Gene signature discovery may predict response to immune therapy

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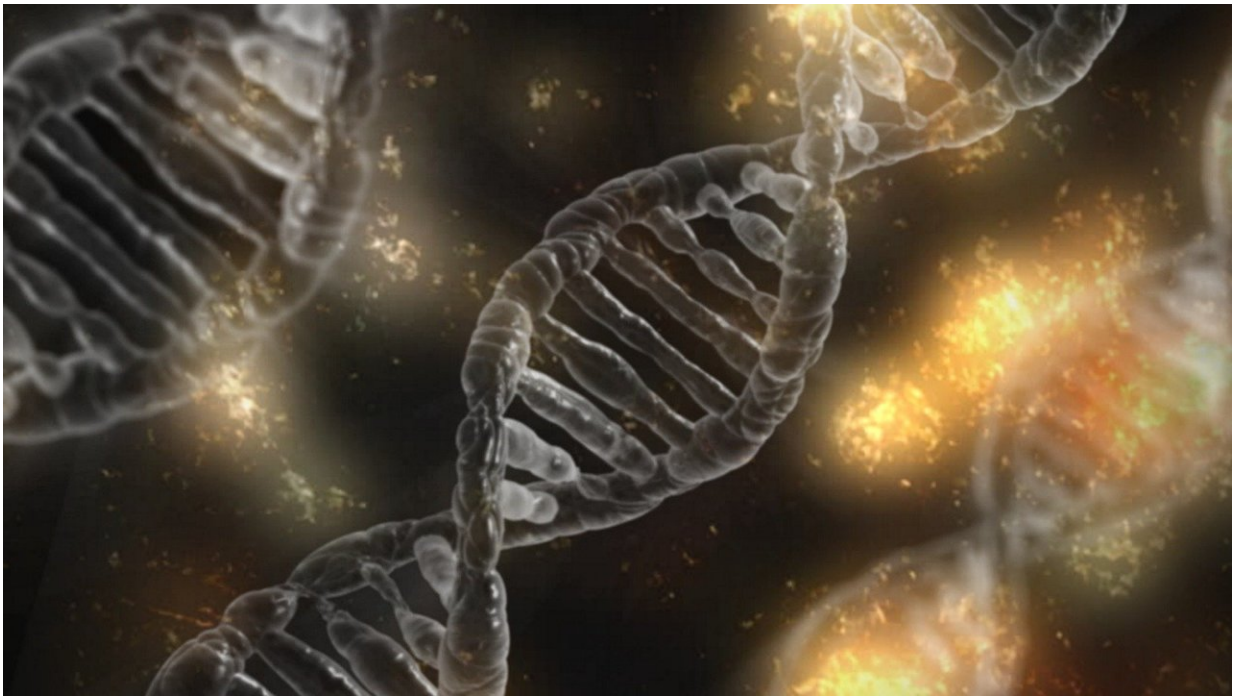

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Scientists led by Dr. Daniel De Carvalho at Princess Margaret Cancer Centre have discovered a gene signature biomarker that may predict which patients will respond—or not—to immune therapy.

The findings are published online today in *Nature Communications*.

Dr. De Carvalho, principal investigator, says the gene signature relates to the body's molecular network called the extracellular matrix (ECM) that underpins and physically supports cells. For cancer patients with the gene signature, the research suggests the ECM can stiffen around the diseased cells to form a barrier that immune cells simply cannot penetrate.

"The ECM gene signature associated with response to immune therapy is important because as of today we do not have a very good way to predict which patient will respond or which patient will not respond," says Dr. De Carvalho, Senior Scientist at the cancer centre, University Health Network.

The multi-institutional scientific team used a big data approach and examined available data across thousands of patient samples from many different cancers to find that in some patients the immune cells were not penetrating the tumour, despite the fact these patients had molecular markers that would predict immune response.

"That's when we started to think that ECM could be playing a role in actually physically blocking the immune system."

With further experimental study to validate the biomarker, Dr. De Carvalho says the research lays the foundation for a new therapeutic strategy to focus first on ways to disable the ECM to enable immunotherapy.

"The ultimate goal is to find a biomarker that can help the clinician decide if a patient should receive immunotherapy or not. For those who will not respond, the answer could be the patient would first receive a drug to target the ECM, and then be able to respond to immune therapy."

More information: Ankur Chakravarthy et al, TGF-β-associated

extracellular matrix genes link cancer-associated fibroblasts to immune evasion and immunotherapy failure, *Nature Communications* (2018). DOI: 10.1038/s41467-018-06654-8