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AstroPath: Astronomy Meets Pathology to Characterize the Tumor MicroEnvironment

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Multispectral, multiplex immunofluorescence (mIF) enables the study of the complex tumor microenvironment (TME) through quantification of key immunomodulatory marker co-expression patterns on specific cells and spatial relationships between different cell types. We have developed a detailed, automated, multi-step approach to mIF staining and image analysis that can support the standardization of results across large, multi-institutional datasets. Our framework for assay development and associated data quality standards for mIF are likely to become universal performance standards for multiple commercial and open source hardware and software offerings. Such universal standards facilitate scaling, particularly important as Tumor-Immune Atlases with billions of cells are generated. These Atlases will be mined by thousands of laboratory and clinical investigators, amplifying the discovery, similar to sky surveys in astronomy.

Using expertise developed over 20 years in astronomy we have built AstroPath to scale up to whole slide analysis by combining a robust hardware infrastructure with a complex processing workflow. We perform automated 35 to 45-band imaging with six Vectra-3 and Vectra Polaris microscopes from Akoya BioSciences. These are then processed, flat-fielded, unwarped, calibrated, segmented, stitched, and loaded into a database. The database and the integrated visual interface, modelled after the SDSS SkyServer, can display complex spatial and multicolor data interactively.

Using the AstroPath pipelines, we have processed 3 cohorts of 235 slides which have all been ingested into the AstroPath database. They contain a total of 184,320 High Powered Fields, 226,619,428 detected cells, of which our unique statistical sample contains 97,041,546 cells, with full geometric boundaries for their nuclei and membranes. In order to support the TME studies, the databases contain precomputed neighbors within 25 microns to each cell, for a total of 3.5 billion cell pairs, with their respective phenotypes. In order to do this, we had to do complex image processing over 8.7 trillion pixels. For comparison, the Sloan Digital Sky Survey (SDSS) has collected about 6.4 trillion raw pixels from the sky over 16 years of imaging.

Our group brings together astronomers from the SDSS, physicists having analyzed LHC data, Machine Vision and Deep Learning experts with pathologists working on cancer. We have heavily relied on lessons from sky surveys. Over the last two years we have worked very hard to adopt theses to multiplex imaging in a systematic fashion. The resulting AstroPath platform demonstrates the feasibility of an automated system feeding into an open public database. It will also lead to open-source tumor-immune Atlases with billions of spatially mapped single cells, enabling analyses at unprecedented scales. Our talk will describe the main features and components of the AstroPath system, and how lessons learned in astronomy have enabled us to short circuit the whole design and implementation process.

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