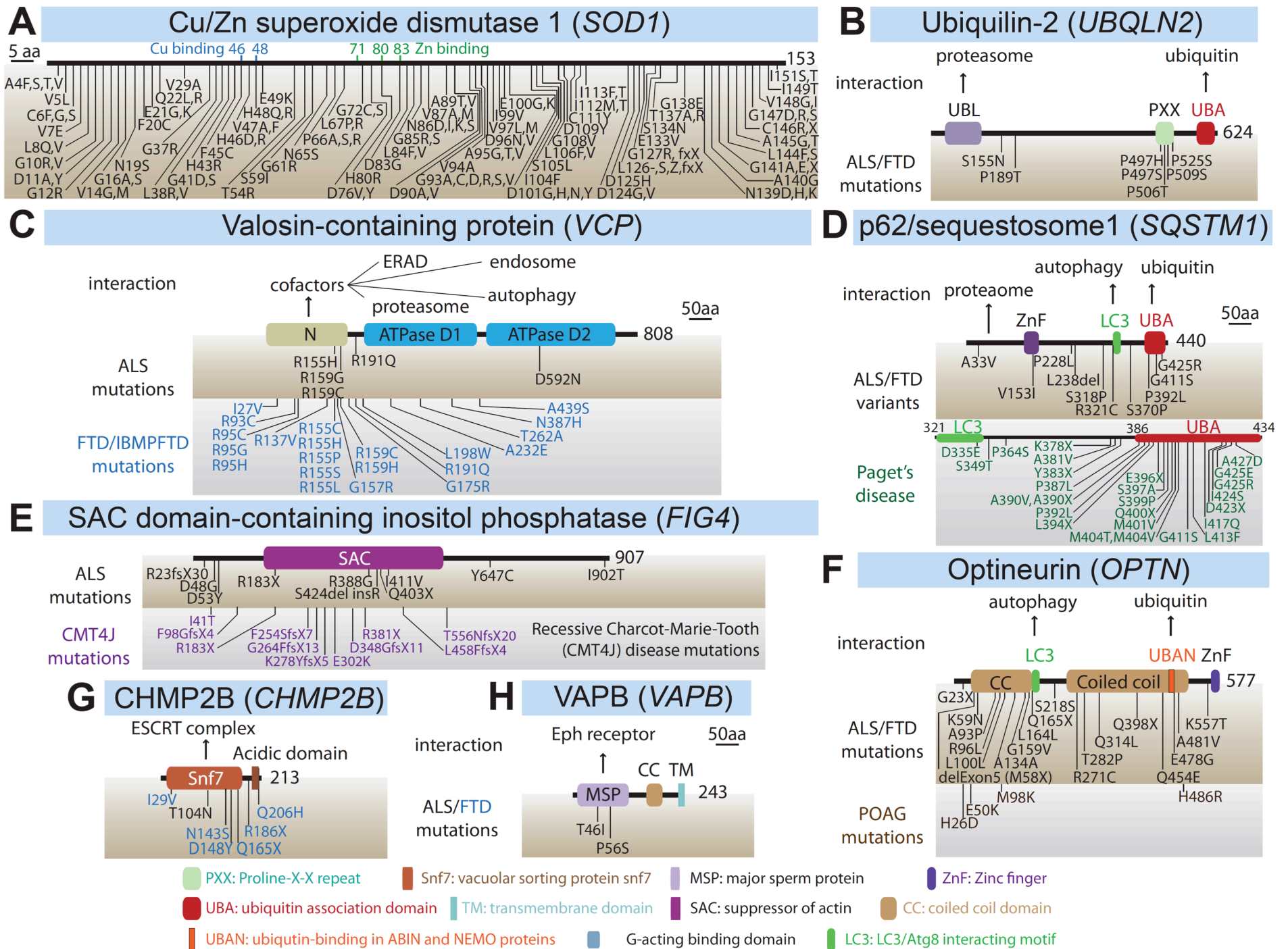


**Supplemental Figure 1. ALS/FTD-linked mutations in genes involved in RNA homeostasis**

Schematic and domain representation of ALS/FTD-linked mutations in genes involved in RNA homeostasis. Proteins are drawn to scale and protein domains and key residues are indicated. FUS/TLS, EWSR and TAF15 collectively form the FET family. Note that mutations in senataxin (SETX) can give rise to ALS and Ataxia-ocular apraxia 2, whose mutations are distinct from those in ALS.



**Supplemental Figure 2. ALS/FTD-linked mutations in genes involved in protein homeostasis**

Schematic and domain representation of ALS/FTD-linked mutations in genes involved in protein homeostasis. Proteins are drawn to scale. Protein domains, interacting partners and key residues are as indicated.