

P016 Functional characterization of several structural domains of the deubiquitinating enzyme USP25

Amanda Denuc¹, Anna Bosch²,

Roser Gonzàlez-Duarte¹ and Gemma Marfany¹

¹ Dept. de Genètica; Facultat de Biologia; Universitat de Barcelona; E-08028 Barcelona; SPAIN

² Present address: Biobanc; Hospital Clínic; IDIBAPS; E-08036 Barcelona; SPAIN

The deubiquitinating enzymes are the most poorly known family of proteins involved in the ubiquitin/proteasome system, even though the human genome encodes around one hundredth of its members. USP25 is a deubiquitinating enzyme (DUB), whose gene is located on human chromosome 21. Although nearly ubiquitously expressed, USP25 shows high levels of expression in testis, skeletal and heart muscle, as well as in actively-replicating regions of the developing brain. There are several isoforms produced by alternative splicing and some of them are tissue specific. We previously have shown that the specific muscle isoform interacts specifically with 3 sarcomeric proteins, and that the over-expression of the specific isoform, but not that of the more ubiquitous protein, rescues some of the substrates from proteasome degradation, thus providing grounds for the physiological relevance of the enzyme. In silico analyses have predicted several protein domains with as yet unascertained function. By constructing and over-expressing several deletion mutants of the enzyme we analyzed their contribution to catalytic activity, substrate recognition, subcellular localization and post-translational modifications.