New detailed immune-profiling method uses only DNA from blood

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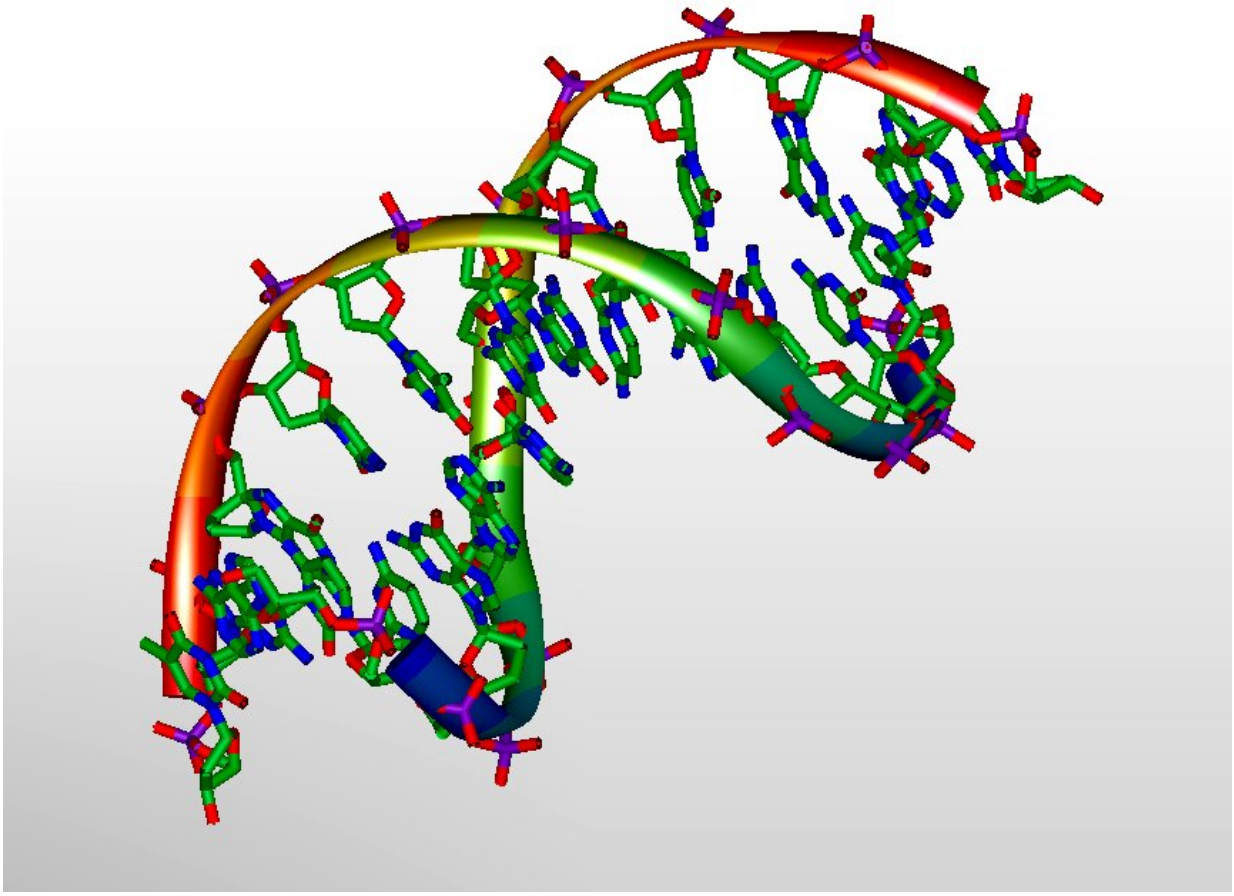

3D-model of DNA. Credit: Michael Ströck/Wikimedia/ GNU Free Documentation License

Flow cytometry is a powerful and complex technology used to count, sort or measure characteristics of cells and to detect biomarkers. It's also widely used in research, as well as in clinical studies and diagnosis of disorders such as blood cancers. However, flow cytometry requires intact and usually fresh cells, that must be processed promptly to preserve cell integrity and surface markers. Those surface (and a few nuclear) markers are used to identify immune cell types.

Researchers at Dartmouth's and Dartmouth-Hitchcock's Norris Cotton Cancer Center (NCCC), in collaboration with the Brown University School of Public Health, University of California, San Francisco (UCSF), and University of Kansas Medical Center (KUMC), introduce a novel immune-profiling method capable of reporting specific immune cell types using only DNA from blood rather than from fresh cell samples. Their method, "Enhanced cell deconvolution of peripheral blood using DNA methylation for high-resolution immune profiling," is newly published in *Nature Communications*.

"Our technology requires minimal input to use blood DNA samples stored under different conditions," says lead author Lucas A. Salas, MD, MPH, Ph.D., member of NCCC's Cancer Population Sciences Research Program (CPS) and Assistant Professor of Epidemiology at the Geisel School of Medicine at Dartmouth. "This is ideal in population epidemiological research and potentially for clinical settings where samples cannot be processed immediately."

"Our paper details a new method that offers a powerful alternative to conventional flow cytometry based on blood DNA rather than intact living cells," adds co-author John Wiencke of the UCSF Institute for Human Genetics.

The new approach offers the opportunity to ask and answer questions about the immune system in health and disease using the millions of

stored blood samples from biobanks in the U.S. and worldwide—samples that already exist for other reasons. In the clinical setting, the complete cell blood count (CBC) differential is used routinely to diagnose patient conditions and is limited to five general immune cell types. In the new method, immune cell identification is extended to include twelve immune cell types, including several that are not determined with CBC, such as naïve and memory T and B cells.

Large-scale human population studies and clinical trials can now access detailed information about individual immune status in a standardized, cost-effective manner, without some of the limitations of existing methods. The advancement paves the way for new research of systemic immune factors in disease and aging. "Not only does the approach return more than double the number of cell types compared with standard clinical methods, but because it doesn't depend on surface markers or intact cells, it can be used with either fresh or archival blood," says Salas.

When the method was applied to cancer patients, immune profile responses to chemotherapy and radiation therapy were observed. Corresponding author and CPS co-Director Brock C. Christensen, Ph.D., is investigating how this new method may help predict response to immunotherapy. "Detailed immune profiling with our new method is expected to uncover biomarkers of response to existing and emerging cancer immunotherapies as well as to other immunomodulatory drugs," says Christensen. "This technology also has great potential in advancing cancer immunoprevention efforts."

The team's next steps are to evaluate the many potential uses for this new tool to understand how it will best and most immediately benefit clinicians and patients. Such technology could elicit a paradigm shift in the way clinicians, patients and researchers harness and understand information about the immune system in health and disease.

More information: Enhanced cell deconvolution of peripheral blood using DNA methylation for high-resolution immune profiling, *Nature Communications* (2022). DOI: 10.1038/s41467-021-27864-7