Characterization of an Ubiquitin Ligases TRAC-1 (T-cell Ring Protein in Activation), RNF114, RNF138 and RNF166

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Ubiquitination has long been known to target damaged proteins for degradation. Ubiquitination is also recognized to modulate the function, localization and interaction of target proteins. Recently, it has become clear that ubiquitination is crucially involved in the regulation of T-cell functions. The RING domain of protein TRAC-1 was identified in a functional screen for T-cell regulators. This protein contains a C3HC4 RING domain, three zinc-finger-like domains and a UIM domain. Protein BLAST searches with RING domain of TRAC-1 revealed that homologous sequences are present in other human proteins: RNF114 (Zfp313), RNF138 (NARF) and RNF166. The similarities between TRAC-1 and its family members suggest that these proteins may be involved in similar activities. Little is known about the targets for ubiquitination by TRAC-1, RNF114 and RNF138 proteins and how their functions are regulated in the cells. Furthermore, no data have been published on RNF166. The present study seeks to better characterize the ubiquitin ligases TRAC-1, RNF114, RNF138 and RNF166 in order to clarify some aspects of their biology. Our preliminary results suggest that none of these proteins are phosphorylated by PKC or CKII *in vitro* assays. TRAC-1 ubiquitinates itself and these events result in its short life inside the cells. Using experiments *in vivo*, we showed that mutations in all of the 8 lysine residues present in TRAC-1 resulted in an increased stability of this protein, when compared to wild-type protein.

Keywords: RING finger protein, TRAC-1, Ubiquitination, Ubiquitin ligase

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