The Role of BCL3 Dysregulation in the Pathogenesis of Asthma and Lung Cancer

Laila salameh[1,2] , Poorna Manasa Bhamidimarri[1], Noha Elemam[1] , Rakhee K. Ramakrishnan[1], Qutayba Hamid[1] ,Bassam Mahboub[2], Saba Al Heialy[3], Rifat Hamoudi[1]

1 University of Sharjah, Sharjah Institute for Medical Research-College Of Medicine, Sharjah, United Arab Emirates 2 Rashid Hospital, Dubai Health Authority, United Arab Emirates 3 Collage of Medicine, Mohammed Bin Rashid University of Medicine and Health Sciences, Dubai, United Arab Emirates.

Rational:

Asthma and lung cancer are two diseases that affect the lungs and are both complex and heterogeneous. There could be common mechanisms at work in the evolution of these two diseases. Extrinsic and intrinsic factors may influence the evolution of lung cancer away from the chronic inflammation found in severe asthma. Our previous study showed B-cell lymphoma 3-(BCL3) as one of the common genes that is dysregulated in both lung cancer and severe asthma(1). BCL3 is a proto-oncogene and a member of the IκB family involved in the transcriptional regulation of many NF-κB target genes. However, the role of BCL3 in the pathogenesis of asthma is still largely undefined. We, therefore, aimed to investigate the functional role of BCL3 in the pathogenesis of asthma and lung cancer.

Methods:

Baseline expression of BCL3 was examined in normal (BEAS-2B) and asthmatic bronchial epithelial cells (DHBE), and lung cancer cell lines (A549) by using qRT-PCR and western blotting. The functional role of BCL3 was examined by overexpressing BCL3 in normal and asthmatic epithelial cells as well as silencing BCL3 in lung cancer cell lines. Cellular apoptosis and proliferation assays were performed to understand the effect of BCL3 dysregulation on cell growth.

Results:

Lung cancer cells (A549) showed significantly higher expression of BCL3, both at mRNA and protein levels, as compared to BEAS-2B and DHBE. Overexpression of BCL3 in normal and asthmatic cells led to an increase in proliferation rate with concomitant reduction in apoptosis rate. At the same time, silencing BCL3 in lung cancer cells led to decreased proliferation rate and increased apoptosis rate at different time points.

Conclusions:

The present study is, to the best of our knowledge, the first report addressing the involvement of BCL3 in asthmatic bronchial epithelial cells and lung cancer cells and investigating its role in the pathogenesis of asthma and lung cancer. Further investigation is required to decipher the molecular function of BCL3 to expand our understanding on the therapeutic potential of this biomarker.

1. Salameh L, Bhamidimarri PM, Saheb Sharif-Askari N, Dairi Y, Hammoudeh SM, Mahdami A, et al. In Silico Bioinformatics Followed by Molecular Validation Using Archival FFPE Tissue Biopsies Identifies a Panel of Transcripts Associated with Severe Asthma and Lung Cancer. Cancers (Basel). 2022;14(7).