DOI 10.18699/WIBSB-2018-22

Promoter-pathway analysis approach to interpretation of microarray data of the antitumor peptide CIGB-552

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Key words: CIGB-552, cytotoxic peptide, promoter analysis, pathway analysis

Motivation and Aim: CIGB-552 is a novel synthetic peptide derived from the antimicrobial peptide LALF32-51 (Limulus sp) which has been shown to be a potential candidate for the anticancer therapy and one of its useful property is the cell-penetrating capacity. COMMD1 is a newly recognized pleotropic protein that plays an important role in inflammation, hypoxic response and cell survival. Others have also demonstrated that COMMD1 levels are reduced in some cancers, which is associated with reduced survival. A strategy is presented that allows a causal analysis of co-expressed genes, which may be subject to common regulatory influences. Promoter analysis for potential transcription factor (TF) binding sites in combination with a network-based analysis of the upstream pathways that control the activity of these TFs is shown to lead to hypothetical master regulators.

Methods and Algorithms: Transcriptomics studies were conducted for the identification of molecular mechanism and cellular targets of CIGB-552 peptide. TF analysis was conducted using iRegulon and geneXplain. Networks were visualized in Cytoscape.

Results: The result of the promoter analysis comprises enriched TF-binding motifs for each cluster of up- and down-regulated genes. When we followed the upstream activation pathways of the TFs potentially involved in the (co-)regulation of the differentially expressed genes, we found the potential master regulator of the up-regulated genes. Altogether, we noticed that the suggested master regulators are involved in promoting tumor progression and/or apoptosis.

Conclusion: In this study, we show that CIGB-552 regulates pathways that are known to play essential roles in apoptosis or cancer development.

References

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