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Simple, Portable Test Could Make Blood Transfusions Safer

Medical Diagnostics: A chip-based magnetic nanosensor analyzes microvesicles, particles linked to blood quality

By Prachi Patel

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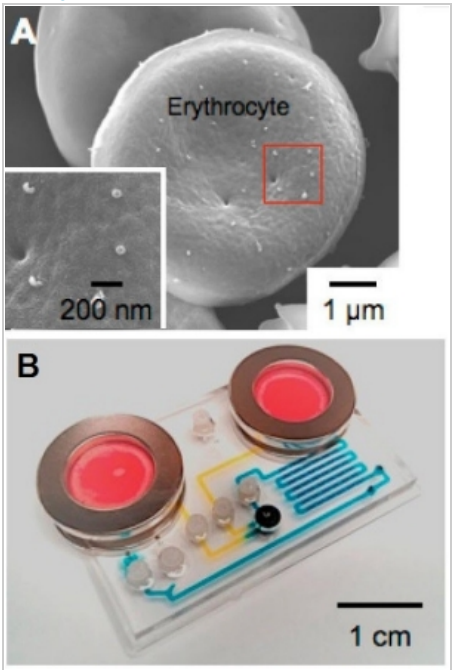

Blood Work
A scanning electron micrograph shows microvesicles (A, inset) budding on the surface of red blood cells. Researchers have developed a chip-based sensor (B) that quickly counts microvesicles and detects their protein content in 150-µL blood samples. Blood samples go in one of two microfluidic inlets (red), pass through a filter that isolates and channels microvesicles into a reservoir (dark blue), where researchers add reagents to anchor them on polymer microbeads and magnetically tag them for micro-NMR analysis.
Credit: *ACS Nano*

Blood meant for transfusion has a limited shelf life. Although blood banks routinely discard red blood cells after 42 days, even unexpired blood samples can sometimes cause adverse transfusion reactions. To avoid these situations, clinics would benefit from a standard test to measure the effect of aging on blood quality. Researchers have now developed a **fast, accurate sensor to gauge a blood sample's quality** by analyzing tiny particles shed from blood cell membranes (*ACS Nano* 2013, DOI: **10.1021/nn405016y**).

Many types of cells shed microvesicles, small fragments of cell membrane surrounding bits of protein and RNA. Recent studies suggest that the concentrations of these microvesicles in stored blood could indicate blood quality (*Curr. Opin. Hematol.* 2010, DOI: **10.1097/MOH.0b013e32833ec217**). But the 200-nm-wide particles are difficult to detect and characterize. Known techniques take hours, and either significantly underestimate counts or cannot analyze single vesicles. A test to study and count the vesicles accurately could provide a new way to measure blood quality and improve transfusion safety.

To that end, **Hakho Lee** and his colleagues at **Massachusetts General Hospital** have developed a chip-based sensor that uses a miniaturized nuclear magnetic resonance system to accurately count microvesicles as well as detect the proteins that they carry. Processing a blood sample takes half an hour, and blood banks could deploy this portable system easily, Lee says. The sensor extends seven years of work on a technology that the team has developed to detect proteins and microbes.

The research team analyzed microvesicles shed by red blood cells, which build up over time in stored blood. The chip has two parts: a microfluidics device and the miniature NMR. A 150-µL blood sample flows through the inlet to a membrane filter that permits the small microvesicles to enter a reservoir. There, the vesicles adhere to polymer microbeads coated with antibodies that bind to a protein abundant in the vesicles. Then the researchers attach magnetic nanoparticles to the anchored microvesicles with a second set of antibodies, selected to target their proteins of interest.

Finally, the researchers transfer the sample to their laptop-sized micro-NMR system. The signals from the labeled microvesicles

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allowed them to measure the total number of vesicles and the quantity of various proteins on the vesicles. A light-scattering counting technique confirmed the microvesicle count.

The microvesicle concentration in the blood samples increased as the samples aged, and the rate of this increase varied for different samples. In addition, the researchers could estimate the amount of unstructured hemoglobin inside the microvesicles. This protein, known to damage blood vessels and cause cell death, could be one cause of the transfusion reactions with older blood samples, Lee says.

The medical community has not reached a clear consensus about the role of microvesicles and blood sample age in safety, says **Niels Lion**, a researcher in the blood transfusion unit at the **University Hospital of Lausanne**, in Switzerland. The lack of an adequate analytical tool at a reasonable cost is one reason microvesicles are not used as a blood quality index. “This smart device has the potential to dramatically reverse that situation,” he says.

Circulating microvesicles have appeared in a number of disease states, Lion adds, so the device could have applications beyond transfusion. “The possibility of probing antigens at the surface of microvesicles while counting them could provide completely new ways to approach the search for diagnostic markers, especially in cancer research.”

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