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Uncovering Time-resolved Regulation from Proliferating to Resting B Cell Progenitors by Network-based Multi-omics Data Integration

Abstract:
Whereas stages of B cell progenitor differentiation have been well characterized, our understanding of how regulatory programs govern the associated dynamics between discrete stages of differentiation is rudimentary. To fill this gap, we perform a time-resolved multi-omics profiling that delineates the sequential regulatory changes in mouse during the transition from proliferating to resting pre-B cells. First, we identify time-derived functional modules (clusters) of coding genes and micro-RNAs; next, our methodological approach is to construct regulatory networks by characterizing the functional modules using many layers of regulatory information: RNA-seq, miRNA-seq, RRBS-seq and DNase-seq. We identify novel TFs associated with early stages of pre-B cell differentiation. Moreover, we recovered signatures linked to with the cell-cycle arrest such as FoxO1 and E2f1. Furthermore, our networks assess the functional role of miRNA, DNA Methylation, and enhancers. We exploit single-cell RNA-seq data to validate transitional changes in networks. Finally, we address two questions: the role of the newly discovery TFs in the regulation of primary mouse B-cells, and their relevance as novel targets of human leukemia.

About:
David Gomez-Cabrero is currently a Senior Lecturer at King's College London, UK, and Assistant Professor at the Karolinska Institutet, Sweden. He holds a PhD in Mathematics and has extensive training in quantitative sciences (MSc Statistics, MSc Operations Research). Before landing in Biomedical research he studied two years in Medical School and participated in several Computational Neuroscience related research projects. Dr. Gomez-Cabrero's research interests are (i) pipeline development in bioinformatic analysis, (ii) developing novel data-integration methodologies and (iii) uncovering disease trajectories. David has been collaborating with clinical researchers investigating Multiple Sclerosis, Rheumatoid arthritis, COPD and Cancer among other diseases.