High-Dimensional Single-Cell based functional immuno-metabolism by ZeNITH Identifies Conserved energetic programs in Human and Mouse myeloid cells

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Metabolic interactions between immune cells and tumors represent an emerging hallmark of cancer. However, evidences that support the complex metabolic interactions are difficult to obtain because current methods are not suited for studying heterogeneous samples from human and mouse tissues. We present here, a novel method we have recently developed and patented, called ZeNITH (EP18305110.1, Argüello RJ, et al; Inserm-Transfert). Our method, allows for functionally profile energetic metabolism in single cells by Facs. ZeNITH allows for metabolic deconvolution to analyze in parallel the composition, phenotype a d metabolic function in all the cells present in a sample. ZeNITH is performed rapidly ex vivo and after deconvolution it allows to determine in parallel the metabolism profile of up to 37 different cell types present in one sample. We used this method to compare the metabolic profile of human and mouse blood and bone marrow derived DCs. Moreover, we analyzed solid tumors from mouse and human patients. we observed that while bone marrow derived DCs are less glycolytic than the the dendritic cells in the tumors and that blood Monocytes show increased but heterogenebut levels of mitochondrial dependence. Moreover, we have performed paralleled single cell RNA-seq and ZeNITH of the same human tumor samples and identified a small set metabolic genes that strongly correlate with functional metabolic profile of human myeloid cells. ZeNITH allowed us to identify a conserved metabolic profile evolution of monocytes to macrophages differentiation upon migration into tumors. ZeNITH has the potential to contribute to immuno-classify cancers and define treatment response profiles in patients and represents a unique opportunity to explore new fields of immune-metabolism research.

Keywords : Novel method, dendritic cells, macrophages, tumor, metabolism
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