Macromolecular Crystallography Unit

Master Project – ITQB 2009

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A Master project is proposed to carry out structural studies of an important biological system that is involved in the protection of DNA against stress conditions (e.g. radiation and oxidative damage). The protein concerned is called Dps. This family of proteins is widespread amongst bacteria and archaea and is considered to be functionally close to the human ferritin analogues in terms of the iron-storage capacity; the mechanisms by which the protein interacts with the DNA are not known, it is being proposed that these type of proteins can have a chromatin-type function in prokaryotes.

The work proposed will be focused on the structural determination of both Dps in different conditions: metals, DNA, and from several mutants which will be produced à prior. The results will provide new insights for an understanding of the mechanisms by which the DNA is protected.

Deinococcus radiodurans (*Dr*) is an aerobic bacterium extremely resistant to ionising radiation, desiccation, as well as to several other stress conditions. There are two Dps (prokaryotic **D**NA- binding **p**roteins from **s**tarved cells present in this organism: DR2263 (Dps1) and DRB0092 (Dps2). These two proteins are unique as the only examples of Dps known to date with particularly long N-terminal extensions compared to the other family members. Dps can store iron and bind DNA to protect it from oxidative stress. Structural and biochemical characterization of these features are important to understand the highly effective mechanisms that allow *Dr* to recover from remarkably high levels of cellular damage under the various stress conditions. We have already determined the high-resolution X-ray crystal structures of the two Dps in two different stages of their activity: the apo and one iron-bound form. Both proteins share the same overall structure with other members of the family: a hollow sphere (which stores variable amounts of iron) composed of 12 identical subunits (each a four-helix bundle) (Figure 1). However, in both forms for the two proteins the electron density for the N-terminal extension of each subunit could not be located, probably due to degradation and the inherent disorder and flexibility of these extensions.

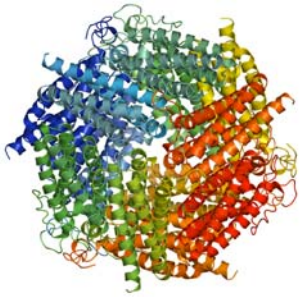

Figure 1. Dps2 overall structure determined by X-ray crystallography.