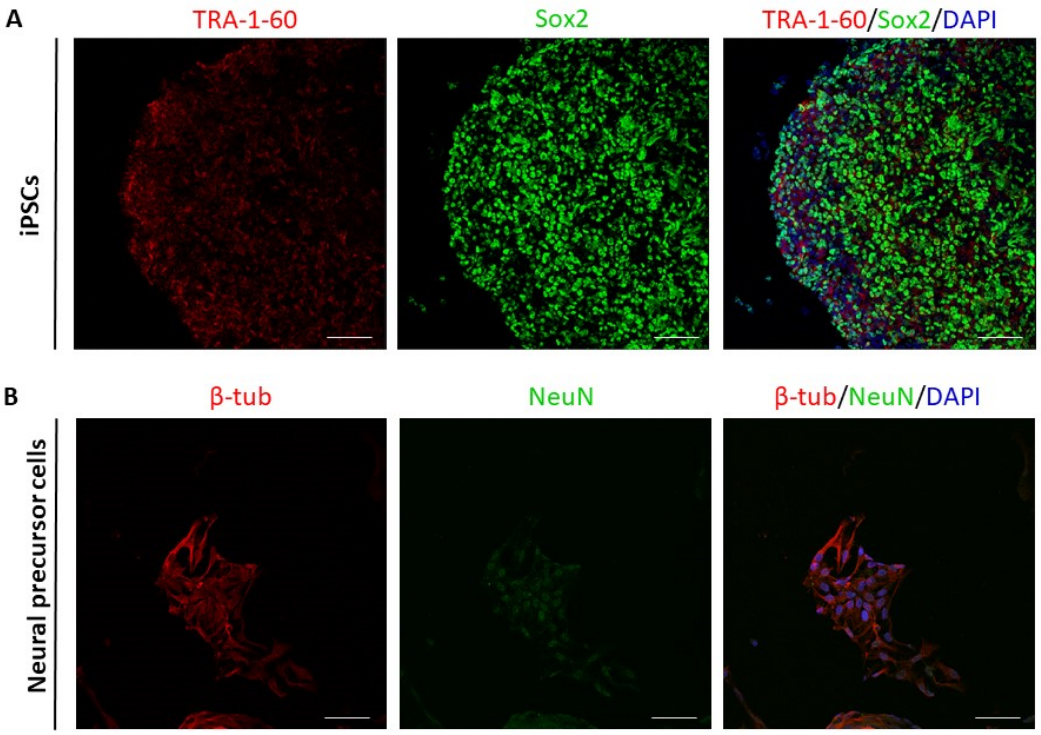
Supplemental Figure 2. Apoptotic events in control and IAHSP iPSCs

Flow cytometry analysis of apoptotic events in control (left column) and IAHSP (right column) iPSCs (n = 2 iPSC lines per group) using annexin V-FITC apoptosis detection kit. Percentages of Annexin V-positive apoptotic cells (red squares) in each sample are reported



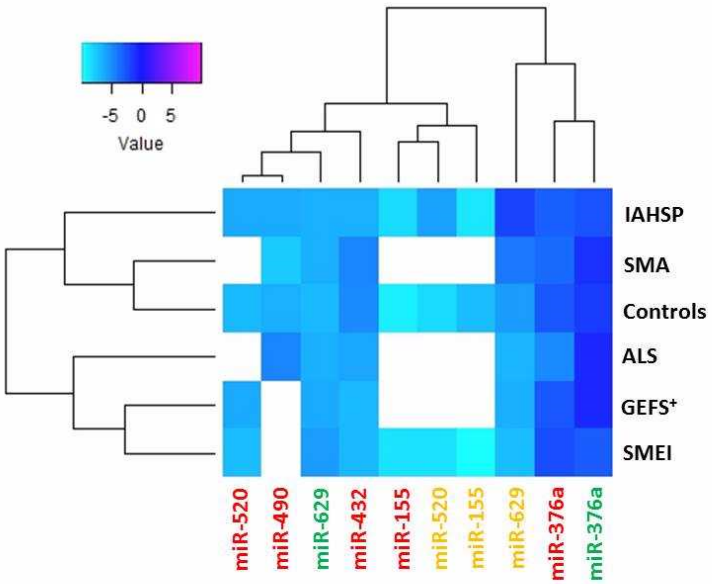
Supplemental Figure 3. Generation of iPSCs and EBs by reprogramming fibroblasts from familial epilepsy patients (GEFS+ and SMEI)

Representative images of iPSC clones obtained from an healthy control and two patients affected by familial epilepsy, one with generalized epilepsy with febrile seizure plus (GEFS+) and one with severe myoclonic epilepsy at infancy (SMEI) (A). Representative image of iPSC clone-derived EBs from the healthy control and the GEFS+ and SMEI patients. Magnification bars: 80 μm



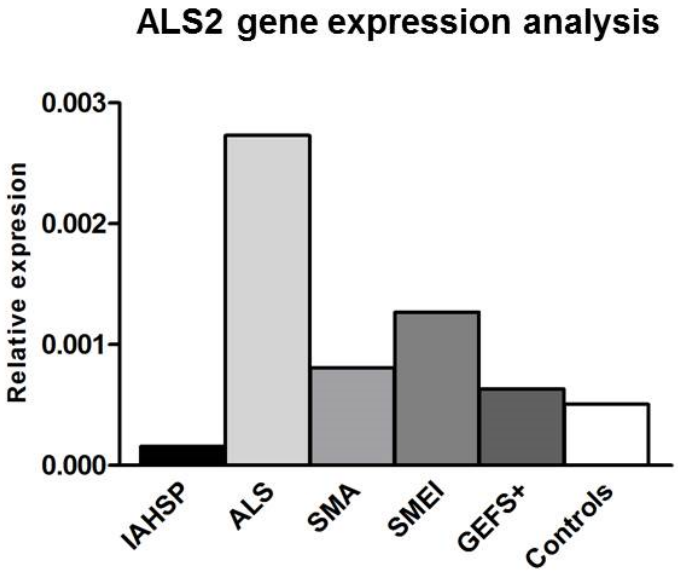
Supplemental Figure 4. Generation of iPSCs, neuronal precursors cells by reprogramming fibroblasts from motor neuron disease patients (ALS and SMA)

(A) Representative images of an iPSC colony obtained from SMA patient's fibroblasts positive for the stem cell markers TRA-1-60 (red), SOX2 (green). iPSCs were obtained also from ALS and healthy subject fibroblasts. (B) Representative images of neural precursors obtained from SMA iPSCs positive for β-tub (red) and NeuN (green). Neural precursors were obtained also from ALS and healthy iPSCs. Nuclei are stained with DAPI (blue). Scale bars: 70 μm



Supplemental Figure 5. Heat map representation of the expression levels of not validated miRNAs in healthy control, pathological control, and IAHSP fibroblasts, iPSCs, and neuronal cells

Heat map of not validated miRNAs having comparable expression levels in fibroblasts (green), iPSCs (red), and neuronal cells (orange) obtained from four healthy subjects, two patients with motor neuron diseases (MNDs), one with ALS and one with SMA, and two patients affected by neurological diseases other than MNDs, one with generalized epilepsy with febrile seizures plus condition (GEFS+), and one with severe myoclonic epilepsy at infancy (SMEI). miRNAs levels were reported as log 2-transformed relative expression and normalized against U6 endogenous control. Rainbow scale color is representative of expression level values from negative (light cyan) to positive (magenta). White boxes indicate undetected miRNAs



Supplemental Figure 6. ALS2 gene expression levels in IAHSP neuronal cells. Transcriptional expression analysis of ALS2 gene in neuronal cells derived from iPSCs of the IAHSP patient (black histogram), ALS (light gray histogram), SMA (gray histogram), SMEI (dark gray histogram), GEFS^{+} (darker gray histogram) and controls (white histogram) expression levels was expressed as relative values (2-ΔCt) normalized with endogenous control 18s in triplicate. ALS2 gene expression levels were lower than to healthy controls, ALS, SMA, SMEI and GEFS^{+} cells. This suggest that an altered transcriptional regulation might occur for ALS2 gene, underlying the complexity of combinatorial gene control mechanisms in IAHSP, and other ALS2 gene-related diseases