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Programmed cell death (apoptosis) is essential for human life. In its intrinsic pathway, the Bcl-2 (B-cell lymphoma 2) protein family regulates cell life and death by controlling permeability of the mitochondrial outer membrane (MOM). However, the molecular basis of cell protection by its anti-apoptotic Bcl-2 members remains elusive due to the lack of detailed structural insight into their action at the MOM to ensure its integrity. To provide atomic-level insight into their functioning, we will use the founding member of this family, the human anti-apoptotic Bcl-2 protein itself, whose involvment in p53 regulation and its overexpression plays a notorious role in many cancers and their treatment resistance. However, for a long time, obtaining sufficient protein was cumbersome due to its insolubility as a membrane protein and low yields. Therefore, we establishes an expression and purification protocol [1] to produce routinely mg amounts of the fully functional full-length human isoform 2 of Bcl-2 (Bcl-2(2)) which can also be isotopically labelled as $^{15}N/^{13}C/^{2}H$ versions, ideally suited for neutron and NMR studies. The protocol even allows to generate residue specific Bcl-2 mutants and various constructs [2].

1. Aden, A.U. Mushtaq, A. Dingeldein, M. Wallgren, **G. Gröbner**. A novel recombinant expression and purification approach for the full-length anti-apoptotic membrane protein Bcl-2. Protein expression and purification. 172 (2020) 105628.
2. A. Ul Mushtaq, J. Aden, T. Sparrman, M. Hedenstrom, **G. Gröbner**. Insight into Functional Membrane Proteins by Solution NMR: The Human Bcl-2 Protein-A Promising Cancer Drug Target. Molecules 26 (2021) 1467, 1-14