SELMA Diagnostics
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Building a better early cancer diagnostic

Semi-virtual SELMA Diagnostics is harnessing its SELMA technology to identify changes in circulating DNA taken from blood samples to create diagnostic tests for early cancer detection, diagnosis and treatment.

Although many cancers arise from inherited changes or are triggered by environmental factors, more than half of cases of cancer result from spontaneous genetic changes. Existing tests can identify people at risk for cancers that run in families, and doctors can advise lifestyle changes. However, it is harder to spot cancers that arise from unexpected genetic changes. SELMA Diagnostics was founded in Denmark in 2015 by CEO Andreas Kunding and partners. The company's aim is to create simple and sensitive chip-based tests to identify changes in DNA circulating in the bloodstream, allowing very early-stage detection and treatment. SELMA Diagnostics has operated semi-virtually so far, using collaborations to gain access to samples, expertise and chip fabrication.

The technology behind the name

Fragments of circulating tumor DNA (ctDNA) can be used as blood biomarkers for cancer. In the early stages the biomarker levels are extremely low, with the concentration increasing as the disease progresses. SELMA, which stands for single enzyme-linked molecular analysis, is designed to detect and profile ctDNA at the single-molecule level.

The SELMA chip has capture probes attached to its surface that are designed to catch hold of specific fragments of ctDNA. Several thousands of capture probes are attached in a capture feature 10 µm in diameter, which in turn is duplicated 50,000 times to produce a large array on an area of a few square millimeters. A flow channel guides the sample and liquid reagents across the chip, such that—similar to ELISA technology—the DNA becomes labeled with an enzyme. The surface of the microfabricated chip is treated so that a detection liquid forms individual micro-droplets at the site of each capture feature, with single-enzyme (and hence single DNA) detection within seconds (Fig. 1a).

SELMA's array regeneration feature uses repeated rounds of detection to increase the sensitivity and reduce the number of false positives. The biomarkers are covalently locked to the capture probes, and the detection cycle is run several times. While the false positives may appear at different array sites in each round because of the detection probe picking up normal DNA, only the true positives will persist at the same location (Fig. 1 b, c).

Compared with PCR testing, the SELMA technology can work with much smaller fragments of DNA. It also does not require DNA amplification as a step, reducing amplification bias, off-target sequencing and false positives. Direct detection means that sample preparation is simpler, the analysis process is faster and the process can be automated more easily than PCR techniques.

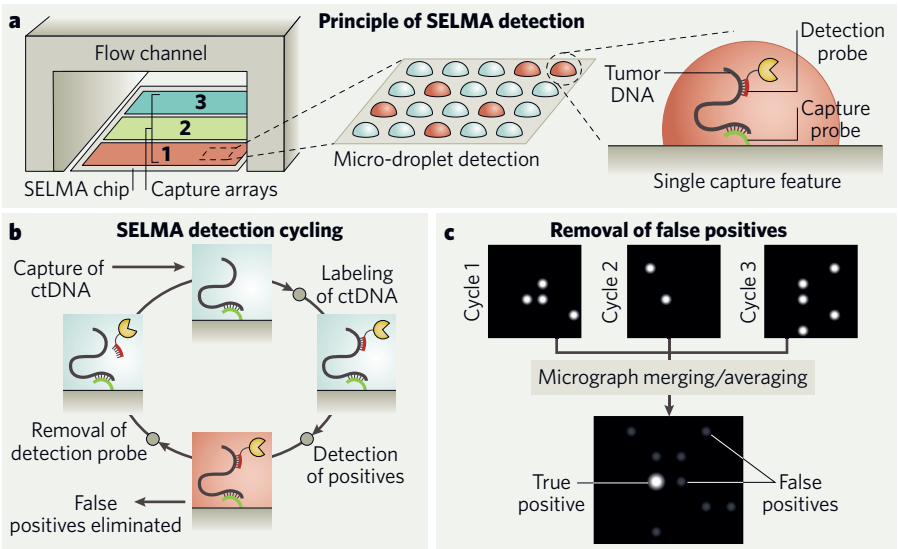

Fig. 1 | SELMA technology in depth. a, A SELMA chip consists of capture regions targeting specific DNA-sequences. When infused with detection liquid several thousand micro-droplets form on the capture regions leading to a bright color change in droplets hosting labeled ctDNA. **b**, A detection cycle includes labeling of ctDNA, detection of single ctDNA molecules followed by removal of detection probes to regenerate the array. **c**, False-positives are eliminated by SELMA detection cycling. Merging of micrographs from consecutive cycles allows signals from droplets repeatedly appearing at the same position (true positives) to become amplified, whereas signals from randomly occurring false-positive droplets are attenuated.

Because a single capture array hosting 50,000 micro-droplets can fit on an area of a few square millimeters, but the total chip surface is far greater (hundreds of square millimeters), a single chip can be partitioned into several distinct capture arrays, allowing for a higher degree of multiplexing than digital droplet PCR.

The next steps

The diagnostic stage of the SELMA system is automated but requires a manual blood sample processing step. The company plans to automate the sample preparation step and then integrate this into the diagnostic device.

SELMA Diagnostic's initial focus is on colorectal cancer diagnosis in collaboration with the Danish Cancer Society, with medium-term plans for a lung cancer diagnostic and long-term plans to create a pan-cancer diagnostic on a single slide.

"The timescale for the colorectal cancer test will depend on the resources available. We have received funding from public and private sources, and are seeking further investment to speed up the development process. Once funding is in place, it would be around a year to creation of a dedicated instrument for automated analysis, and then 2–4 years for validation of the colorectal cancer test," said Kunding. "We would like to work with partners who can support us through the validation and qualification steps and help us to get the tests into diagnostic and therapeutic guidelines."

A pan-cancer test would look for 150–200 different mutations linked with 20 common cancer types in a single blood sample. Clinical validation of this would take a long time, perhaps at least a decade, but according to Kunding, the company will be able to learn from its single cancer diagnostics and from its competitors in the field, such as Menlo Park-based GRAIL.

"Our motivation is to support early diagnosis and better treatment for cancer," said Kunding. "A low-cost and automated diagnostic device that could provide an answer in less than an hour could make a big difference by helping doctors to carry out routine screens on asymptomatic patients."

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