entre níveis elevados de índice de saturação da transferrina e a presença de SM. A hiperferritinemia demonstrou relação significativa com componentes da SM, sobretudo com resistência à insulina, dislipidemia, aumento da circunferência abdominal e alterações no metabolismo lipídico. É válido destacar também o aumento da ferritina em pacientes do sexo masculino, sugerindo influência hormonal na regulação do ferro. Parâmetros como hepcidina elevada, capacidade de ligação do ferro reduzido e transferrina baixa também favorecem o aumento da gordura visceral. Outro ponto verificado na análise dos artigos, foi que a elevação de hepcidina, estimulada por inflamação crônica, promove o acúmulo intracelular de ferro, levando à sobrecarga tecidual e disfunção do tecido adiposo, principalmente em pacientes obesos, a qual está diretamente relacionada à progressão da resistência insulínica e da adiposidade visceral. Discussão: Os achados evidenciam que a hiperferritinemia é um marcador clínico importante na SM, fato que evidencia a sobrecarga de ferro e a inflamação crônica. Outros fatores como triglicerídeos elevados, obesidade abdominal e sexo masculino se mostraram importantes preditores da ferritina elevada, indicando risco cardiovascular e metabólico aumentado. Outro ponto de destaque é que a hepcidina parece desempenhar papel central na retenção de ferro e sua deposição tecidual, potencializando a disfunção do tecido adiposo e agravando a resistência insulínica. Diante disso, a utilização em conjunto de marcadores como ferritina e hepcidina podem oferecer melhor entendimento do perfil de pacientes com SM. Conclusão: Os estudos analisados demonstraram uma associação consistente entre a hiperferritinemia e a SM, sobretudo com resistência à insulina, dislipidemia e obesidade abdominal. Esses achados indicam que níveis elevados de ferritina sérica podem evidenciar não apenas a sobrecarga de ferro, mas também processos inflamatórios e disfunções metabólicas. Além disso, a ferritina, em conjunto com marcadores como a hepcidina, apresenta potencial como biomarcador complementar na avaliação do risco metabólico.

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SPHEROMAP CYTOMETRY: A PLATFORM TO EVALUATE STRATEGIES ENHANCING IMMUNE CELL INFILTRATION IN IMMUNOCOMPETENT SOLID TUMOR MODELS

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Introduction: The failure of immunotherapies in solid tumors, including pancreatic ductal adenocarcinoma (PDAC), is often attributed to poor immune cell infiltration and a highly immunosuppressive tumor microenvironment (TME). PDAC, in particular, is characterized by a dense stromal matrix and hypoxic gradients that create physical and functional barriers to immune cell entry. Developing therapies that enhance T-cell infiltration into solid tumors requires preclinical platforms that recapitulate key features of the immunocompetent TME. **Aim:** Here, we present SpheroMap Cytometry, an innovative spatial flow cytometry method designed to quantitatively assess immune cell localization within tumor spheroids under physiologically relevant conditions. **Material and methods:** Heterotypic spheroids were generated by co-culturing CAPAN-1 pancreatic tumor cells with either HS-5 bone marrow stromal or umbilical cord-derived mesenchymal stromal cells (UC-MSCs). After 24 hours aggregation 100,000 PBMCs (pre-activated or not) were added to infiltrate spheroids. The Image-iT Green Hypoxia probe was applied to define hypoxic regions, and after 72 hours spheroids were enzymatically dissociated and analyzed for T-cell markers (CD3, CD4, CD8, CD25, CD127) using flow cytometry. **Results:** In tumor-HS-5 spheroids, pre-activation of PBMCs increased $CD3^+$ infiltration into the hypoxic core (79.3% *vs.* 66.2% $p < 0.01$), doubled the proportion of $CD8^+$ cells (46.1% *vs.* 24.8%), and significantly raised $CD8^+CD25$high cells (39.8% *vs.* 9.7% $p < 0.001$). However, this was accompanied by a rise in $CD4^+CD25^+CD127^-$ regulatory T cells (Tregs) from 18.3% to 48.9% ($p < 0.001$), indicating that T-cell activation enhances cytotoxic infiltration but also promotes suppressive phenotypes. In contrast, spheroids formed with UC-MSCs showed reduced $CD8^+$ infiltration and enhanced Treg induction, consistent with the known immunomodulatory effects of mesenchymal cells. Notably, $CD8^+$ infiltration and activation profiles differed significantly between normoxic and hypoxic compartments, demonstrating that oxygen gradients critically modulate immune cell function and localization. In another study (abstract is also being presented at this event) using SpheroMap Cytometry technique, we found that hypoxia also modulates the stromal component, favoring the emergence of cancer-associated fibroblasts with a myofibroblast profile, which contributes to desmoplasia through extracellular matrix deposition, leading to immunosuppression by excluding immune cells. **Discussion and conclusion:** These findings highlight the complex interplay between hypoxia, stromal context and immune activation in determining the quality and distribution of infiltrating lymphocytes. SpheroMap Cytometry enables precise quantification of these dynamics, making it an ideal platform for testing therapies aimed at overcoming immune exclusion. The ability to track lymphocyte phenotypes within spatially defined tumor compartments makes this approach well-suited to evaluate the impact of checkpoint inhibitors, CD73/adenosinergic pathway blockers and next-generation CAR-T cell therapies in immunocompetent models. This study was funded by the São Paulo Research Foundation (FAPESP) Brazil, process #2022/12856-6; the Brazilian Federal Agency for Support and Evaluation of Graduate Education (CAPES); and the National Council for Scientific and Technological Development (CNPQ).

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