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A tale of tumors

Recent technological advances for studying the biology of tumors have expanded our understanding of cancer.

Cancer is one of the most complex and elusive problems in biological research. While decades of research in the field of tumor biology have propelled our understanding of the pathophysiology of cancer, which in turn has enabled interventional and therapeutic strategies, there remain many unanswered questions surrounding this disease.

At *Nature Methods*, we have been closely following progress in this field, especially as recent technological developments advance our ability to investigate the molecular bases of cancer. In this issue, we feature several pieces highlighting recent methods development in this field. These papers and other related content are also available in an online Collection.

The field of cancer research has always been heavily reliant on model animals for modeling the in vivo complexities of human cancers. However, these models fail to fully recapitulate genetic, immune and metabolic features observed in vivo in humans. In addition, the use of animals poses ethical considerations. These challenges are discussed by Kuperwasser and colleagues in their Perspective[1], in which they delve into emerging 2D and 3D organoid systems for modeling tumors in vitro.

One of the key things to keep in mind when developing a high-fidelity tumor model system is that it should capture not only key features of the tumor cells but also the relevant structures and functions of the surrounding tumor microenvironment. In the last few years, research has increasingly pointed towards the critical role of the tumor microenvironment in tumor initiation, progression and response to intervention. In their Review[2], Nia et al. describe the four physical hallmarks of cancer and the tools and models available to advance the emerging field of physical oncology.

It is an established fact that the stromal and immune compartments exert their effects on the tumor and vice versa. However, the involvement of the microbiome in oncogenesis and metastasis or whether it plays any role at all remains a fierce debate in the community. Ma, Spakowicz and colleagues present a Perspective[3] that clarifies some of the confusing terminology in this space and envisages technological and analytical strategies that will generate reliable insights into the properties of the tumor microbiome.

It would be remiss to discuss technological advancements in a field and not mention the burgeoning role of artificial intelligence (AI) approaches. Cancer biology research, like many fields, is being revolutionized by the recent breakthroughs in AI technologies. In a previous Comment[4] published in *Nature Methods*, Fan et al, discuss how AI-based tools have enabled the interpretation of large-scale multimodal cancer genomic datasets. Additionally, deep learning-based causal discovery methods can now unlock complex genetic and epigenetic relationships that control tumor growth and progression. In another past Comment[5], Quail and Walsh address how spatial proteomics combined with computer vision has been used to explore spatial organization of tumors and immune cells within the microenvironment.

To explore new ways to foil cancer, some researchers are returning to classic concepts in cancer evolution. In this issue's News Feature[6], journalist Vivien Marx investigates how scientists assess tumors as multidimensional, constantly evolving entities in their current and future work.

Indeed, advances in cancer genomics methods now allow researchers to investigate drivers of tumor evolution. A research paper[7] by Wu et al. reports Clonalscope, a method that leverages copy number alterations to identify genetically distinct cancer subclones. Recently, we also published SAVANA[8], an algorithm for detecting somatic structural variants and copy number alterations, key genomic features that underpin cancer driver mutations.

Nature Methods aims to champion technology and methods development for basic biological research. Cancer biology studies tend to have a clinical and translational bent, but they must be bolstered by basic biological research for understanding the fundamental origins and mechanisms that lead to cancer. Thus, we are very excited by new tools that open a window into the biology and behavior of tumors, and we welcome manuscripts in this area. Cancer research is a vast and complicated area with serious implications for human health, but still comprises many underexplored genres. We are watching this space for novel methods, models and resources that enable studies into the tumor microbiome, the tumor metabolome, cancer evolution, tumor-immune crosstalk and more.

References

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