

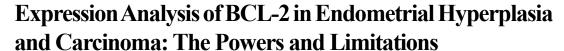
Archives of Razi Institute Journal "Arch. Razi Inst."

Journal Homepage: https://archrazi.areeo.ac.ir/

Letter to Editor







Zohreh Jadali1* (1)

1. Department of Immunology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.



How to cite this article Jadali Z. Expression Analysis of BCL-2 in Endometrial Hyperplasia and Carcinoma: The Powers and Limitations. Archives of Razi Institute Journal. 2025; 80(5):1089-1090. https://doi.org/10.32598/ARI.80.5.3396



Dear Editor

read the ar which exan mia-2 (Bcl dometrium,

read the article by Krishna Kumar et al. which examined B-cell lymphoma/leukemia-2 (Bcl-2) expression in normal endometrium, endometrial hyperplasia, and endometrial adenocarcinoma [1].

They showed increased BCL-2 expression in endometrial hyperplasia compared to healthy endometrium. Moreover, BCL-2 levels were lower in endometrioid adenocarcinoma than in endometrial hyperplasia. The authors suggested that alternative mechanisms, other than failure of apoptosis, may be implicated in endometrial carcinogenesis. These findings are important because BCL-2 expression plays an important role in maintaining a favorable antiapoptotic microenvironment, which influences tumor progression. Moreover, it is vastly upregulated in most cancers, allowing cancer cells to continue growing and dividing. For these reasons, BCL-2 has been a hot topic in cancer research, including endometrioid adenocarcinoma, and several studies about

this issue have been published recently. Unfortunately, various papers have reported conflicting results. For instance, some investigators have observed increased expression of BCL-2 in endometrial carcinoma, particularly in low-grade endometrioid types, while others have found its reduced expression in people with this carcinoma [2]. Addressing the root causes of these conflicts is complex because myriad different molecules involved in apoptosis regulation —and BCL-2 makes up only a small fraction among them. In fact, BCL-2 is a member of a large family of proteins, which consists of various anti-apoptotic members (such as BCL-2 or BCL-xL) and pro-apoptotic members (like BAX and BAK). They exhibit specific patterns of activation, localization and response to signaling molecules. All of these can influence multiple cell fate choices, with the outcomes of cell death or survival. On the other hand, deregulation of both pro- and anti-apoptotic BCL-2 proteins plays an important role in the pathogenesis and progression of cancers. Therefore, simultaneous assessment of the proand anti-apoptotic members of this family provides more reliable information about the behavior of these complex

* Corresponding Author:

Zohreh Jadali, PhD.

Address: Department of Immunology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.

Tel: +98 (21) 6462267

E-mail: zjadali@razi.tums.ac.ir, zjadali@yahoo.co.uk



Copyright © 2025 The Author(s)

molecules. Moreover, there is no unifying model for the physiological function of this family. For instance, researchers have found that anti-apoptotic BCL-2 proteins can become proapoptotic, whereas proapoptotic proteins may encourage cells to survive [3]. The existence of alternative and uncharacterized isoforms of many of the BCL-2 family members adds an extra dimension of complexity [4]. Therefore, scientists should be cautious in interpreting the results of surveys on the clinicopathological significance and expression patterns of BCL-2 in endometrial carcinoma.

Recent studies also indicate that silencing of BCL-2 induces massive p53-dependent apoptosis (BCL-2/p53 apoptotic pathway). This means that the combination of p53 activation and BCL-2 suppression can mutually induce apoptosis. Activated p53 downregulates BCL-2 and upregulates BAX expression in favor of apoptosis [5]. Therefore, reduced expression of BCL-2 protein does not necessarily reflect a reduction of apoptosis.

Altogether, BCL-2 family proteins are the master regulators of apoptosis, and the interplay among their family members is essential for the regulation of cell fate. The proper regulation of apoptosis is vital in various aspects of life, such as normal development of multiple tissues, homeostasis, and disease biology. Therefore, understanding the roles of BCL-2 family members in these processes can provide deeper insight into cancer and accelerate the development of new anticancer therapies.

[5] Kirkin V, Joos S, Zorniga M. The role of Bcl-2 family members in tumorigenesis. Biochim Biophys Acta. 2004; 644(2-3):229-49. [DOI:10.1016/j.bbamcr.2003.08.009] [PMID]

References

- [1] Krishna Kumar K, Upadhyaya K, Cn RT. Bcl-2 May Contribute to Evolution of Endometrial Hyperplasia, but It Isn't a Factor in Subsequent Carcinogenesis. Arch Razi Inst. 2024; 79(4):827-32. [DOI:10.32592/ARI.2024.79.4.827] [PMID]
- [2] Ghorbanniadelavar Z, Jalali Nadoushan M, Soltanipur M. Comparison of B-cell lymphoma 2 (BCL-2) expression in disordered proliferative endometrium and simple endometrial hyperplasia. Rev Esp Patol. 2024; 57(4):265-72. [DOI:10.1016/j.patol.2024.05.005] [PMID]
- [3] Hardwick JM, Soane L. Multiple functions of BCL-2 family proteins. Cold Spring Harb Perspect Biol. 2013; 5(2):a008722.[DOI:10.1101/cshperspect.a008722] [PMID]
- [4] Saddam M, Paul SK, Habib MA, Fahim MA, Mimi A, Islam S, et al. Emerging biomarkers and potential therapeutics of the BCL-2 protein family: The apoptotic and anti-apoptotic context. Egypt J Med Hum Genet. 2024; 25:12. [DOI:10.1186/ s43042-024-00485-7]