A universal DNA nano-signature for cancer

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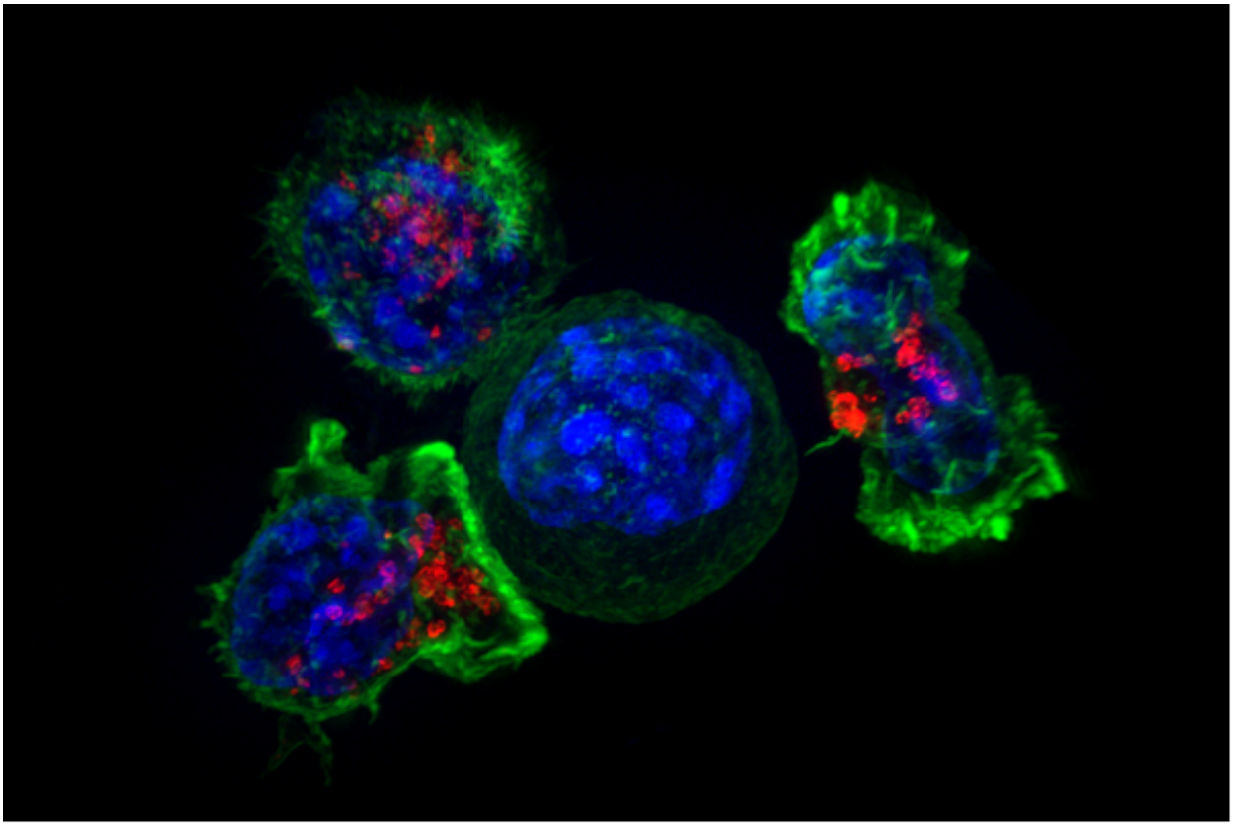

Killer T cells surround a cancer cell. Credit: NIH

Researchers from the University of Queensland's Australian Institute for Bioengineering and Nanotechnology (AIBN) have discovered a unique nano-scaled DNA signature that appears to be common to all cancers.

Based on this discovery, the team has developed a novel technology that

enables cancer to be quickly and easily detected from any tissue type, e.g. blood or biopsy.

The study, which was supported by a grant from the National Breast Cancer Foundation and is published in the journal *Nature Communications*, reveals new insight about how epigenetic reprogramming in cancer regulates the physical and chemical properties of DNA and could lead to an entirely new approach to point-of-care diagnostics.

"Because cancer is an extremely complicated and variable disease, it has been difficult to find a simple signature common to all cancers, yet distinct from healthy cells," explains AIBN researcher Dr. Abu Sina.

To address this, Dr. Sina and Dr. Laura Carrascosa, who are working with Professor Matt Trau at AIBN, focussed on something called circulating free DNA.

Like healthy cells, cancer cells are always in the process of dying and renewing. When they die, they essentially explode and release their cargo, including DNA, which then circulates.

"There's been a big hunt to find whether there is some distinct DNA signature that is just in the cancer and not in the rest of the body," says Dr. Carrascosa.

So they examined epigenetic patterns on the genomes of cancer cells and healthy cells. In other words, they looked for patterns of molecules, called methyl groups, which decorate the DNA. These methyl groups are important to cell function because they serve as signals that control which genes are turned on and off at any given time.

In healthy cells, these methyl groups are spread out across the genome.

However, the AIBN team discovered that the genome of a cancer cell is essentially barren except for intense clusters of methyl groups at very specific locations.

This unique signature—which they dubbed the cancer "methylscape", for methylation landscape—appeared in every type of breast cancer they examined and appeared in other forms of cancer, too, including prostate cancer, colorectal cancer and lymphoma.

"Virtually every piece of cancerous DNA we examined had this highly predictable pattern," says Professor Trau.

He says that if you think of a cell as a hard-drive, then the new findings suggest that cancer needs certain genetic programmes or apps in order to run.

"It seems to be a general feature for all cancer," he says. "It's a startling discovery."

They also discovered that, when placed in solution, those intense clusters of methyl groups cause cancer DNA fragments to fold up into three-dimensional nanostructures that really like to stick to gold.

Taking advantage of this, the researchers designed an assay which uses gold nanoparticles that instantly change colour depending on whether or not these 3-D nanostructures of cancer DNA are present.

"This happens in one drop of fluid," says Trau. "You can detect it by eye, it's as simple as that."

The technology has also been adapted for electrochemical systems, which allows inexpensive and portable detection that could eventually be performed using a mobile phone.

So far they've tested the new technology on 200 samples across different types of human cancers, and healthy cells. In some cases, the accuracy of cancer detection runs as high as 90%.

"It works for tissue derived genomic DNA and blood derived circulating free DNA," says Sina. "This new discovery could be a game-changer in the field of point of care cancer diagnostics." It's not perfect yet, but it's a promising start and will only get better with time, says the team.

"We certainly don't know yet whether it's the Holy Grail or not for all cancer diagnostics," says Trau, "but it looks really interesting as an incredibly simple universal marker of cancer, and as a very accessible and inexpensive technology that does not require complicated lab based equipment like DNA sequencing."

More information: Abu Ali Ibn Sina et al, Epigenetically reprogrammed methylation landscape drives the DNA self-assembly and serves as a universal cancer biomarker, *Nature Communications* (2018). DOI: 10.1038/s41467-018-07214-w

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