New technology to tackle treatment-resistant cancers

February 3 2012

Free-flowing cancer cells have been mapped with unprecedented accuracy in the bloodstream of patients with prostate, breast and pancreatic cancer, using a brand new approach, in an attempt to assess and control the disease as it spreads in real time through the body, and solve the problem of predicting response and resistance to therapies.

In comparison to a previous generation of systems, the researchers state their test showed a significantly greater number of high-definition circulating tumour cells (HD-CTCs), in a higher proportion of patients, by using a computing-intensive method that enables them to look at millions of normal cells and find the rare cancer cells among them.

Their results, published today, Friday 3 February 2012, in IOP Publishing's journal Physical Biology, could help reveal the mechanisms behind the spread of solid tumours from one organ or tissue to another – mechanisms that have, until now, remained a mystery.

Dr Jorge Nieva, an oncologist at Billings Clinic leading the study, said: "This technology will allow scientists to move away from mouse and cell culture systems and speed the delivery of cures for cancer in people. This is the technology we have been waiting for to solve the problem of resistance to chemotherapy drugs."

Senior technology author of the study, Professor Peter Kuhn, said: "In the future, our fluid biopsy can effectively become the companion to the patient for life. If we can assess the disease in real time, we can make

quantitative treatment decisions in real time. These decisions include predictive decisions about therapeutic response, diagnostic decisions and prognostic decisions about outcome."

The researchers, based at the Scripps Physics Oncology Center in La Jolla, California, were able to find five or more CTCs in each milliliter of blood in 80% of the 20 patients they tested with prostate cancer; 70% in the 30 patients with breast cancer; and 50% in the 18 patients with pancreatic cancer.

The authors also report that their test showed significantly better results when compared with the commercial test, CellSearch®, which uses a slightly less accurate approach which effectively reduces the sample from approximately 50 million cells to just 5,000 before conducting fluorescent imaging, meaning important cells you wish to study could be lost.

In 7.5 mL of blood, the CellSearch® test found two or more CTCs in 5 out of the 15 patients tested whereas the new test found two or more CTCs in a single milliliter of blood in 14 out of the 15 patients tested.

The dyes used in this new approach contain antibodies that target, and then attach to, specific proteins that are expressed by the CTCs. Once attached, they fluoresce and allow the researchers to observe them. The result is a set of high resolution digital images that retain the intricate details of the cells and allow the researchers to effectively analyse them in the laboratory. Also striking is the quality of the images.

"The high definition method gives a detailed portrait of these elusive cells that are caught in the act of spreading around the body. It's unprecedented – we've never been able to see them routinely and in high definition like this before," says diagnostic pathologist Kelly Bethel, MD, the senior clinical investigator on Kuhn's team.

"The science behind this approach, and the ability to obtain more detailed information about CTCs in a timely fashion, opens up opportunities to address some of the outstanding problems in cancer, such as drug-resistance. This is an example that bringing a physical sciences approach to a medical need has potential for profound consequences to greatly benefit cancer patients," said Dr Larry Nagahara of the National Cancer Institute.

More information: The published version of the paper "Fluid biopsy in patients with metastatic prostate, pancreatic and breast cancers" D Marrinucci et al. 2012 *Phys. Biol.* 9 016003 is available at iopscience.iop.org/1478-3975/9/1/016003

Provided by Institute of Physics

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