



Structural and functional abnormalities in cancer and psychiatric diseases

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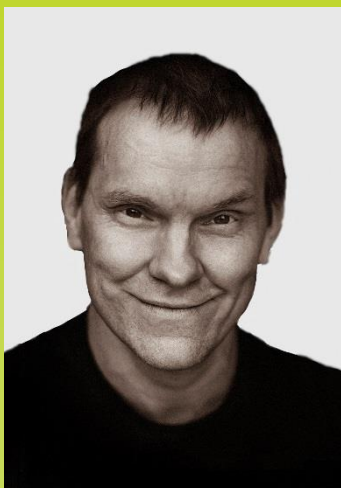
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Abstract:

Intratumoral heterogeneity is a critical factor when diagnosing and treating patients with cancer. Marked differences in the genetic and epigenetic backgrounds of cancer cells have been revealed by advances in genome sequencing, yet little is known about the phenotypic landscape and the spatial distribution of intratumoral heterogeneity within solid tumors. Our research group has developed a new diagnostic pipeline termed DIPCO, using three-dimensional light-sheet microscopy of cleared solid tumors, to identify structural abnormalities of phenotypic heterogeneity, in the epithelial-to-mesenchymal transition and in angiogenesis, at single-cell resolution in whole formalin-fixed paraffin-embedded biopsy samples. We also show that the DIPCO pipeline can identify structural abnormalities to determine tumor stage and stratify patient prognosis from clinical samples with higher accuracy than current diagnostic methods.

The CACNA1C gene is a well-established candidate risk gene in multiple psychiatric disorders, including bipolar disorder, schizophrenia and major depression, and it encodes a voltage-gated Ca²⁺ channel. However, the mechanism by which the CACNA1C gene imposes its risk is not known. Our research group has used transgenic mice to show that deletion of *Cacna1c* results in signs of increased anxiety. Magnetic Resonance Imaging scans of these animal revealed structural abnormalities in the brain anatomy. Examining their spontaneous Ca²⁺ activity showed functional abnormalities that was confirmed by mathematical modeling. We hypothesize that spontaneous Ca²⁺ activity is driven by functional pacemaker cells, expressing slightly more voltage-gated Ca²⁺ channels than non-pacemakers.

事前登録不要 No prior registration is necessary.

