

Whole-tissue phenotyping of clinical samples using light sheet microscopy

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 tumours. Here, we developed a pipeline for three-dimensional light-sheet microscopy of whole formalin-fixed paraffin-embedded (FFPE) biopsy samples, which allow us to clear solid tumours and identify unique patterns of phenotypic heterogeneity at single-cell resolution. We also show that cleared FFPE samples can be re-embedded in paraffin after examination for future use, and that our tumour-phenotyping pipeline can determine tumour stage and stratify patient prognosis from clinical samples with higher accuracy than current diagnostic methods, thus facilitating the design of more efficient cancer therapies.

Affiliation

Karolinska Institutet

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Primary author(s) : Mr KANATANI, Shigeaki (Karolinska Institutet); Dr TANAKA, Nobuyuki (Karolinska Institutet); Ms KACZYNSKA, Dagmara (Karolinska Institutet); Prof. UHLÉN, Per (Karolinska Institutet)

Presenter(s) : Mr KANATANI, Shigeaki (Karolinska Institutet)

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