Understanding gene regulatory networks (GRNs) in muscle-invasive bladder cancer (MIBC) subtypes

Bladder cancer is not just a single disease, there are many different kinds of bladder cancer each presenting with different symptoms, genetic features and prognosis. We must learn what genetically differentiate each subtype in order to enhance treatment by designing targeted therapy which contributes to achieve effective precision medicine

Zhang et al. (2021) delve deeply into this complexity by analysing gene regulatory networks (GRNs) in muscle-invasive bladder cancer (MIBC). GRNs are systems that control how genes communicate with one another in MIBC, which assist in revealing how genetic regulation varies across subtypes and impact disease outcomes. Muscle invasive bladder cancer is a type of cancer that is aggressive and genetically diverse. Worldwide we are currently facing the “one size fit all “challenge when it comes to treatment. However, this variability is not taken into account by the majority of treatments. For many people, this can result in unneeded side effects and poor outcomes.

Five molecular subtypes were identified by the researchers through the analysis of gene expression data from more than 400 MIBC patients using sophisticated computational techniques. Then, in order to understand how gene connections change among subtypes, they constructed differential gene regulatory networks. Their research highlights important genes such as NOTUM, SERPINI1, and FGFR1 that showed both expression and regulatory variations within subtypes, indicating that they may be useful treatment targets or biomarkers.

They also discovered two basic pathways that were consistently disrupted across subtype comparisons which were cytokine-cytokine receptor interaction and neuroactive ligand-receptor interaction. Cytokine-cytokine receptor interaction is responsible for regulating immune response and inflammation while neuroactive ligand-receptor interaction is usually related with neural communication but also shown impact to cancer progression, making the two pathways attractive targets for therapeutic research. Below are two figures showing the two important pathways.

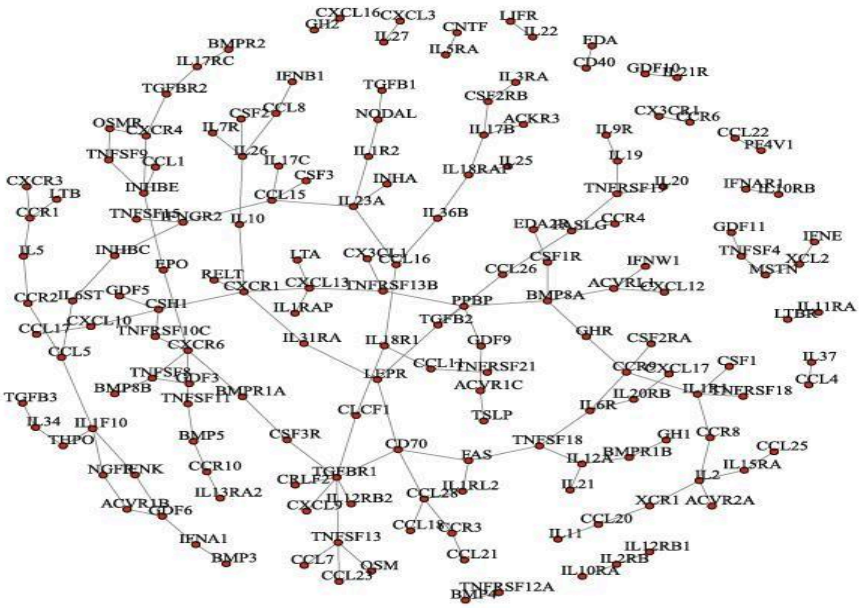

Fig. 5 Differential networks on Cytokine-cytokine receptor interaction between Luminal and Neuronal. The node represents the gene on the pathway, and the edge is the regulatory differences between the two subtypes

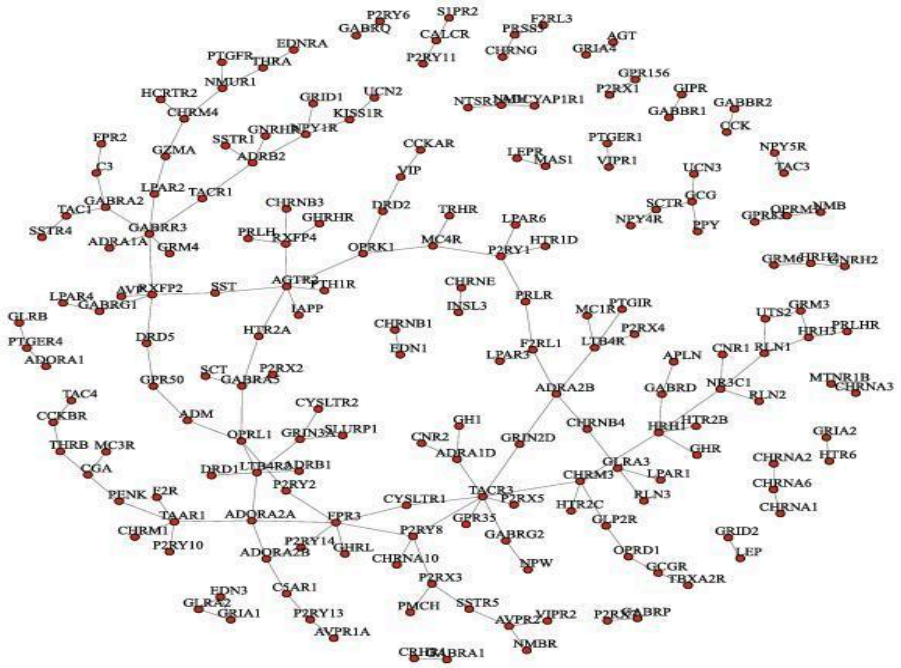

Fig. 6 Differential networks on Neuroactive ligand-receptor interaction between Luminal-infiltrated and Basal-Squamous.The nodes represents the gene on the pathway, and the edge is the regulatory differences between the two subtypes

This study brings us closer to tailored bladder cancer treatment by identifying the distinct regulatory "fingerprints" of each subtype. With more study, particularly with single-cell technology, we may soon be able to customize medicines to the genetic wiring of an individual's cancer.

References:

Zhang Y, Chen Q, Gong M, Zeng Y, Gao D. (2021). Gene regulatory networks analysis of muscle invasive bladder cancer subtypes using differential graphical model. BMC Genomics 22 (Suppl 1). 22: 863. https://doi.org/10.1186/s12864-021-08113-z