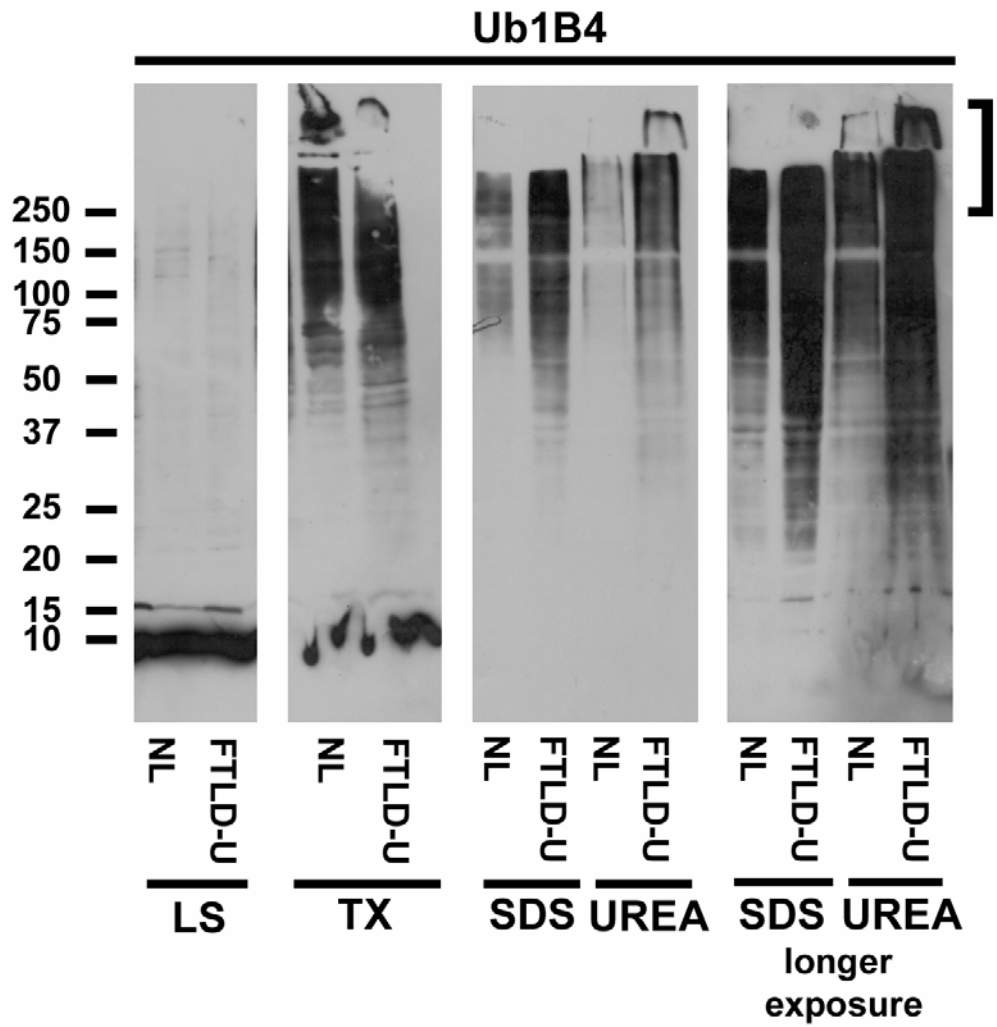


**Supplementary Figure 1. FTLD-U brains accumulate more abundant high Mr ubiquitinated proteins than controls.** Sequential biochemical fractions of cortical gray matter from FTLD-U (case 11) and a NL control were separated by 5-20% gradient Tris-glycine SDS-PAGE and immunoblotted with the anti-ubiquitin antibody Ub1B4. The bracket indicates portion of the blot to which high Mr (> 250 kD) proteins from the stacking gel were transferred. For each fraction, equal volumes of sample from each brain were loaded. The mobility of molecular mass markers (kD) is depicted on the left.

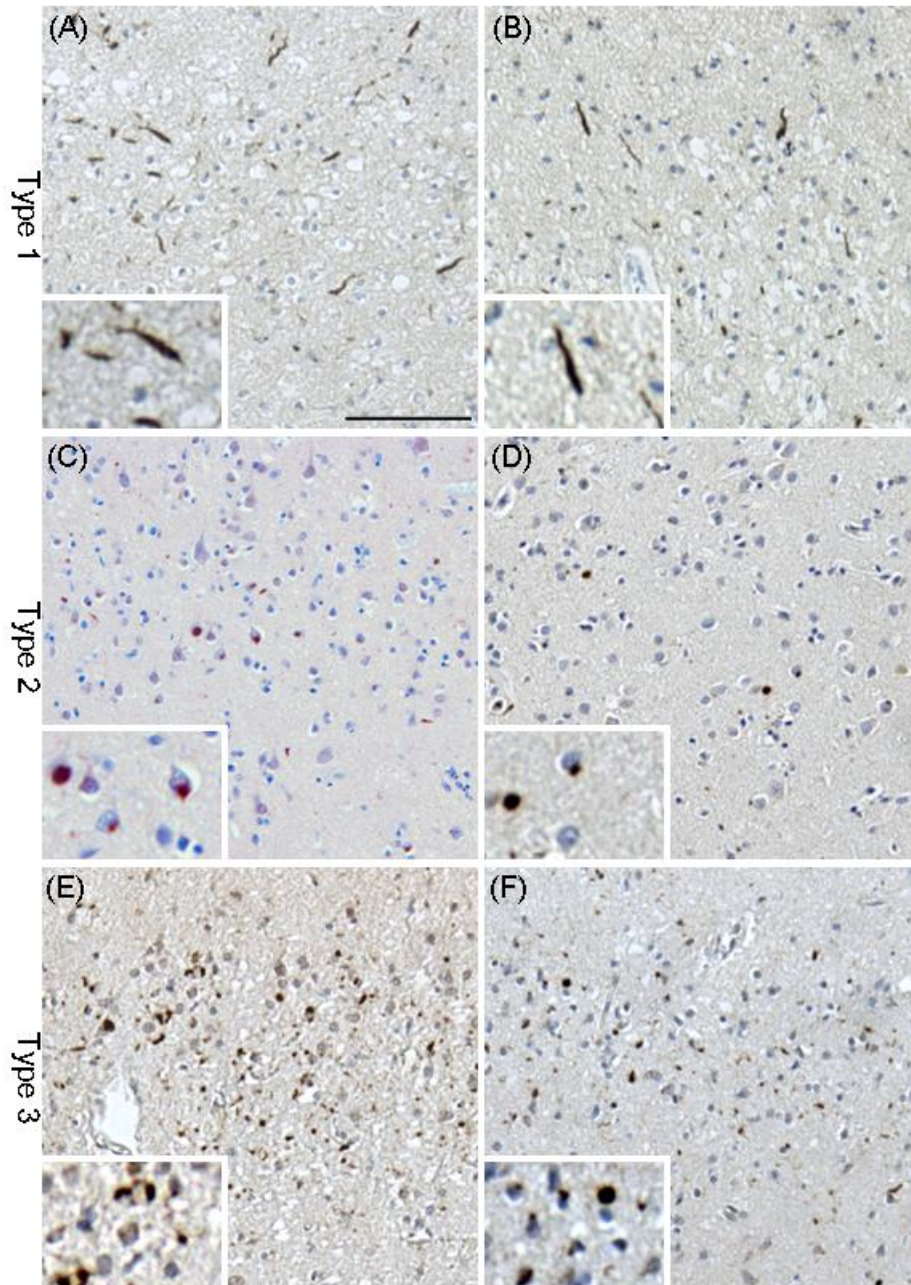
**Supplementary Figure 2: FTLD-U types based on ubiquitin immunohistochemistry** (A, B) Type 1: Abundant neuritic pathology in the superficial layers of temporal (A, case 1) and frontal cortex (B, case 8). (C,D) Type 2: Ubiquitin-positive cytoplasmic inclusions in temporal (C, case 14) and frontal cortex (D, case 15). (E,F) Type 3: Numerous cytoplasmic inclusion and small neuritic profiles in the superficial layers of temporal (E, case 19) and frontal cortex (F, case 20). Scale bar in A corresponds to 100  $\mu$ m (A-F) and 50  $\mu$ m (inserts in A-F).

**Supplementary Figure 3: Immunoblot analysis of cell lysates from ubiquitin transfected QBI 293.** QBI 293 cells transfected with pMT 123 vector containing the cDNA for HA-octameric ubiquitin precursor (a gift from C. Pickart) were treated with 10  $\mu$ M lactacystin or medium for 24 h. The cells were extracted with RIPA and the lysates were separated on 5-20% gradient Tris-glycine SDS-PAGE, transferred to nitrocellulose, and immunoblotted with Ub1B4, MAb 137, or MAb 244. The data showed that MAb 137 and MAb 244 were not immuno-reactivity toward free ubiquitin or ubiquitinated proteins.

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Supplementary Figure 3

