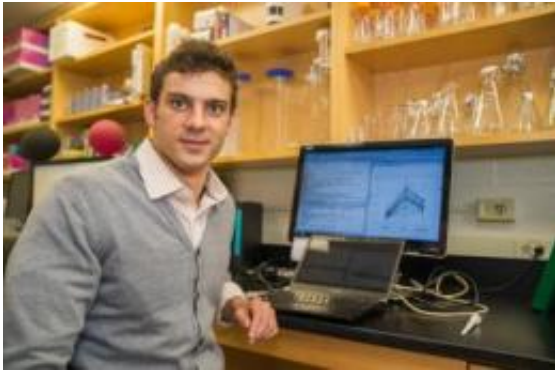


Blood cells may offer telltale clues in cancer diagnosis

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Devin Koestler is a biostatistician whose research is focused on the development and application of statistical methods for analyzing genomic data. Credit: Eli Burakian

Postdoctoral Research Fellow Devin Koestler is a biostatistician in the Geisel School of Medicine at Dartmouth. He develops and applies statistical methods to large volumes of data, seeking new approaches for understanding disease, cancer in particular. Koestler and his colleagues are investigating the potential use of white blood cell variation as a diagnostic, predictive, and research tool in the study of non-blood cancers.

"There is promise here for a new diagnostic tool," says Koestler. "What we show here is not ready for immediate clinical utility, but I think it is on the right path."

Koestler is working in the Quantitative Biomedical Sciences program with Professors Margaret Karagas and Jason Moore. His focus is the development of computational and statistical tools for investigating the process of DNA methylation.

In methylation, a molecule known as a [methyl group](#) (chemically CH₃—three [hydrogen atoms](#) and one carbon) attaches itself to the DNA. When this occurs, the DNA function can change dramatically. An example might be the methyl group blocking the expression of a tumor-suppressing gene.

Koestler is the first author on a paper with Karagas and a host of colleagues from Dartmouth, Brown University, Oregon State University, the University of Minnesota and the University of California. Its subject is methylation in leukocytes ([white blood cells](#)) and their association with [cancer](#) in tissues and organs other than blood, such as bladder or [ovarian cancers](#).

"When we have an illness or a disease, that does something to our immune system," Koestler explains. "It responds by providing whatever cells are necessary to combat that threat. In the blood, the leukocytes supply that immune response."

Methylation has been studied in biopsied cells from cancer patients, in comparison to cells of cancer-free individuals. "Those studies have compellingly shown there are very striking differences in methylation patterns between cancer and cancer-free subjects," Koestler says. "This brought us to also look at patterns of methylation in blood."

The new studies, in which Koestler took part, showed differences in methylation patterns in the leukocytes of [cancer patients](#) versus cancer-free individuals. There are different types of leukocytes, referred to as subsets, each of which exhibits its own signature methylation pattern.

The proportions of these identifiable subsets shift, depending on the kind of disease they may be combating.

Using data from studies of ovarian, bladder, and head and neck cancers, the researchers demonstrated statistically significant correlations between the specific cancers and the methylation signatures that characterize leukocyte subsets.

"What made our study unique is that we had the methylation data on the individual leukocytes themselves, enabling us to connect the dots, and better understand the mechanisms underlying the results from previous studies."

Analyzing the relative proportions of the leukocyte types in the blood sample can help predict the onset of a particular cancer or identify and diagnose a cancer in progress. The alternative of sampling a patient's blood is far preferable to undergoing an invasive surgical biopsy.

The advantages of using methylation patterns to assess proportions of white blood cell subtypes in cancer research extend beyond the bedside to the lab bench. Archival blood samples frozen and stored at some time in the past can now be used as research material, whereas existing methods typically require fresh blood samples with intact cells to assess white blood cell subtypes.

Provided by Dartmouth College

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