Lab in a Drop

Analysis and diagnosis in a chip format are coming of age, but their practical application has been limited because until now, the sample usually had to be prepared separately and on a nonminiaturized scale. Jürgen Pipper and his team at the Institute of Bioengineering and Nanotechnology in Singapore want to change this.

They have now developed a rapid test for genetic diagnosis that combines the preparation of biological samples with a polymerase chain reaction (PCR) on one chip. As they report in the journal *Angewandte Chemie*, the "laboratory device" for all steps in this system is a single drop containing magnetic nanoparticles, which is moved across the chip by a magnetic field.

PCR allows gene sequences to be duplicated and identified—to identify a disease trigger, for example. In this process, the sample must cycle through a specific sequence of temperatures. Because of the slow heating and cooling processes, laboratory PCR usually takes several hours. The new chip PCR requires only minutes, including for the sample preparation.

In contrast to other chip-based methods, the actual sample, such as a drop of blood, can be placed directly on the PCR chip, where it is mixed with a drop that contains magnetic particles. These particles are equipped with antibodies on their surface, antibodies that bind specifically to the interesting cells in the blood.

By moving a magnet underneath the chip, a droplet containing the bound magnetic particles is physically pulled out of the blood droplet and moved on to the next station—a droplet of washing liquid. The magnetic droplet is combined with the washing droplet and then pulled out again through movement of the magnet. Another droplet then delivers the enzymes and reagents necessary for cell disruption.

The last station is the PCR station. After combination with a reagent droplet, the magnetic droplet is moved around like a clockwork, passing again and again through four different zones set to the temperatures necessary for PCR. Each cycle lasts 8 seconds. A fluorescence detector over one of the zones monitors the progress of the PCR (real-time PCR) and indicates whether the desired gene sequence is present and in what amount.

With their new PCR chip, the researchers were able to isolate 30 cells implanted with the genetic information for a green-fluorescing protein from 25 µL of blood, concentrate them 100-fold, wash them, rupture them, and detect the gene for the green protein by real-time PCR—all within just 17 minutes!

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