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Researchers develop simple method to characterize immune cells in tumors

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Despite recent achievements in the development of cancer immunotherapies, only a small group of patients typically respond to them. Predictive markers of disease course and response to immunotherapy are urgently needed. To address this need, researchers at The Tisch Cancer Institute (TCI) at the Icahn School of Medicine at Mount Sinai have developed a new method of analyzing multiple tissue markers using only one slide of a tumor section to better understand immune response occurring locally. Named MICSSS, for multiplexed immunohistochemical consecutive staining on a single slide, the new technique helps characterize human cells involved in immune responses at the tissue site, before and after treatment with immunotherapy. The research, published today in the journal *Science Immunology*, may help define new biomarkers to predict patient outcome.

In cancer, having a measurable immune response at the tumor site has been associated with improved outcome of patients with various types of cancers. Recent studies have shown that tumor-infiltrating immune cells consist of different subtypes with distinct functions, and that their frequency, localization, and organization in cancer tissues end up either promoting antitumor immunity or, in some cases, preventing it; both of these eventually affect the patient's outcome. However, a lack of methods to characterize the complex relationships between immune and cancer cells and the difficulty of obtaining enough tissue to do so with standard methods hampers the ability to study the mechanisms at play.

"Our goal was to get a better understanding of immunologic responses at

the tumor site while addressing the need for high-dimensional analysis using as little tissue as possible," said Sacha Gnjatic, PhD, Associate Professor of Immunology, Hematology, and Medical Oncology at TCI, who was the senior co-author of this study with Miriam Merad, MD, PhD, Professor of Oncological Sciences, Hematology, and Medical Oncology at TCI. "We need more comprehensive analyses of the immune microenvironment of tumors, as part of our immune monitoring to inform treatment and predict outcomes for cancer patients."

Lead author Romain Remark, PhD, a postdoctoral fellow working in the laboratories of Dr. Gnjatic and Dr. Merad, helped develop a new method to look at multiple tissue markers and detect expression of biological markers with just one tissue section slide. Researchers applied the MICSSS technique to tumor tissue sections of melanoma and lung cancers. This enabled views of co-expression of markers on the same cells while sparing material from tissues.

"The MICSSS technique helps us characterize the distribution of complex cell subsets in tumor tissues without cross-reactivity between staining cycles," said Dr. Remark. "In contrast to other available methods, our approach is not as reliant on proprietary reagents or instruments and should be easier to adapt because it follows the same staining steps currently implemented throughout all pathology labs."

If the MICSSS method is proven successful in mapping other tumor types (hepatocellular carcinoma, colorectal, breast, head and neck, or pancreatic cancers), the investigators believe it may be useful beyond just cancer. It offers the ability to reuse any slide from a tissue sample, up to 10 times, and to characterize multiple parameters with standard chromogen staining. Researchers have begun to apply MICSSS to characterize immune and tissue markers of diabetes, HIV-related kidney pathology, inflammatory bowel disease, and atherosclerosis.

"We hope to implement MICSSS as part of the Human Immune Monitoring Center at TCI to characterize the types of immune cells infiltrating various cancers and other disease for their density, localization in the tissue, and diversity," said Dr. Merad.

More information: "In-depth tissue profiling using multiplexed immunohistochemical consecutive staining on single slide," *Science Immunology*, sciencemag.org/lookup/doi/10.1 … 6/sciimmunol.aaf6925

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