BIC Augments the Proliferative Effects of miR-155 in Diffuse Large B Cell Lymphoma Via Downregulation of Tumor Suppressor and Anti-Apoptotic Targets

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Diffuse Large B Cell Lymphoma (DLBCL) is the most common form of Non-Hodgkin's Lymphoma. Current chemotherapy fails in approximately 50% of patients; consequently, understanding DLBCL pathogenesis is crucial to improving treatments. Non-coding RNAs, including microRNAs and long non-coding RNAs (lncRNAs) are linked to gene regulation and potentially oncogenic. miR155 (microRNA) and its host gene, BIC (lncRNA) are overexpressed in DLBCL, but only miR155 has a demonstrated role in DLBCL. To investigate BIC's role in DLBCL, three distinct plasmids (BICmiR overexpressing BIC and miR155, BICdel overexpressing BIC alone, and empty vector) were created and transfected into U2932 cells. BIC overexpression independently enhanced cell proliferation, as BICdel cells significantly increased proliferation compared to empty vector, suggesting a role for BIC beyond hosting miR155. Additionally, increased BIC expression in BICdel cells prompted increased miR155 levels, suggesting potential regulation through positive feedback. To better understand BIC and miR155 functions, potential BIC and miR155 targets were computationally rank ordered via Spearman's ρ analysis of RNA-Seq data from the TCGA-DLBC database and identified by subsequent Gene Set Enrichment Analysis. Candidate targets were verified: BICmiR cells showed decreased expression of NRAS, VAV2, and CDC42 compared to BICdel cells, suggesting three novel miR155 targets. In both BICdel and BICmiR cells, IRF4 and CFLAR were downregulated, suggesting two novel BIC targets. Collectively, the data suggests distinct functions for miR155 and BIC in DLBCL, and further research into the role of BIC may aid in the development of more effective DLBCL therapies.