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Single-cell sequencing in cancer

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The area of cancer research has developed a lot in the last few decades. Tumours begin as a single cell but gradually show different morphological and phenotypic profiles described as tumour heterogeneity. Intra-tumour heterogeneity plays a critical role in immune evasion and metastasis, posing a challenge to personalised cancer therapy. With the advancement of single-cell sequencing techniques, we are able to identify tumour cells as well as immune cells within the tumour microenvironment. Understanding genomic alteration at single-cell resolution helps us to identify intra-tumour heterogeneity accurately and allows us to boost the immune response against malignant cells. Among various single-cell sequencing methods, small conditional RNA (scRNA) sequencing is vastly used. A study used scRNA sequencing to identify malignant cells which respond to checkpoint immunotherapy and malignant cells which are resistant to immunotherapy within the same tumour-microenvironment. The single-cell proteomic method is applied to characterise the functional states of immune cells in melanoma patients before and after immunotherapy. The recent development of the sc-epigenomics method allows us to identify the cell to cell variability within the tumour population by profiling epigenetic modifications and chromatin status. It also aids in understanding the mechanism of tumour growth. Further, a study used single-cell cytometry by time-of-flight (sc-CyTOF) along with scRNA sequencing to reveal the remodelling of lymphoid and myeloid intra-tumoural compartments during immune checkpoint therapy. The information derived from single-cell high-throughput sequencing is invaluable for predicting targetable mechanisms of resistance to cancer immunotherapy including melanoma, renal carcinoma and non-small cell lung cancer. Single-cell sequencing technologies can provide more information to understand intra-tumour heterogeneity, immunoediting etc. This technique may ultimately help us in manipulating immunity with therapy and vaccines, which might hopefully eliminate or suppress tumour phenotype in cancer patients.

Keywords: Single-cell sequencing, Intra-tumour heterogeneity, Checkpoint immunotherapy, Tumour-microenvironment, Epigenomics

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