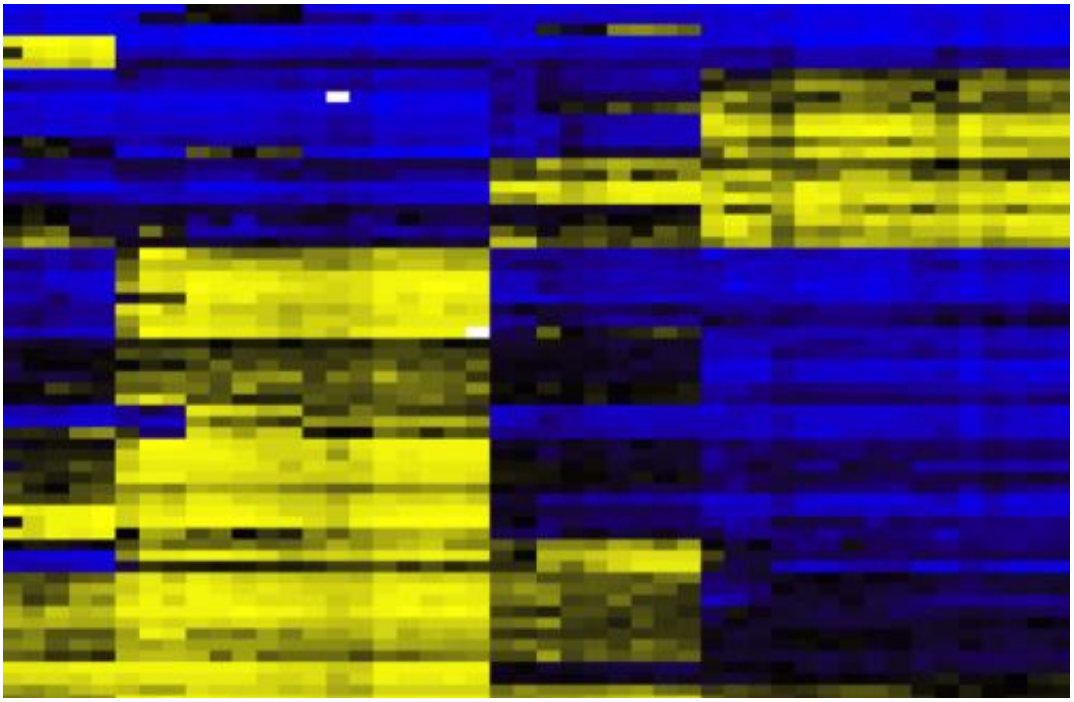
An inventive new way to profile immune cells in blood

March 5 2014



A new technique based on microarrayss distinguishes cell types in blood by looking at signature degrees of methylation in DNA. Yellow represents no methylation, and blue represents full methylation. Credit: Kelsey Lab/Brown University

When a person becomes sick or is exposed to an unwelcome substance, the body mobilizes specific proportions of different immune cells in the blood. Methods of discovering and detecting those profiles are therefore useful both clinically and in research. In a new paper in the journal

Genome Biology, a team of scientists describes a new and uniquely advantageous way to detect them.

All the current means of counting immune cells in a blood sample require whole cells, said Karl Kelsey, professor of epidemiology at Brown and corresponding author, but the new system relies on something far less ephemeral: DNA. Its use of hardy strands of genetic material allows it to handle even archived samples where cells have lost their physical integrity.

All of a person's immune cells—in fact, nearly all of their cells—have exactly the same DNA, but what makes a kidney cell different from a brain cell or a T-cell distinct from a B-cell are chemical alterations known as epigenetic marks. Those cause a cell's genes to be expressed in the particular way that makes them different. One type of those alterations is methylation, and every kind of cell has its own methylation signature.

"Once you understand the unique and really immutable signature that directs the differentiation of the cell, then you can use that and you don't need the cell anymore," Kelsey said.

So the new test detects those methylation signatures in a blood sample and, with the help of sophisticated algorithms, counts up how many cells of each type are in the sample. In the experiments reported in the paper, Kelsey, lead author William Accomando, and colleagues counted up the following major immune cell types, or leukocytes: T-cells, B-cells, NK cells, monocytes, eosinophils, basophils, and neutrophils.

Based on their tests using fresh human blood samples from more than 80 donors, they report that their technique's accuracy performed at par in a direct comparison with three "gold standard" methods: "manual five-part differential," "CBC with automated five-part differential," and

"fluorescence activated cell sorting."

In further experiments they showed that their technique works to detect the mixtures of immune cells associated with known diseases and that the technique works with blood exposed to storage conditions such as freezing and the addition of anticoagulants.

Moreover, in their experiments the team showed that to distinguish among and count those various immune cell types, they only needed to measure a few dozen methylation marks in the DNA. What's sufficient to constitute a signature, in other words, can be quite short.

The main ingredients of the method, Kelsey said, are libraries of methylation signatures of cells. Kelsey's lab determined the ones needed for this study, but big new epigenetics research consortia in Europe and the United States are poised to produce many more, greatly expanding the versatility of the proprietary method to cover more immune cells and other cell types as well.

In addition to the algorithms and the libraries, the test also requires some hardware, such as commercially available methylation microarrays.

The method has proven feasible enough that many other epidemiology research labs are already using it, Kelsey said. Brown University has also applied for a patent on the technique. He said it has the potential to be cheaper and faster than current techniques, although he didn't measure that in the paper.

More information: genomebiology.com/2014/15/3/R50

Provided by Brown University