

Unveiling the radiation resistance mechanisms of

Deinococcus radiodurans

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Deinococcus radiodurans is the most radiation resistant organism so far identified. It is a gram-positive bacterium, and besides its high resistance to different types of radiation, it is also able to endure extreme conditions of desiccation and oxidative stress.^{1,2} The proposed mechanism that avoids cell death relies on the protein protection against oxidation,³ promoted by the oxidative stress generated under these extreme conditions. Therefore, the organism contains enzymatic systems, such as superoxide dismutase and catalase, which are able to detoxify reaction oxygen species. Moreover, it contains a highly efficient non-enzymatic system that involves small complexes of manganese and other small molecules, such as phosphate.⁴ Currently, neither the homeostasis of Mn nor the intracellular localization and formation of these small complexes are yet fully understood. We have been addressing this question by studying two proteins, the DNA-binding proteins under starved conditions (Dps1 (*dr2263*) and Dps2 (*drb0092*)). In our studies we have used a multidisciplinary approach to examine these proteins both *in vitro* and *in vivo*.⁵⁻⁸ Our results showed that these proteins have the ability to store Mn and Fe as well as to bind/protect DNA under *in vitro* conditions.⁷ Moreover, structurally these proteins share a highly conserved dodecameric structure, although under *in vivo* conditions, Dps1 assumes different oligomeric forms.^{5,6,8} Now, we propose to study the formation and hydrolysis of polyphosphates, its association with Mn and post-translational modifications that arise under stress conditions. Different techniques will be used to address these questions, namely biophysical, X-ray crystallography, NMR, MS, fluorescence microscopy and X-ray microanalysis using the scanning electron microscope. This project will develop in the MX-Unit at ITQB and in collaboration with our in-house Labs - Cell Physiology and NMR (Prof. Helena Santos and Dr. Luís Gafeira) and Mass Spectrometry Facility UniMS (Dr. Isabel A. Abreu). The outcomes of this project will be crucial to hint potential breakthroughs in future applications, such as the development of methodologies to protect cells against injury associated with radiotherapy and radiation emergencies.⁹

References:

- [1] White et al (1999) *Science* **286**: 1571.
- [2] Slade & Radman (2011). *MMBR* **75**: 133.
- [3] Daly et al (2007) *PLoS Biol* **5**: e92.
- [4] Daly et al (2004) *Science* **306**: 1025.
- [5] Romao et al (2006) *JBIC* **11**: 891.
- [6] Cuypers et al., (2007) *JMB* **371**: 787.
- [7] Santos et al (2015) *FEBS J* **282**: 4307.
- [8] Santos et al (2017) *JMB* **429**: 667.
- [9] Gupta et al (2016) *PLoS One* **11**: e0160575.