

A Web-Based Systems Immunology Toolkit Allowing the Visualization and Comparative Analysis of Publically Available Collective Data to Decipher Immune Regulation in Early Life

Authors : Mahbuba Rahman, Sabri Boughorbel, Scott Presnell, Charlie Quinn, Darawan Rinchai, Damien Chaussabel, Nico Marr

Abstract : Collections of large-scale datasets made available in public repositories can be used to identify and fill gaps in biomedical knowledge. But first, these data need to be made readily accessible to researchers for analysis and interpretation. Here a collection of transcriptome datasets was made available to investigate the functional programming of human hematopoietic cells in early life. Thirty two datasets were retrieved from the NCBI Gene Expression Omnibus (GEO) and loaded in a custom, interactive web application called the Gene Expression browser (GXB), designed for visualization and query of integrated large-scale data. Multiple sample groupings and gene rank lists were created based on the study design and variables in each dataset. Web links to customized graphical views can be generated by users and subsequently be used to graphically present data in manuscripts for publication. The GXB tool also enables browsing of a single gene across datasets, which can provide information on the role of a given molecule across biological systems. The dataset collection is available online. As a proof-of-principle, one of the datasets (GSE25087) was re-analyzed to identify genes that are differentially expressed by regulatory T cells in early life. Re-analysis of this dataset and a cross-study comparison using multiple other datasets in the above mentioned collection revealed that PMCH, a gene encoding a precursor of melanin-concentrating hormone (MCH), a cyclic neuropeptide, is highly expressed in a variety of other hematopoietic cell types, including neonatal erythroid cells as well as plasmacytoid dendritic cells upon viral infection. Our findings suggest an as yet unrecognized role of MCH in immune regulation, thereby highlighting the unique potential of the curated dataset collection and systems biology approach to generate new hypotheses which can be tested in future mechanistic studies.

Keywords : early-life, GEO datasets, PMCH, interactive query, systems biology

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