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The BHP2 protein - an evolutionary perspective on the intrinsic apoptotic pathway

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Apoptosis or programmed cell death is a crucial response to perturbations in physiological conditions, allowing an organism to determine if a given cell can be eliminated when unneeded, damaged or dangerous for the organism. In this mechanism the B-cell lymphoma 2 (Bcl-2) protein family plays an important role in regulating the homeostasis [1].

Sponges are the phylogenetically oldest existent members of the Metazoa phylum. It has been demonstrated that *Geodia cydonium* (*G. cydonium*) and *Suberites domuncula* possesses polypeptide sequences with high sequence similarity to Bcl-2 protein members [2]. The study of these proteins is highly relevant for the understanding of the evolution of apoptosis across species. BHP2, a *G. cydonium* pro-survival Bcl-2 protein, has been shown to be involved in apoptotic pathway [3].

In this study the BHP2 protein biochemical characterisation using ITC as well as its structure determination in complex with a BH3-only peptide has enable us to shine light on the sponges apoptosis mechanism and compare it to others previously characterized such as the mammalian and viral. A better understanding of how apoptosis evolved across species might yield value information for rational drug design.

References:

- [1]- Kvansakul M et al. (2014) *Method Enzymol.* 544, 44-79.
- [2]- Wiens M et al. (2000) *J. Mol. Evol.* 50, 520-531.
- [3]- Wiens M et al. (2001) *Cell Death Differ.* 8, 887-98.

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