Gene name: **BCL2**

External Ids for BCL2 Gene: HGNC: 990 NCBI Gene: 596 Ensembl: ENSG00000171791 OMIM®: 151430 UniProtKB/Swiss-Prot: P10415

NCBI Gene Summary for BCL2 Gene: This gene encodes an integral outer mitochondrial membrane protein that blocks the apoptotic death of some cells such as lymphocytes. Constitutive expression of BCL2, such as in the case of translocation of BCL2 to Ig heavy chain locus, is thought to be the cause of follicular lymphoma. Alternative splicing results in multiple transcript variants.

GeneCards Summary for BCL2 Gene: BCL2 (BCL2 Apoptosis Regulator) is a Protein Coding gene. Diseases associated with BCL2 include Follicular Lymphoma and High-Grade B-Cell Lymphoma Double-Hit/Triple-Hit. Among its related pathways are MIF Mediated Glucocorticoid Regulation and TGF-Beta Pathway. Gene Ontology (GO) annotations related to this gene include *protein homodimerization activity* and *identical protein binding*. An important paralog of this gene is BCL2L1.

UniProtKB/Swiss-Prot Summary for BCL2 Gene: Suppresses apoptosis in a variety of cell systems including factor-dependent lymphohematopoietic and neural cells (PubMed:1508712, 8183370). Regulates cell death by controlling the mitochondrial membrane permeability (PubMed:11368354). Appears to function in a feedback loop system with caspases (PubMed:11368354). Inhibits caspase activity either by preventing the release of cytochrome c from the mitochondria and/or by binding to the apoptosis-activating factor (APAF-1)

Tocris Summary for BCL2 Gene: Bcl-2 family proteins contribute to programmed cell death or apoptosis. It is a large protein family and all members contain at least one of four Bcl-2 homology domains. Certain members (Bcl-2, Bcl-XL and Mcl-1) are antiapoptotic, whilst others (Bax, Bak, Bok) are proapoptotic.

Cellular localization: Mitochondria outer membrane, Nucleus membrane, Endoplasmic reticulum membrane, Cytoplasm.

The **BCL2** gene encodes the B-cell lymphoma 2 protein, a pivotal regulator of apoptosis (programmed cell death). By inhibiting apoptotic pathways, BCL2 promotes cell survival, playing a crucial role in maintaining cellular homeostasis and tissue integrity.

Function in Sepsis: In sepsis—a severe systemic inflammatory response to infection—dysregulated apoptosis contributes to immune dysfunction and organ failure. BCL2's anti-apoptotic properties are significant in this context:

- **Immune Cell Preservation:** Overexpression of BCL2 in transgenic mice has been shown to decrease apoptosis in immune cells during sepsis, potentially preserving immune function.
- **Organ Protection:** Administration of BCL2 protein in murine sepsis models reduced apoptosis and improved survival, suggesting a protective role against sepsis-induced organ injury.

Pathways Involved in Sepsis:

- **Intrinsic Apoptotic Pathway:** BCL2 modulates mitochondrial membrane permeability, preventing the release of cytochrome c and subsequent activation of caspases that execute apoptosis.

- **Inflammatory Signaling:** By regulating apoptosis, BCL2 indirectly influences inflammatory responses, as excessive cell death can exacerbate inflammation.

Diagnostic and Prognostic Role:

- **Diagnostic Marker:** Altered expression of BCL2 and related genes has been identified in sepsis patients, indicating its potential as part of a diagnostic gene signature.
- **Prognostic Indicator:** Genetic variants in BCL2 have been associated with a decreased risk of acute kidney injury in septic shock, suggesting a role in patient prognosis.

Therapeutic Implications:

- **BCL2 Inhibition:** In oncology, BCL2 inhibitors like venetoclax are used to induce apoptosis in cancer cells. However, in sepsis, where preventing excessive apoptosis is beneficial, BCL2 inhibition may not be advantageous.
- **BCL2 Augmentation:** Enhancing BCL2 function could mitigate sepsis-induced apoptosis, preserving immune cell populations and organ function. Further research is needed to explore this therapeutic strategy.

Apoptosis pathway: