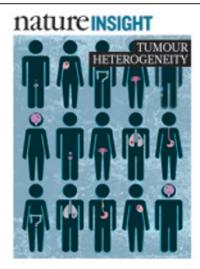


nature INSIGHT

TUMOUR HETEROGENEITY

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Cancer is not one but many diseases. It is different in each patient and continuously evolves into a progressively complex interplay of diverse tumour cells with their changing environment.

In an insightful and prescient 1976 paper, Peter Nowell proposed the now prevailing view of cancer as a process of clonal evolution, in which successive rounds of clonal selection give rise to tumours with diverse genetic and other molecular alterations that may necessitate 'personalized' therapies. Functional and phenotypic heterogeneity of cancer cells has also long been recognized, with experiments as early as the 1930s demonstrating that some but not other cells from mouse tumours could give rise to new tumours when transplanted.

The picture that has emerged over the past few decades — especially with the advent of more sophisticated model systems and technologies — is of even greater than anticipated genetic, phenotypic and functional heterogeneity and plasticity within tumours and between primary tumours and metastases. Adding to this bewildering complexity is the heterogeneity of the tumour micro-environment, inflammatory stimuli, the immune response, mechanical stresses, therapeutic intervention and many other factors, such as diet and the microbiota. These continuously changing environmental influences affect which cancer cell subpopulations are able to survive, proliferate, spread and resist therapy.

If every cancer, and perhaps every cancer cell, is unique, and some cancer cell populations are more 'unique' than others, this needs to be taken into consideration for the improvement of cancer diagnoses and prognoses, for the treatment and monitoring of each patient and for the design of clinical trials to evaluate new therapies.

This Insight covers some of the key topics relevant to the fast-moving field of cancer research, ranging from the basic understanding of tumour heterogeneity to translational cancer research and clinical trials. We hope to have captured some of the most exciting recent developments in this area.

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Barbara Marte
Senior Editor

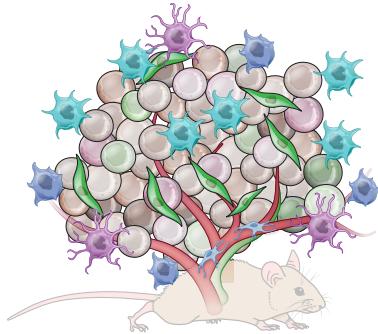
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