Journal of Interdisciplinary Histopathology, 2022
VOL 10, NO. 12, PAGE 02

PERSPECTIVE

Open Access

Digital Histopathology of the Tumor Microenvironment

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ARTICLE HISTORY
Received: 26-Nov-2022, Manuscript No. EJMJIH-22-80475; Editor assigned: 28-Nov-2022, PreQC No. EJMJIH-22-80475 (PQ); Reviewed: 12-Dec-2022, QC No. EJMJIH-22-80475; Revised: 19-Dec-2022, Manuscript No. EJMJIH-22-80475 (R); Published: 27-Dec-2022

Description

Innovative tools that allow for a coordinated investigation of the tumour microenvironment and the cellular phenotypes caused by somatic mutations and post-translational changes are crucial for the advancement of cancer research. Understanding tumorigenesis and cancer progression now requires the ability to identify and quantify the actual phenotypes of individual cell populations in situ that is, in their tissue environment, due to the large number of genes, multiplied by differential splicing as well as post-translational protein modifications. Optical equipment and imaging methods are experiencing a renaissance as a result of the demand for quantitative analyses. With the advent of precision medicine, automated analysis of an ever-increasing number of cellular markers and their spatial context measurement have become more and more important to comprehend the molecular mechanisms underlying various disease progression pathways in specific patients.

A significant worldwide health issue is cancer. Over the next 20 years, there will likely be a 70% increase in the number of new cancer cases. Exploring the genomic, transcriptomic, and proteomic nature of cancer is essential for comprehending and utilising treatments for the treatment of cancer because it is believed that cancer results from a deranged genome. The extracellular matrix, which is made up of nearby blood vessels, fibroblasts, signalling cells and molecules, and the microenvironment surrounding the tumour cells are all highly interdependent compartments.

The cancer genome, transcriptomic, and proteome have recently been identified as potent sources of diagnostic, prognostic, and predictive markers/biomarkers as a result of detailed profiling of cancer cells/tissues. In this regard, spatially mapped cellular gene expression has emerged as a key technique to comprehend the localization and complex multicellular interactions of proteins, RNA, and DNA inside cells found in both the tumour and the TME. A deeper understanding of the heterogeneity of the TME both between persons and within the same tumour sample can be achieved by investigating the tumor's cellular organisation environment at the level of the individual cell as well as the cell's interactions with neighbouring cells.

All of the aforementioned studies are excellent illustrations of how tissue cytometry can offer the theoretical foundation for next-generation digital pathology, the cutting-edge technology that makes precision medicine possible in both clinical settings and academic research. By addressing the ideas of next-generation digital pathology using imaging-based tissue cytometry in conjunction with multiplexing and RNA ISH technologies as an emerging and crucial technique within precision diagnostics, and by discussing various applications, we are going a step further in this article.

Multiplexing staining techniques are increasingly important in research and clinical settings to achieve high-content phenotyping, optionally in conjunction with the application of genetic markers for well-defined DNA loci as well as total RNA or specific mRNA measurements, particularly for the purpose of assessing the complex immune and tumour microenvironment status in patients with cancer, graft versus host disease, and other pathological conditions related to immune Assessment of immune cell populations and different immune cell markers is necessary in clinics for prognosis, diagnosis, and choosing the therapeutic intervention strategy. The number of markers that conventional IHC/IF staining techniques can simultaneously detect within a tissue section is a limitation.

The acquisition of a region of interest on the stained slide, at the very least, is the initial step in a tissue cytometry/next-generation digital pathology workflow. The subsequent computer-assisted quantitative picture analysis is the second and even more crucial stage. A fully automated computerised platform for the detection and numerical quantification of stained markers in de-

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fined cell subpopulations in relation to particular histological structures is the goal of next-generation digital pathology technology. It aims to shift the workflow away from visual observation with a standard microscope and subjective estimations, which are funnelled into scoring schemes describing marker expression with "+/++/+++."

The tumour needs neoangiogenesis and the consequent vascularization just like healthy tissues need. Both normal and malignant tissue types require oxygen and nutrients for cell survival and growth, as well as for the elimination of carbon dioxide and metabolic wastes. Tumor angiogenesis is characterised by an uncontrolled, inefficient, frequently incomplete (and thus leaky) growth of new blood vessels within the tumour tissue in order to supply the tumour mass with oxygen and nutrition, in contrast to controlled neoangiogenesis in healthy tissues.

There are several application fields that support next-generation digital pathology, such as RNA ISH analysis, conventional and/or multiplexed immunophenotyping, and tumour microenvironment blood vessel detection. High-dimensional data mining is one of the new challenges brought on by new staining technologies that enable a greater number of markers, and it is this challenge that next-generation digital pathology platform providers need to address.