1290 QUANTITATIVE CELL MORPHOLOGY FEATURIZATION IN MULTIPLEXED IMMUNOFLUORESCENCE IMAGES REVEALS TUMOR SUBTYPES IN CANCER MICROENVIRONMENTS

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Background Cell morphology, the study of cellular form and structure, provides valuable insights into the diverse characteristics and functions of different cell types. Cell morphology is also indicative of cellular activities and processes, such as cell division, migration, differentiation, and responses to environmental cues. With advances in multiplexed immunofluorescence (mIF) imaging techniques, a powerful technique that allows spatial characterization of dozens of molecules at subcellular resolution, examining in situ cell morphology at scale is possible. Along with molecular information gleaned from mIF imaging, morphology features provide an additional axis of information that can help characterize tumor microenvironments and their component cells. Here, we describe a suite of morphology metrics and their applied utility in characterizing tumor microenvironments.

Methods To thoroughly understand the cells, their neighborhoods, and their interactions using cell morphology in multiplexed immunofluorescence images, we developed a suite of tools for cell morphology featurization and analysis. The extracted morphology features include measurements of each single cell in four categories: orientation, area, length, and shape. These features are derived from cell segmentation, and use both cell intrinsic shape information, as well as contextual information about the relative orientations or alignment of cells. Using the new morphology features, we enhanced analysis methods for cell type phenotyping, cell morphology quantification, tissue partition, and clinical outcome predictions.

Results Our analyses show that the new quantitative cell morphology features reveal cell type morphology quantification, improve cell phenotyping, and uncover tumor subtype morphology. We computed morphology characteristics in a renal transplant sample and quantitatively summarized the morphological differences between distal and proximal tubular cells. We performed cell phenotyping on a head and neck cancer sample and revealed three morphologically distinct subtypes in a CD15-/Ki67- population of tumor cells. We also analyzed a head and neck cancer sample and found that CD15- tumor cells and CD15+ tumor cells have distinct morphologies.

Conclusions Harnessing the quantitative cell morphology features in addition to protein expression patterns, we were able to perform comprehensive analyses on multiplexed immunofluorescence imaging data for distinct tissue subtypes in multiple aspects - morphology characteristic summarization, cell phenotyping, and cell subtype analysis. We showed that cell morphology features and analysis methods presented here may help uncover novel cellular functions and gain critical insights into disease processes and therapeutic interventions.

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