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Perspective

A New Approach to Detect Prostate Cancer

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DESCRIPTION

Due to the high levels of variability, it has been challenging to pinpoint particular molecular subtypes associated with different stages of localized prostate cancer. The variability that exists at the single-cell level is hidden by bulk tests, which represent a population average. In this study, single cells from 18 prostate tumours that were flash-frozen had their accessible chromatin regions sequenced. It has been seen that high-grade tumours is lost the chromatin characteristics that low-grade prostate cancer cells. Despite this loss, FOXA1, HOXB13, and CDX2 transcription factor binding sites are enriched in high-grade tumours, suggesting a common trans-regulatory mechanism. It has been discovered two distinct genes that are highly accessible in high-grade prostate tumours and that encode neural adhesion molecules. Using cyclic immunofluorescence, we demonstrate the expression of *NRXN1* and *NLGN1* in prostate cancer epithelial, endothelial, immunological and neural cells. Our findings give us a better understanding of the active gene regulatory networks in early prostate tumours, which is important for the disease's molecular stratification.

For patients with localized prostate tumours, tumour heterogeneity in prostate cancer presents a considerable challenge for molecular stratification. It is generally known that only a small percentage of clinically diagnosed cases of prostate cancer progress to fatal metastatic disease. However, the prostate gland's substantial variability both inside and among its several tumour foci leads to the disease's complex evolutionary pathways. Many times, the molecular heterogeneity within a tumour focus causes incorrect tumour grade classification and inefficient therapeutic treatment strategies. The bulk analysis of tumours, which records a population-average of various cell types in the tumour, is where the majority of the genomic and epigenomic information on prostate cancer that has been gathered so far comes from. As a result, there are three issues that arise: The heterogeneous cell states within a single histopathological tumour grade are excluded from the analysis; and the epithelial, endothelial, myeloid, lymphoid, nerve, and other stromal cells that contribute to the progression of prostate cancer are reduced to a single component. As a result, the dynamic bidirectional communication between these different components is not captured.

The secret to characterizing the huge diverse landscapes of prostate cancer lies in recently developed single-cell technology. 20 single cells from localized prostate tumours had their entire genomes recently sequenced, which revealed significant cell-to-cell variance in mutations and intricate sub clonal paths. This technique is now being used on a small number of tumours. However, there are currently no studies that describe localized prostate cancer utilizing these high-throughput single-cell methods.

It's crucial to record the chromatin accessibility profiles of cells in low-grade and high-grade tumours in order to highlight the transformative alterations in localized prostate tumours that cause aggressive illness. Non-coding regulatory sequences are found in open chromatin regions of cells in addition to promoter regions of actively transcribed genes. The active gene regulatory networks that trigger changes in cell state are reflected in these sequences. In light of this, ATAC-seq (Assay for Transposase-Accessible Chromatin Sequencing) technology offers a technique to identify Cis- and Trans-Regulators of cell states during tumour progression.

Determining the risk of advancement is necessary to comprehend the change from a disease that is indolent to one that is aggressive. Confounding factors, such as the surgical margin status for patients who underwent radical prostatectomy surgery, the presence or absence of extracapsular extension, and lymph node involvement, exist even though it is crucial to appropriately stratify tumours based on the Gleason Pattern (GP) and score. These other variables are taken into account by the Cancer of the Prostate Risk Assessment Post-Surgical (CAPRA-S) score and post-radical prostatectomy nomo gram, which offer approaches to determine the likelihood of disease recurrence.

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