Queen Mary Innovation

Opportunity 2016084

Megakaryocytes and CTCs as a Prognostic marker in Cancer

A novel biomarker for the prognosis of cancer. Using patient samples, it was demonstrated that the number of circulating megakaryocytes was associated with patient survival. For patients with advanced prostate cancer the larger the difference between the number of mesenchymal CTCs and megakaryocytes strongly correlated to poor survival.

Background

Prostate cancer is the most common cancer in Western men, also being the second most frequent cause of cancer-related death. The majority of prostate cancer deaths are caused by metastases, which are thought to be seeded throughout the body by circulating tumour cells (CTCs). In fact, even prior to a metastatic tumour being clinically evident, large numbers of CTCs can be detected in the circulation. However, current CTC analysis mainly focuses on cells expressing epithelial-specific markers, despite the fact the downregulation of these markers has been described during epithelial–mesenchymal transition (EMT), a key process in cancer metastasis. As such CTCs undergoing EMT as part of the metastatic process may be missed.

The Problem

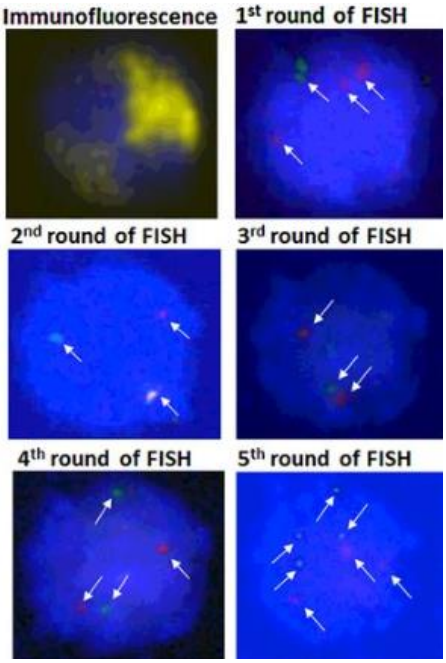
Current criteria for risk stratification of newly diagnosed prostate cancer are mainly based on clinical features, including serum PSA, clinical stage, and biopsy/surgical specimen Gleason score. However, these are often not sufficient to distinguish between indolent and aggressive disease, requiring the establishment of new biomarkers for disease diagnosis and prognosis. Current CTC technologies, such as CellSearch®, mainly rely on the capture and identification of those CTCs that express epithelial phenotype-specific markers epithelial cell adhesion molecule (EpCAM) and cytokeratin (CK). However, CellSearch® has been reported to detect fewer than two CTCs per sample in metastatic prostate cancer patients. As such, better methodologies and biomarkers are required to improve the accurate prognosis of cancer.

Invention: Benefits & Application

This invention describes a novel technique which allows the confirmation of the malignancy of CTCs with a mesenchymal phenotype, achieved through performing multiple rounds of fluorescence in situ hybridization (FISH) following immunofluorescence staining. This technique allows the simultaneous identification of epithelial and mesenchymal cell features and genomic alterations, confirming the malignancy of the cells. In addition, using the Parsortix system, researchers at QMUL demonstrated that an increase in circulating megakaryocytes in blood samples from prostate cancer patients were correlated with a good prognosis in progressive disease and the combination of CTC and megakaryocyte count may effectively predict survival in advanced disease.

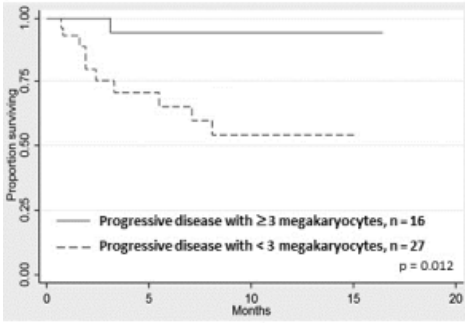
Queen Mary University of London

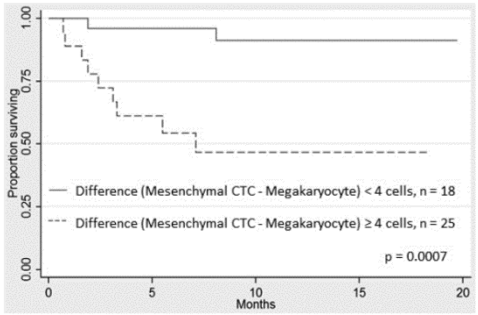
Contact:
Dr Mark Gurden
Commercialisation Manager
m.gurden@qmul.ac.uk



Five rounds of FISH on CTCs

FISH on one CK−/VIM+/CD45− CTC postimmunostaining. First round: AR (red) and 6q16 (green). Second round: RP11-476D17 (red) and RP11-95I21 (green). Third round: C-MYC (red) and NKX3.1 (green). Fourth round: RB1 (red) and PTEN (green). Fifth round: CCND1 (red) and 16q22.1 (green). Arrows, FISH signals.





Megakaryocytes are prognostic for survival

Kaplan-Meier curves for overall survival showed that progressive prostate cancer patients with:
(1) less than 3 megakaryocytes had a significantly shorter survival rates ($p = 0.012$).
(2) a number difference between mesenchymal CTCs and megakaryocytes of no less than four had even poorer survival ($p = 0.0007$)

Patents

A patent has been granted in Europe and is pending in the US
Patent application: WO2018073381A1

Lead Inventor

Prof Yung-Jie Lu
Professor of Molecular Oncology, Barts Cancer Institute, Queen Mary University of London.

Inventors Profile:
https://www.bartscancer.london/staff/professor-yong-jie-lu/

Publication

Lei Xu; Xueying Mao; Tianyu Guo; Pui Ying Chan; Greg Shaw; John Hines; Elzbieta Stankiewicz; Yuqin Wang; R. Tim D. Oliver; Amar Sabri Ahmad; Daniel Berney; Jonathan Shamash; Yong-Jie Lu, *The Novel Association of Circulating Tumor Cells and Circulating Megakaryocytes with Prostate Cancer Prognosis.* Clin Cancer Res (2017) (https://doi.org/10.1158/1078-0432.CCR-16-3081).

Contact:
Dr Mark Gurden
Commercialisation Manager
m.gurden@qmul.ac.uk