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Online seminar via ZOOM

Liquid Biopsies in Lung Cancer

SPEAKER
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ABSTRACT:

In my presentation I will exemplify the multiple uses of circulating tumour cells (CTC) and ctDNA in lung cancer research. CTC number using the ‘gold standard’ CellSearch platform (that identifies epithelial cells) before treatment in Non Small Cell Lung Cancers (NSCLC) and Small Cell Lung Cancers (SCLC) is prognostic for overall and progression free survival. Cellsearch CTCs are scarce in NSCLC but prevalent in SCLC where they can be used as a pharmacodynamic biomarker for treatment response and to measure predictive biomarkers. In this regard, we developed a single SCLC CTC copy number alteration (CNA) classifier that predicts chemotherapy response that can be used alongside ctDNA analysis for therapy monitoring.

Obtaining clinical tumour biopsies to study metastasis in SCLC is particularly challenging. We derived mouse models from patients CTCs (we termed CDX) to explore biology and test new therapies. Our biobank of >45 CDX models, some generated pre- and post-patient therapy, allows analysis of tumour heterogeneity, therapy resistance and biology of progressing disease. CDX cells metastasise to the same organs in mice as commonly observed in patients.

Using labelled CDX cells, we developed new workflows to study SCLC metastasis to the liver and the brain. SCLC cells exhibit plasticity and can undergo vasculogenic mimicry (VM) adopting endothelial cell behaviours to form blood vessels, a process that worsens prognosis and supports metastasis. ctDNA is also prevalent in SCLC and I will describe routine monitoring of SCLC with ctDNA CNA and a new liquid biopsy based on ctDNA methylation that increases sensitivity for detection and allows us to subtype a patient’s SCLC.

In our NSCLC CTC studies within the UK TRACERx consortium, we showed that CTCs in the pulmonary draining vein of stage I-IIIa patients at surgery with curative intent predicts recurrence risk. In a case study we identified a lethal subclone that gave rise to metastasis 10 months later in the pulmonary vein at surgery. I will also briefly highlight discuss the potential for CTCs within a multimodal liquid biopsy for the earlier detection of NSCLC.

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