Team Lead Proposal

Tony Liang, Jeffrey Tang, Aditi Srinivasan, Sam Munn

University of British Columbia

2024-01-29

Background

Cytokines are small intercellular signalling protein that regulate immune responses by acting on various pathways

There are two types of cytokines (Type 1 or Type 2)[1]:

- Type 1 favours the development of strong cellular immune responses
- Type 2 favour a strong humoral immune response

Regulatory mechanisms in the context of cytokine induced signaling is well studied but there is limited ability to link back these cytokine induced activities on all gene expression activity partially due to short half-lives and pleiotropy[2]

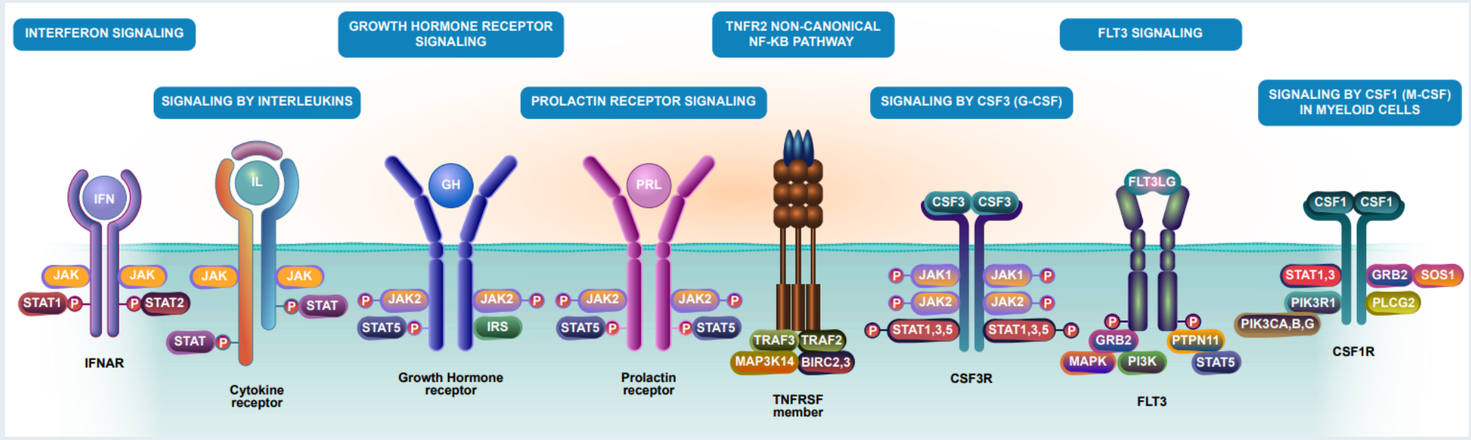

Figure 1: Cytokine secretion occurs and response to inmmmune stimuli and act briefly locally at very low concentration [3]

Question/Hypothesis

- Can we leverage cytokine stimulated perturbation data to better understand gene expression using bulk RNA sequencing data comparing to control?
- Other than the interleukin genes (*IL-6*, *IL-10*, *IL-12*, etc.), which other genes demonstrate a change in expression level when a cytokine response is triggered?

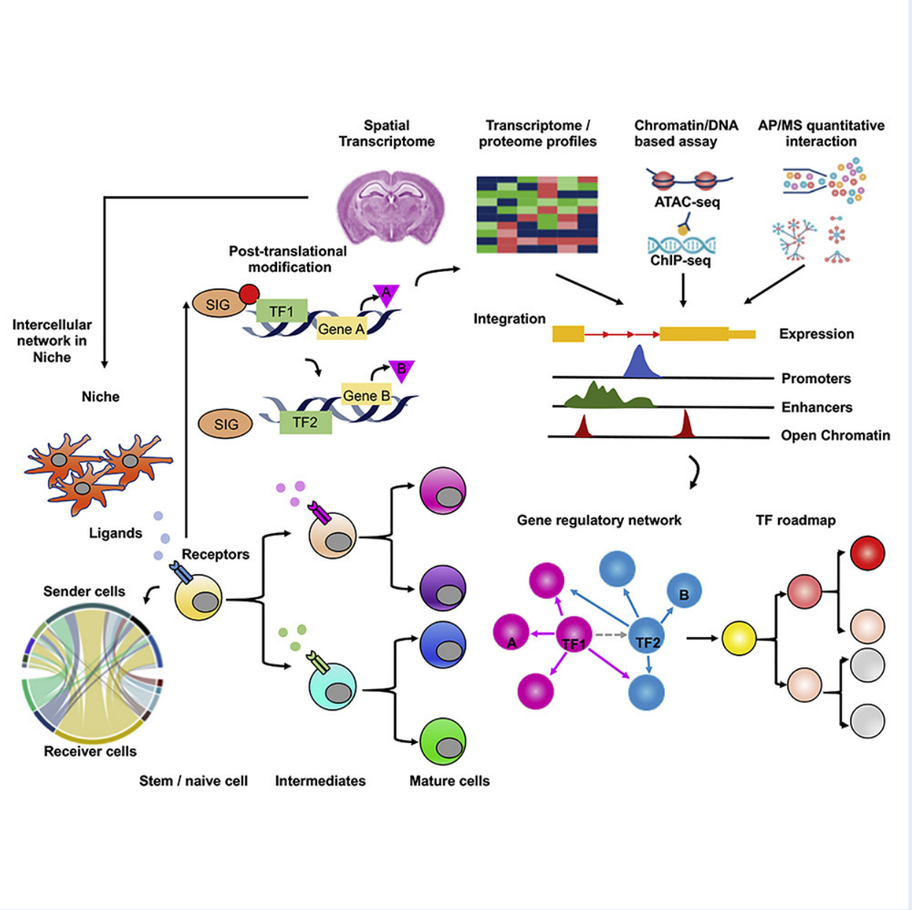

Figure 2: Network Approaches for Dissecting the Immune System[1]

Data Source

Retrieved from public database GEO[1]

Table 1: Metadata of dataset to benchmark from GEO

GSE ID	Data Type	Number of patients	Sequencing platform	Dataset Description
GSE231345	RNA-Seq	60	NextSeq 2000	Induced gene expression in response to IL-6 and IL-10 in macrophage cells in mice
GSE241939	RNA-Seq	168	NextSeq 2000	Differential gene expression in live mice after IL-12 was adminstered using nanospheres
GSE220433	RNA-Seq	20	Illumina NovaSeq 6000	Recovery of gene expression in exhausted T cells is induced by Ibrutinib

1. Gene Expression Omnibus, public funtional genomics data repository at here

Analysis Plan

How will you answer your main research question?

- We propose performing differential expression analysis on a series of cytokine stimulated mice samples
- Next we will perform enrichment analysis to see what genes are influenced by the cytokine-specific stimulant comparing this with control
- We may propose some gene regulatory networks based on the relationships of genes and assess if the hub gene is the cytokine

Questions?

References

Hao Shi, Koon-Kiu Yan, Liang Ding, Chenxi Qian, Hongbo Chi, and Jiyang Yu. 2020. “Network Approaches for Dissecting the Immune System.” *iScience* 23 (8): 101354. https://doi.org/https://doi.org/10.1016/j.isci.2020.101354.

Jiang, Peng, Yu Zhang, Beibei Ru, Yuan Yang, Trang Vu, Rohit Paul, Amer Mirza, et al. 2021. “Systematic Investigation of Cytokine Signaling Activity at the Tissue and Single-Cell Levels.” *Nature Methods* 18 (10): 1181–91.

Lucey, Daniel R, Mario Clerici, and Gene M Shearer. 1996. “Type 1 and Type 2 Cytokine Dysregulation in Human Infectious, Neoplastic, and Inflammatory Diseases.” *Clinical Microbiology Reviews* 9 (4): 532–62.

Resch, Klaus. 2005. “Cytokines.” In *Principles of Immunopharmacology*, edited by Frans P. Nijkamp and Michael J. Parnham, 45–61. Basel: Birkhäuser Basel. https://doi.org/10.1007/3-7643-7408-X_4.