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Investigating cytokines as biomarkers for macrophage therapy of advanced lung cancer

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nTTP-GCT-Cohort 2025

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Background

Cell-based therapies have shown great success against blood borne cancer, but the approach has been difficult to adopt to more frequent solid tumors, including non-small cell lung cancer (NSCLC). In principle macrophages–immune cells that can naturally infiltrate tumors – could overcome this problem, but so far their therapeutic utility has remained limited. This is because, traditionally, these cells can't be expanded efficiently in the lab, and once inside the body, tumors can “reprogram” macrophages to support rather than fight cancer.

Researchers in the Sieweke Laboratory have developed a breakthrough method to overcome these challenges. They have created special genetically modified macrophages that can be expanded *ex vivo* and maintain their natural ability to attack cancer cells.

Patient stratification is a critical criterium for the therapeutic success of cellular therapies. Macrophages rely on certain survival signals—including critical cytokines that affect macrophage survival and activity. Tumors like NSCLC often produce enormous levels of such cytokines that vary with tumor size and progression stage. After passing into the blood circulation they can transmit information to monocytes–a macrophage precursor cell–to support growth of new macrophages but also to change their activity and gene expression profile. Patient monocytes exposed to tumor produced cytokines thus possess a distinct transcriptional signature that correlates with tumor burden and stage.

The Project

This project aims to identify gene expression signatures in monocytes of cancer patients as a proxy of cytokine levels in the blood that can be used as a biomarker—as simple measurable signal to predict how well a patient might respond to macrophage therapy. The study will test this in lab-based experiments, with the goal of identifying the right patients for upcoming clinical trials targeting relapsed or treatment-resistant NSCLC.

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