QUEBEC+ NEUTROPHIL MEETINGS

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Directing Granulocytic Networks to Orchestrate Metabolic Sensitivity in Breast Cancer: Adjusting the Spotlight on Anti-Tumor Neutrophils

The tumor microenvironment (TME) is a complex arms race composed of host immune cells, stroma, and ever-adapting cancer cells. Comprising major components of the TME, exploiting tumor-associated inflammation has long been sought for therapeutic purposes. Our group identified inflammatory responses in breast cancer cells that elicit sensitivity to oxidative stressors, namely the complex I inhibitor, phenformin. In our immune-competent murine breast cancer models, sensitivity to phenformin was modest. However, sensitivity was largely improved when combined with TLR3/4 agonists (the dsRNA-mimic, poly I:C; or the synthetic lipid A analog, CRX527). Given the large role of the innate immune system in the generation of this pathogen-associated inflammation, we analyzed systemic and tumor-infiltrating leukocyte diversity in our models by single-cell RNA-sequencing and flow cytometry. Combination therapy induced the expansion of specific CD11b+ Ly6G+ neutrophil populations in the blood and the TME. Using high-throughput proteomics, we highlight differential granule production and frequency which correlates with increased ROS production in cancer cells and synergizes with complex I inhibitors. The granulocyte-dependent tumoricidal synergy between oxidative stress and inflammation has not yet been described, establishing these findings as novel additions to the field of tumor-immune biology.

FRIDAY	TIME
9 February 2024	09:00-10:00 am

Zoom Meeting ID:
814 254 6865

For more information:
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