Whole-organ analysis of the tumor microenvironment by tissue clearing

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Stochastic and proliferative events initiating from a single cell can disrupt homeostatic balance and lead to fatal disease such as cancer metastasis. To overcome metastasis, it is necessary to detect and quantify sparsely-distributed metastatic cells throughout the body in the early stages. Here we demonstrate that CUBIC (clear, unobstructed brain/body imaging cocktails and computational analysis)-based cancer (CUBIC-Cancer) analysis with a refractive-indices (RI) optimized protocol enables comprehensive cancer cell profiling in whole body and organs. CUBIC-Cancer analysis is applicable to a dozen mouse models using several cancer cells and spatio-temporal quantification of metastatic cancer progression at single-cell resolution. CUBIC-Cancer analysis is applicable to profiling of the remodeling of the tumor microenvironment. The scalable analytical pipeline with these three modalities would contribute to overcome incurable metastatic diseases.