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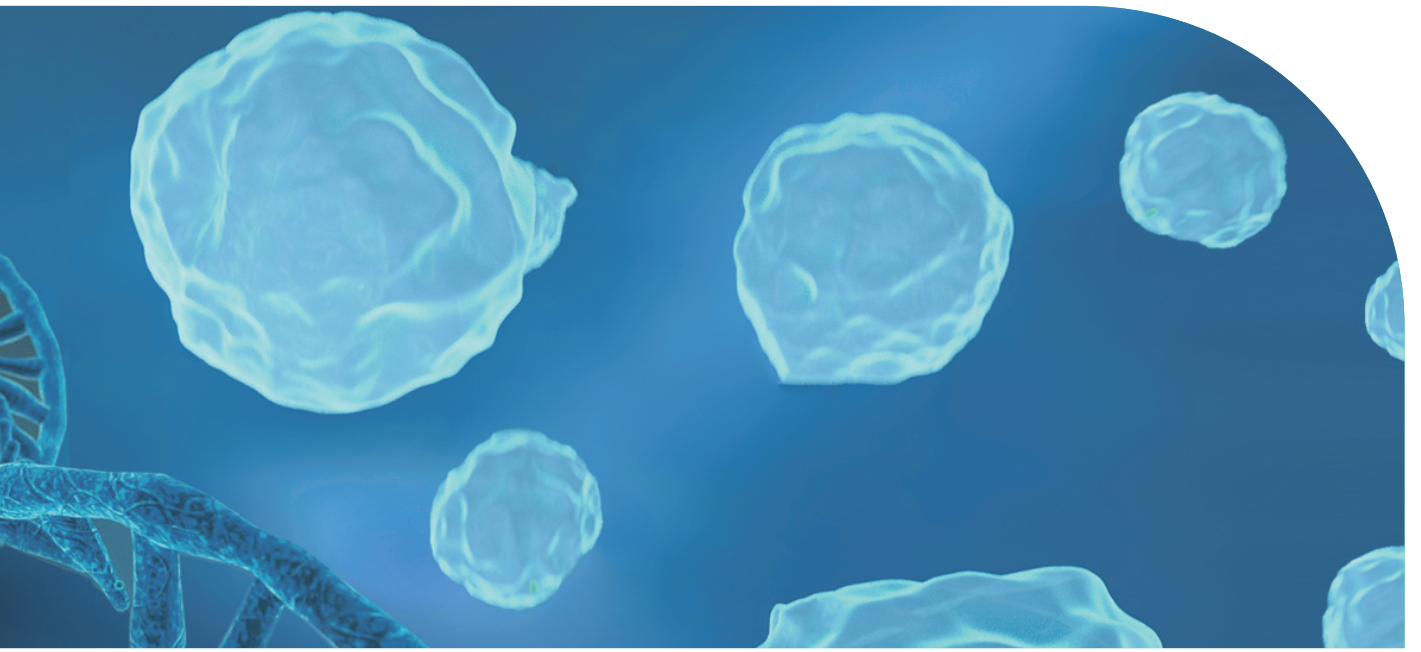


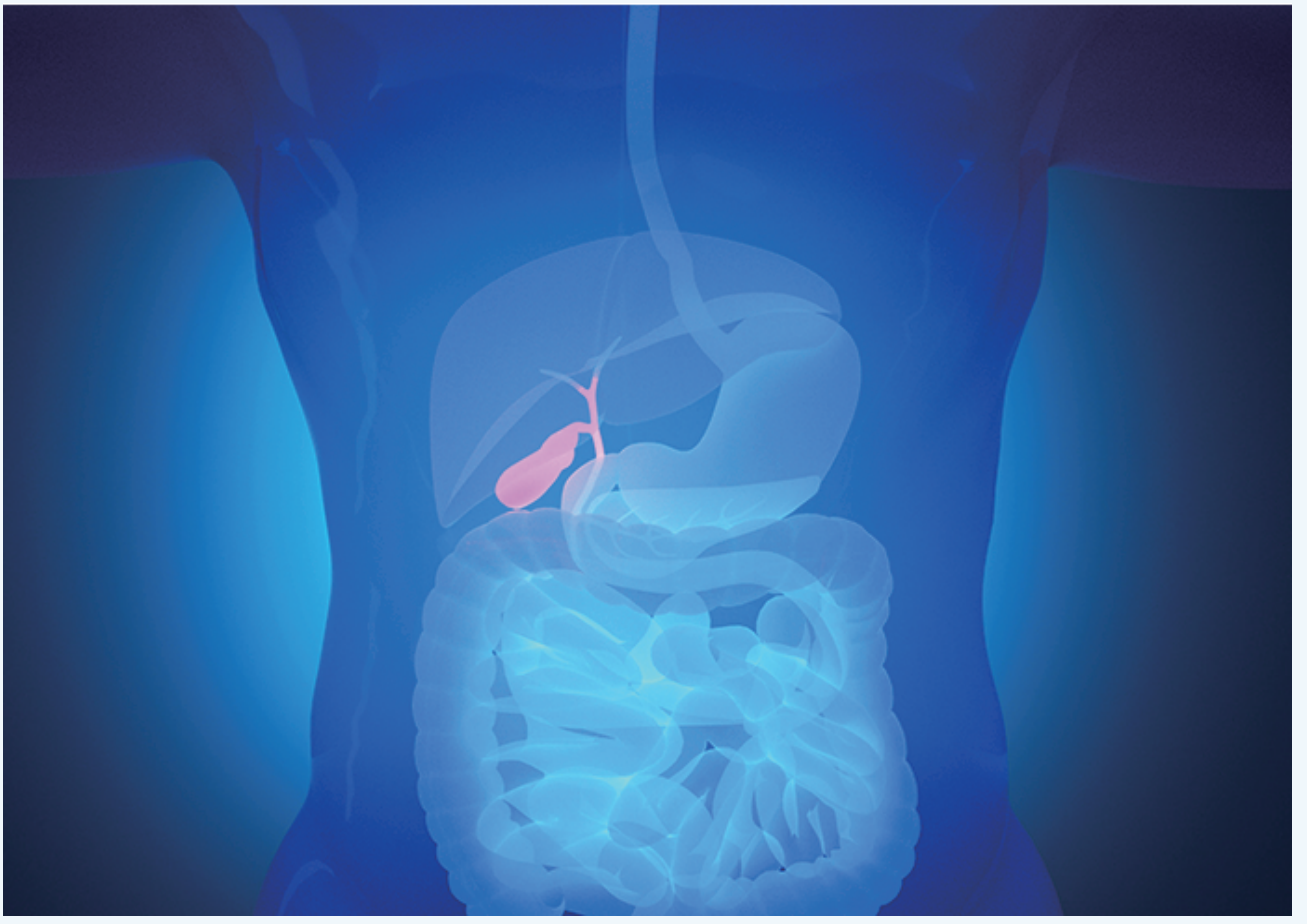
Single-cell RNA-sequencing atlas reveals an MDK-dependent immunosuppressive environment in ErbB pathway-mutated gallbladder cancer

Advancing Genomics, Improving Life

Case Study

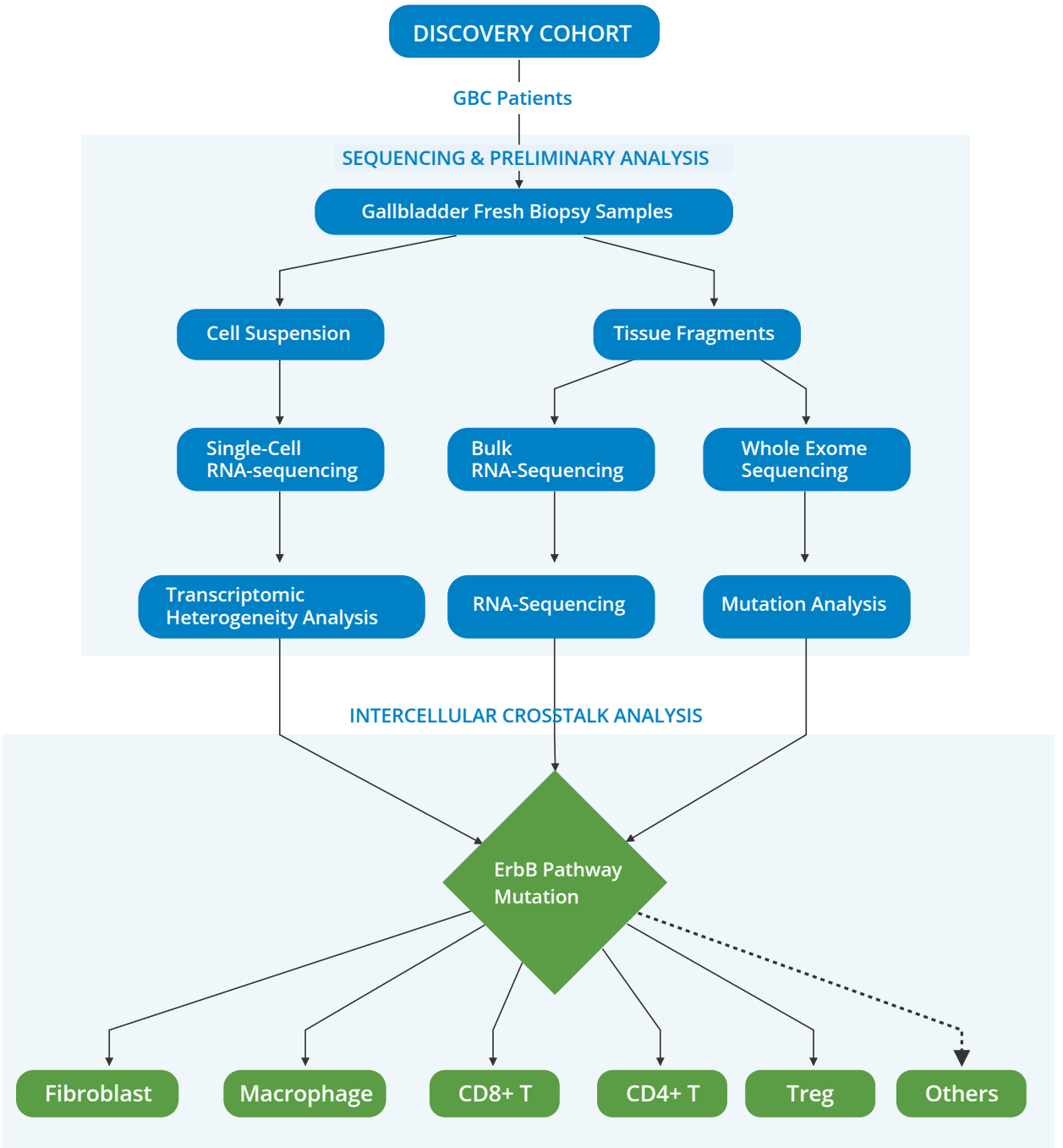
Introduction

Gallbladder carcinoma (GBC) is the most common cancer of the biliary tract and the sixth most common type of gastrointestinal cancer worldwide. Growing evidence suggests that genomic alterations acquired during oncogenesis help tumor cells to escape immune surveillance. ErbB signaling is the most extensively mutated pathway that mediates anti-tumor immunity. This study took advantage of the newly created scRNA-seq technology to test the hypothesis that individual cellular components of the tumor microenvironment (TME) in GBC function differentially to participate in ErbB pathway mutation-dependent tumor progression.



Research Strategy

- This study engaged single-cell RNA-sequencing to reveal transcriptomic heterogeneity and intercellular crosstalk from 13 human GBCs and adjacent normal tissues.
- WES analysis was performed to reveal the genomic variations related to tumor malignancy.
- A variety of bulk RNA-sequencing, immunohistochemical staining, immunofluorescence staining and functional experiments were employed to study the difference between tissues with or without ErbB pathway mutations.



Research Strategy

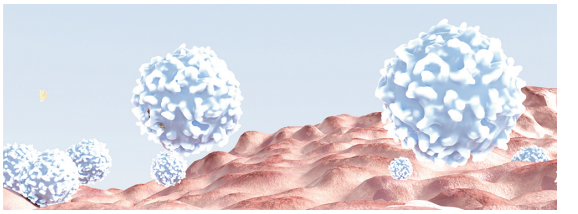
Results

- Tumors with ErbB pathway mutations harbored a larger population of subtype 1 and 2 epithelial cells, Tregs, and M2 macrophages.
- Increased MDK in these tumors interacted with its receptor LRP1 to promote immunosuppressive macrophage differentiation.
- Crosstalk between macrophage-secreted CXCL10 and its receptor CXCR3 on Tregs was induced in GBC with ErbB pathway mutation.

Conclusion

This study provided valuable insights into transcriptomic heterogeneity and the global cellular network in the TME, which coordinately functions to promote the progression of GBC with ErbB pathway mutations; thus, unveiling novel cellular and molecular targets for cancer therapy.

Primary reference, (Zhang et al., 2021)



References

Zhang, Y., Zuo, C., Liu, L., Hu, Y., Yang, B., Qiu, S., Li, Y., Cao, D., Ju, Z., Ge, J., Wang, Q., Wang, T., Bai, L., Yang, Y., Li, G., Shao, Z., Gao, Y., Li, Y., Bian, R., ... Liu, Y. (2021). Single-cell RNA-sequencing atlas reveals an MDK-dependent immunosuppressive environment in ErbB pathway-mutated gallbladder cancer. *Journal of Hepatology, 75*(5), 1128–1141. https://doi.org/10.1016/J.JHEP.2021.06.023

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