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# Human secretory RNases as multifaceted antimicrobial proteins

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Human secretory RNases are wide-spectrum host defense proteins. They are secreted by innate cell types upon infection and constitute a first line immune barrier. Our research group is exploring their mechanism of action at distinct cellular levels.

In this work we compare the three main human antimicrobial RNases: RNase 3 specifically secreted by eosinophils, RNase 6, expressed by neutrophils and monocytes, and RNase 7 predominant in keratinocytes. By applying site directed mutagenesis and peptide synthesis we have identified the main structural determinants for the proteins' cytotoxicity on several Gram negative and Gram positive bacteria species together with Candida albicans yeast. Domains responsible for lipopolysaccharide binding, cell agglutination and membrane destabilization have been located at the protein N-terminus. The identified antimicrobial motives served as a template to design antimicrobial peptides. Protein derived peptides were engineered reproducing efficiently the parental protein antimicrobial properties. Moreover, together with an unspecific membrane lysis killing mechanism, the studied RNases were able to internalize at sublethal concentrations, blocking the cell viability and potentially targeting the cellular nucleic acids.

We can conclude that human antimicrobial RNases work as host multitask proteins contributing to the clearing of the infection focus. Complementary, human RNases can also serve as templates towards a structure- based drug design of novel antimicrobial agents. In particular, potential contribution of the enzymatic activity in the RNases cytotoxicity envisages cellular RNA targeting as an effective strategy for alternative antibiotic development.

## Biography

Ester Boix defended her PhD at the Universitat Autònoma de Barcelona (Spain) and spent 5 years postdoctoral studies at the National Institutes of Health, Bethesda (USA) and Structural Biology Unit, University of Bath (UK). She has been awarded a Ramon y Cajal senior researcher contract in 2002. She is currently an Associate Professor at the Dpt. of Biochemistry and Molecular Biology at the Universitat Autònoma de Barcelona and principal investigator of the research group on Host defense ribonucleases She has published more than 60 papers in peer-reviewed journals; her main interest focusing on the mechanism of action of antimicrobial RNases.

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