Unravelling the mechanism of action of the RNB family of exoribonucleases

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Enzymes from the RNase II-family are ubiquitous and play a crucial role in RNA metabolism. They are involved in virulence, growth and viability, mitotic control and chloroplast biogenesis. *E. coli* RNase II is the prototype of this family. An important breakthrough in the understanding of the mechanism of action of this protein was the resolution of its structure. The 3D structure showed that this protein is formed by four domains, two N-terminal CSD and a C-terminal S1 domains involved in RNA binding, and a central RNB domain, which is responsible for catalysis (Frazão et al, 2006, Nature). Moreover, the co-crystallization of this protein with a RNA molecule allowed seeing which residues are crucial for catalysis; the role of these amino acids was then biochemically confirmed (Barbas et al, 2008; 2009, JBC). RNase R, the other member of this family in *E. coli*, shares 60% of sequence homology with RNase II, however, these proteins behave differently. While RNase II activity is blocked by the presence of secondary structures, RNase R is capable of degrading highly structured RNA. Another difference is that the final degradation product of RNase II is a 4 nt fragment, whereas the end product of RNase R is a 2 nt fragment. We performed a biochemical analysis and constructed several mutants in order to understand the mechanism of action of RNase R. We discovered that the RNB domain from RNase R is sufficient for the degradation of structured substrates (Matos et al, 2009, Biochem J). At the C-terminal, this protein has a lysine-rich tail, which probably helps to unwind the substrate before it enters into the catalytic cavity (Matos et al, 2011, Proteins). A definitive model for RNA degradation by RNase R is still open, and only the resolution of its structure will answer the many questions about its remarkable mode of action.