GBSBC

Genetics, Bioinformatics, & Systems Biology Colloquium

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presents

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Thursday, April 11th 2024 | **12PM** | **Leichtag Auditorium** | **Zoom**

LIVE IN-PERSON with Pizza
*Live stream via Zoom available

"Forecasting pancreatic carcinogenesis through spatial multi-omics"

Combining genomics with mathematical modeling provides a forecast system that can yield computational predictions to anticipate cancer progression and therapeutic response. High-throughput profiling technologies can indicate the molecular and cellular pathways of malignancies, but not the effect of targeting those pathways with therapy. Precision interception requires relating therapies to the cellular phenotypes underlying pancreatic carcinogenesis. This talk presents a hybrid computational and experimental strategy to uncover interactions between neoplastic cells and the microenvironment during pancreatic carcinogenesis. As pancreatic cancer develops, it forms a complex microenvironment of multiple interacting cells. The microenvironment of advanced pancreatic cancer includes a heterogeneous and dense population of cells, such as macrophages and fibroblasts, that are associated with immunosuppression. New single-cell and spatial molecular profiling technologies enable unprecedented characterization of the cellular and molecular composition of the microenvironment. These technologies provide the potential to identify candidate therapeutics to intercept immunosuppression in pancreatic cancer. State-of-the-art mathematical approaches in computational biology are essential to uncover mechanistic insights for high-throughput data for these precision interception strategies.

We have recently applied new machine learning techniques to integrate imaging and spatial transcriptomics to enable comprehensive characterization of the pancreatic precancer microenvironment. Developing targets for interception requires determining which of these cellular and molecular pathways drive subsequent development of cancer. Relating the transcriptional programs in premalignant lesions to carcinogenesis requires mapping their temporal changes across disease stages. To integrate the spatial molecular data from premalignancies and single-cell RNA-seq reference atlases, we developed a transfer learning approach. This integrated analysis identified a switch between fibroblast-induced inflammatory signaling and cellular proliferation in pancreatic cancer cells. We confirmed these transitions also occur in pancreatic cancer patient derived organoids co cultured with fibroblasts using transfer learning from the reference scRNA-seq atlases of pancreatic tumors. This approach demonstrates the potential of computational analysis of multi-omics data in human tissue with organoid models for bidirectional bench to bedside research.

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