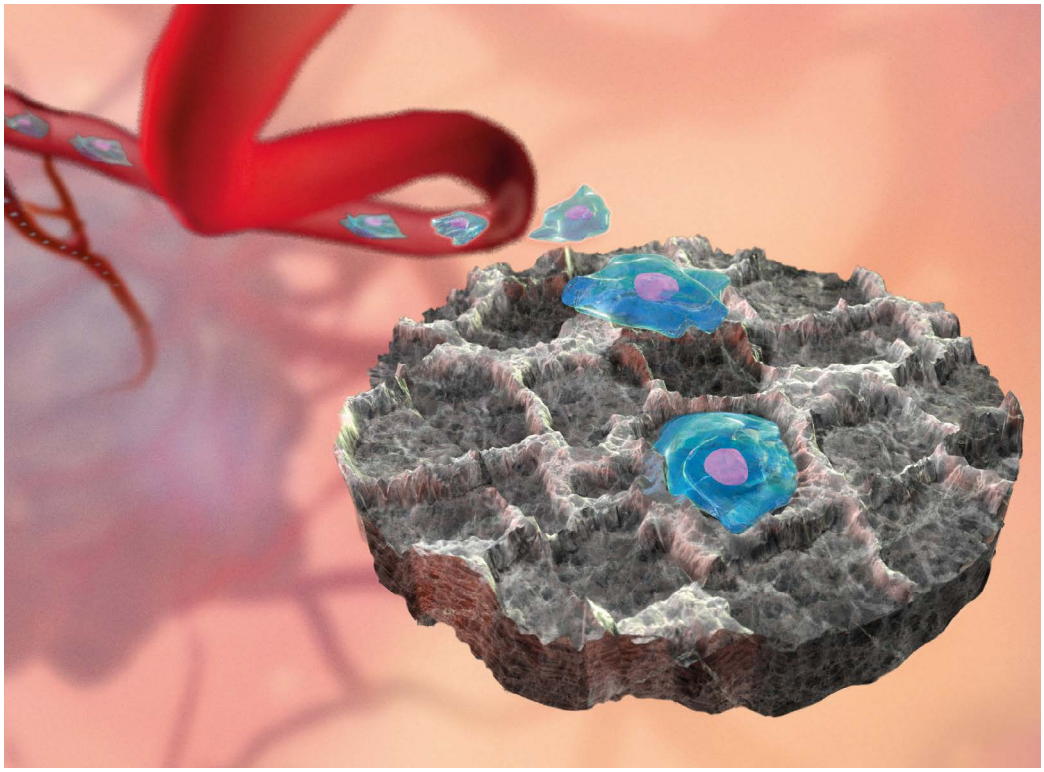
Research round-up

Highlights from cancer-diagnosis studies. By Elizabeth Svoboda



STEPHEN ALVEY, MICHIGAN ENGINEERING

Illustration of a cancer trap that researchers have developed to aid tracking of disease progression.

'Cancer traps' detect early signs of spread

An animal study has shown that implanting a tiny, cell-attracting scaffold below the skin can help physicians to track cancer progression, potentially reducing the need for tissue biopsy.

Researchers have observed that before malignant tumours spread from their primary location to other parts of the body, they deploy circulating tumour molecules that suppress the body's immune response — a strategy that makes it easier for the cancer to infiltrate distant organs. Bioengineer Lonnie Shea at the University of Michigan in Ann Arbor and his team developed a scaffold that could detect and trap circulating immune and cancer cells during the period before a cancer spreads.

The team's minuscule trap is made of biodegradable polyester and designed to be implanted under the skin, near vital organs such as the lungs or bones. The polyester in the implant is porous and attracts immune cells such as macrophages, which in turn coax circulating tumour cells to attach on to the scaffold. The team found that differences in the expression levels of ten genes carried by immune cells can indicate a spreading cancer. In tests on mice, the researchers could distinguish between mice without cancer, mice with non-spreading cancers and mice with metastasizing cancers.

If this method works similarly in humans, the team says, it might be possible to pick up impending metastases at an earlier stage, and thus allow for more effective treatment. And because taking samples from the scaffold is less invasive than a biopsy, the implant could enable physicians to monitor a person's condition more frequently. The scaffolds might even slow the spread of some metastases by stopping circulating cancer cells in their tracks.

Cancer Res. **80**, 602–612 (2020).

Urine test for bladder cancer

An experimental urine test can detect tumour-cell DNA mutations that are present in about 95% of bladder cancers. The results raise the prospect of a simple and quick screening test for bladder cancer.

Some physicians already test people's urine for blood to detect possible cancer. However, this test is not very sensitive — only about one in five people with blood in their urine turn out to have bladder cancer. Bladder-cancer surgeon Richard Bryan at the University of Birmingham, UK, and his team devised a test that detects DNA fragments that enter the blood after detaching from the bladder tumours. The pieces of DNA make their way through the kidneys' filtration system and into urine.

The team evaluated their test on a group of about 260 people with bladder cancer. After sequencing the volunteers' tumours to compile a library of bladder-cancer-related mutations, the team tested people's urine for DNA fragments containing these mutations. The test reliably picked up cancer mutations that are present in the vast majority of bladder cancers, indicating it could be more accurate than current urine-screening tests. The test also detects specific mutations that predict survival rates and the likely disease-free interval before recurrence — data that could allow clinicians to craft more customized treatment plans.

BJU Int. **124**, 532–544 (2019).

RNA fragments signal ovarian cancer

Two-thirds of cases of ovarian cancer are not detected until stage 3 or 4 of the disease, a diagnostic lag that lessens the prospect of effective treatment. Now, researchers have successfully used circulating

microRNAs (miRNAs) — RNA molecules involved in the regulation of gene expression — to distinguish ovarian cancer from benign pelvic growths, raising the hope that the disease could be eventually diagnosed earlier and less invasively.

A team led by pathologist Douglas Oliveira at the University of Copenhagen evaluated 190 blood plasma samples from people with pelvic masses — half benign and half malignant. The researchers sequenced the genes in each plasma sample to evaluate levels of 46 different circulating miRNAs known to be present in people with ovarian cancer or other malignancies.

The team found six miRNAs that were expressed differently in people with ovarian cancer than in people with benign pelvic lumps. Ordinarily, some of these miRNAs are thought to be part of the body's defence system against cancer. When the miRNAs' function is disrupted, however, tumour cells might be able to proliferate more easily.

A blood test to detect expression levels of two of the identified miRNAs, along with levels of a known ovarian tumour marker called CA-125, proved to be 96% accurate at diagnosing ovarian cancer. If the test can be validated in a future study focusing on people with early-stage disease, it could save lives — the five-year survival rate for people with early ovarian cancer is three times higher than the survival rate for those with late-stage disease.

PLoS ONE **14**, e0225249 (2019).

AI identifies more than 20 cancer types

Artificial intelligence (AI) can accurately identify a host of cancer types in a clinical setting, say researchers at Memorial Sloan Kettering Cancer Center in New York — a breakthrough that could fast-track a cancer diagnosis.

Computational biologist Alexander Penson and his team trained a computer to identify various kinds of tumour by feeding it a large data set that contained genetic information from people with advanced cancer. The data set contained information about gene mutations and other anomalies specific to individual cancer types.

The team tested the model on about 7,800 people with a total of 22 kinds of malignancy, including cancer of the breast, colon, prostate, lung, bladder and pancreas. Using the tumour DNA information, the algorithm correctly identified what type of cancer a person had about three-quarters of the time. Some cancers were easier to categorize than others — colorectal cancer, for instance, had a more distinctive genetic profile than ovarian or thyroid cancers. When physicians did not know where in the body a person's cancer had started, the computer identified a probable tissue of origin almost 70% of the time.

The researchers think that this type of AI model could supplement the information that techniques such as a tumour biopsy can provide and help to clarify cancer diagnoses. If the computer's prediction differs significantly from that of a clinician, AI analysis could even change a cancer diagnosis.

JAMA Oncol. **6**, 84–91 (2020).

Risk-adapted screening is best

A study of more than five-million women in Sweden suggests that a personalized breast-cancer screening schedule, based on family history, could lead to quicker and more accurate diagnoses.

To find most cancers but minimize unnecessary testing, many specialists recommend starting mammography screening when a woman has a 2.2% risk of developing breast cancer over a 10-year period. Elham Kharazmi at Germany's National Center for Tumour Diseases in Heidelberg and colleagues analysed the large Swedish data set to work out the ages at which different groups of women reached this threshold. The team calculated each woman's risk on the basis of how many of her first- and second-degree relatives developed invasive breast cancer, and at what ages.

The average woman, according to the study, reaches the 2.2% risk level at the age of about 50 (the age at which the US Preventive Services Task Force recommends biennial mammograms). But there is wide variation in the population. The more close relatives with breast cancer that a woman had, the sooner she reached the risk threshold for screening. For instance, a woman whose sister receives a breast-cancer diagnosis would hit the 2.2% risk level at the age of 40, whereas some women with multiple affected first-degree relatives reach this risk level at just 27 years old.

The researchers propose a comprehensive screening programme in which the age at which a woman begins screening is based on her family history. Such an approach, say researchers at the US National Cancer Institute, could pinpoint breast cancers sooner, make mammography programmes more cost-effective, and reduce rates of breast-cancer over-diagnosis.

JAMA Oncol. **6**, 68–74 (2020).

Screening reduces colorectal cancer

A long-term follow-up of the US Prostate, Lung, Colorectal, and Ovarian Cancer (PLCO) screening trial confirms that people who are screened using a sigmoidoscope — a flexible tube with a camera that scans intestinal walls — have a lower incidence of colorectal cancer, and a lower risk of dying of the disease, than those who are not screened.

For decades, oncologists have debated the merits of screening for colorectal cancer with a sigmoidoscope, and the new National Cancer Institute study aims to put this long-standing debate to rest. In the 1990s and early 2000s, participants in the PLCO trial, aged 55 to 74, were randomly assigned to receive either standard care (no specific screening outside of standard doctor's appointments) or periodic examinations using flexible sigmoidoscopy.

In the follow-up study, 15 years or more after the screening trial began, epidemiologist Eric Miller at the National Cancer Institute and his team reported that participants who received sigmoidoscopy were 18% less likely than those in the control group to have developed colorectal cancer, and they were 25% less likely to have died from the disease.

The benefits of sigmoidoscopy screening were most pronounced in men. The technique is thought to improve health outcomes because it can detect potential cancer precursors known as polyps — tiny, bulbous growths in the colon — that can then be removed before they develop into malignant tumours. The researchers say further studies are needed to clarify how the benefits of sigmoidoscopy might differ with age and gender.

Lancet Gastroenterol. Hepatol. **4**, 101–110 (2019).

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