Genetic signature linked to cancer prognosis identified

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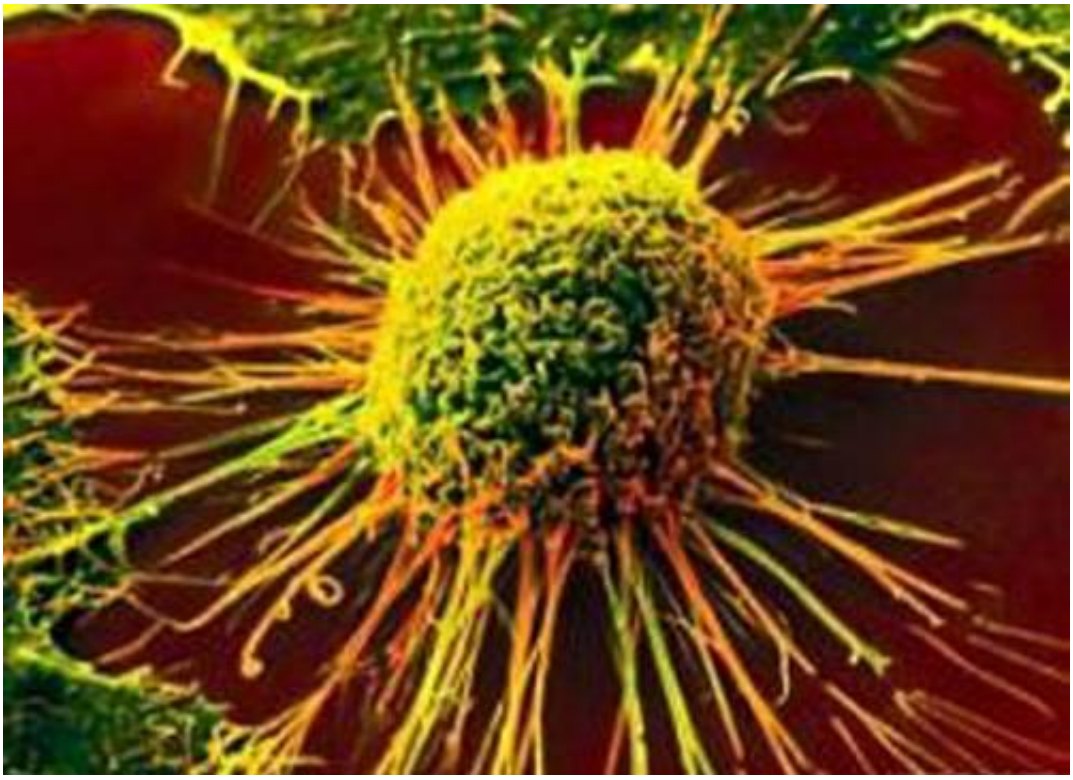

Researchers from the Medical Research Council (MRC) Cancer Unit at the University of Cambridge have identified a genetic signature related to metabolism associated with poor patient prognosis. The results of the analysis of 8,161 tissue samples could in the future help clinicians decide how best to treat a patient as well as aid the development of new targeted

treatments.

For cancer cells to grow and spread they undergo a complex metabolic transformation. This allows the cells to meet the energy needs for the cancer to proliferate. Increasing our understanding of the genes that underpin the changes to metabolic pathways will provide further insight into the events that lead to the spread of cancer within the body.

To this end, Dr Christian Frezza, programme leader, and Edoardo Gaude, a PhD student, from the MRC Cancer Unit, analysed the expression of metabolic genes across 20 different solid cancer types from 8,161 tumour and non-cancerous samples held in The Cancer Genome Atlas (TCGA).

The researchers found that genes related to the OXPHOS pathway - a metabolic pathway in the cell's mitochondria that provides energy to the cell - were significantly down-regulated in the tumour cells from patients with poor clinical outcome. Furthermore, suppression of OXPHOS genes was linked to metastasis, where the cancer spreads to other parts of the body and is linked to even poorer prognosis. Although the link between OXPHOS genes and cancer survival has been found only to be an association at this stage, these results suggest that mitochondrial function might play an important role in metastasis and, therefore, patient prognosis.

Further work is needed to validate these results and to assess to what extent mitochondrial dysfunction contributes to the malignancy of cancer cells.

Dr Christian Frezza said: "Cellular metabolism is known to be a key part of cancer progression. In our work we used data on patient's prognosis to identify a genetic signature related to metabolism that correlated with poor clinical outcome. Using this information, it could be possible in the

future to tailor treatments specific to patients. This genetic signature also gives a new target for the development of drugs that could prevent a cancer from spreading throughout the body."

Dr Adam Babbs, research programme manager for cancer at the MRC, said: "The work will inform future patient stratification efforts and demonstrates the important links between metabolism and cancer. Further validation of this work may allow us to predict with greater accuracy a patient's long term survival and design a treatment strategy personalised to improve their chances of living longer."

The study was published in *Nature Communications*.

More information: Edoardo Gaude et al, Tissue-specific and convergent metabolic transformation of cancer correlates with metastatic potential and patient survival, *Nature Communications* (2016). DOI: 10.1038/ncomms13041

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