A genome-wide polyribosome profiling revealed a post-transcriptional operon as an endogenous defense against inflammation

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Emerging evidence suggests that the transcriptome does not always faithfully represent the proteome. Using Affymetrix GeneChip analysis of the polyribosome-profiled mRNAs from the IFN-γ activated monocytes/macrophages; we have identified a cohort of mRNAs under translation control. These mRNAs encode different chemokines and their receptors. Our subsequent studies have identified these mRNAs as a member of a single posttranscriptional operon regulated by ribosomal protein L13a dependent translational silencing. Release of L13a from 60S ribosomal subunit is required for this process and the silencing is mediated by the presence of GAIT (Gamma Activated Inhibitor of Translation) element in the 3'UTRs of the target mRNAs. To test the physiological consequence of this L13a-dependent translational silencing in macrophage we have created viable macrophage specific L13a-knockout (KO) mice (L13aflox/floxLysMCre+). In these mice the termination of inflammation is severely compromised due to the uncontrolled synthesis of several inflammatory proteins e.g. Chemokine and chemokine receptors. Upon LPS-induced endotoxemia, these animals displayed significantly reduced survival rates and symptoms of severe inflammation. Recently we have tested the relevance of this translational silencing in two other murine models of human disease caused by uncontrolled inflammation e.g. high Fat diet-induced atherosclerosis and DSS induced experimental colitis. Both of these studies revealed the essential role of L13a-dependent translational silencing as an endogenous defense against these diseases. Although no disease related SNPs have yet been reported in L13a gene however, we anticipate that manipulation of such pathways may offer novel therapeutic strategies against human inflammatory diseases.

Biography

Barsanjit Mazumder has completed his PhD at the age of 28 years from Bose Institute, Jadavpur University, India and Postdoctoral Studies from Cleveland Clinic. He is now the Professor of Molecular Genetics, in the Center for Gene regulation in Health of Disease of the Department of Biological Science of Cleveland State University. He has been awarded several major grants from NIH and American Heart Association and published more than 35 papers in high visibility journals including Cell, Molecular Cell, Molecular & Cellular Biology, and Journal of Immunology etc., and served as a reviewer of many funding organizations.

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