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Artificial Intelligence in Tumor Microenvironment Research: Hype, Hope, or Both?

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Tumor microenvironment (TME) is a dynamic and heterogeneous niche, which comprises of tumor cells, immune influx, stromal components and extracellular matrix fragments [1]. Its space and molecular complexity pose a significant challenge to the conventional methods of analysis. The artificial intelligence (AI) can learn trends in big amounts of data which is the solution to this complexity [2]. AI models can identify hidden morphological data, multi-omics, and clinical outcomes and thus provide a systems-level understanding of the TME. The integration of digital pathology results and AI is promising in predicting the presence of immune cells and patient prognosis, suggesting an indispensable role of AI in the future of cancer biology [3].

Artificial Intelligence-based characterization of the TME

Deep learning, one of the AI features, has changed the imaging analysis of cells and tissues. Whole-slide images that are analyzed by convolutional neural networks (CNNs) may determine the tumor margins, the different types of immune cells, as well as the spatial organization in the TME [4]. Machine learning techniques have further been used to combine transcriptomic, proteomic and imaging datasets and have uncovered hitherto unknown connections between cellular states and clinical outcomes [5]. In addition, natural language processing (NLP) tools can be used to extract biomedical literature, and can potentially aid in the identification of potential signaling networks that could be used to suppress immunity and angiogenesis. A set of these methods help to reconstruct the TME landscape on a high-resolution level that overcomes the drawbacks of the traditional histopathological analysis [6].

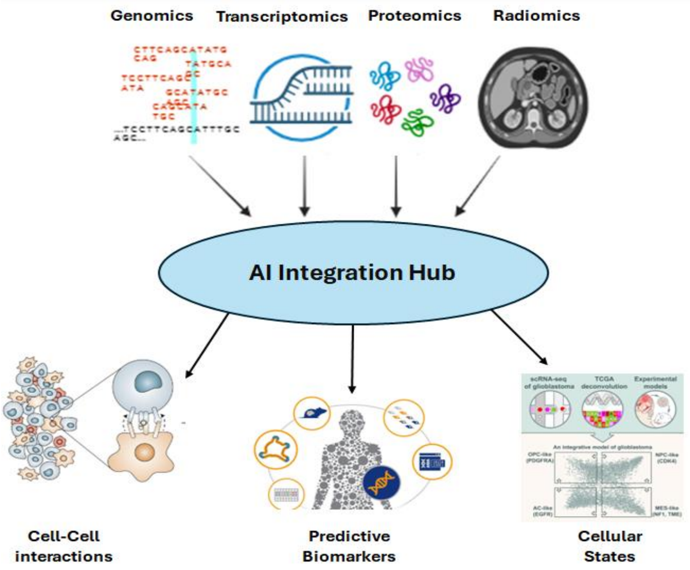

Figure 1: Artificial Intelligence enabled integration of multi-omics and spatial data in tumor microenvironment

Combination of Multi-Omics and Spatial Data

The multiparametric (MP) imaging and spatial transcriptomics technologies generate extensive data, which involve both the localization and gene expression of cells. The AI models that are trained using these datasets are capable of finding important spatial features that are predictive of therapy resistance or immune exclusion [7]. A combination of radiomics and spatial omics can even achieve a greater predictive accuracy, associated with the relationship between imaging phenotypes and molecular change [8]. These integrative models would allow stratification of patients beyond histology, providing a personalized-medicine strategy that specifies treatment based on TME features (Figure 1). Nevertheless, these advantages are highly dependent on the quality of data, harmonization, as well as cross-platform reproducibility [9].

Clinical Usage and Predictive Modeling

Artificial intelligence also plays a significant role in clinical oncology to predict therapeutic response and survival. AI-based models are also able to estimate the response to immunotherapy based on the TME signatures of PD-L1 expression, T-cell density, and stromal activation [10]. Radiomic algorithms also build upon the predictions with a correlation of non-invasive imaging biomarkers with TME composition [11]. Even with these achievements, the standard of linking research to practice is still at a standstill due to the problem of generalizability, model interpretability, and the issue of ethics related to data privacy. However, the regulatory organizations are starting to see the potential of AI-based diagnostic systems, which is a slow transition to clinical integration [12].

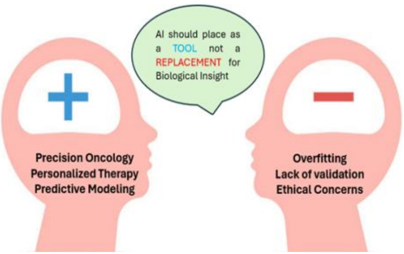

Figure 2: Balancing hype and hope in Artificial Intelligence driven tumor microenvironment research

Problems and Future Projections

Although AI has huge potential, a number of challenges need to be tackled to achieve the maximum significance of AI on TME research. It has little interpretability in the model- black-box, algorithms can detect patterns but are not usually able to provide explanations with respect to biological mechanisms. Lack of data, bias, and heterogeneity between cohorts also pose a reproducibility problem [13]. Further research should be aimed at the explanation of AI structures, creating multi-institutional data stores, and open science collaboration between oncologists, data scientists, and bioinformaticians. The future is not only hype and hope, but with a process of refinement over time, AI can truly be the tool that will lead the next generation of TME-oriented oncology (Figure 2) [14].

Conclusion

AI has shifted the role from a hypothetical invention to a practical tool in the process of decoding the TME. It helps to connect the gap between the large volumes of biological data and practical insight, to discover novel biomarkers and targets of therapy. The success of it, however, lies in the ability of computational intelligence to be synergized with mechanistic biology. The question of whether AI will transform cancer cure or act as a complement to human experience will be decided by the quality of its validation and the openness of its process.

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