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# Scientists identify targets for melanoma immunotherapy

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Using a highly sensitive technology called NanoString, researchers have identified seven targets that could potentially be used to develop new immunotherapies for patients with metastatic melanoma, according to a study published in *Clinical Cancer Research*, a journal of the American Association for Cancer Research.

"We identified seven potential candidate genes that deserve further consideration as targets for melanoma immunotherapy," said Richard Morgan, Ph.D., staff scientist at the Tumor Immunology Section of the Center for Cancer Research, National Cancer Institute (NCI), in Bethesda, Md. "We used NanoString technology because it is very robust, yielding quantitative and extremely reproducible results and, in addition, an antigen expression profile can be constructed for a patient from a very small amount of tumor sample, which makes NanoString a better clinical tool."

NanoString technology allows for the simultaneous measurement of multiple genes that are expressed in higher amounts in tumor cells than in normal cells. Researchers isolate genetic material called RNA from tumor samples, use this technology to measure the amount of RNAs present in tumors, and compare them with those present in normal tissues. Unlike many other technologies that can be used for this purpose, NanoString can detect and measure the expression levels of the genes in a single step, avoiding errors.

"Our laboratory has developed a battery of different antigen receptors to

target a wide range of antigens, and we can engineer human immune cells to recognize the targets in patients' tumors and kill those cells," said Morgan. "The NCI surgery branch is conducting several clinical trials using this technology to treat a variety of cancers."

In these clinical trials, the NCI researchers are treating patients with adoptive immunotherapy, a type of cancer treatment that involves "teaching" the immune cells of a patient to locate specific targets on tumor cells and kill those cells. Identification of the right targets present in a patient's tumor is, therefore, essential for immunotherapy to be successful.

Morgan and colleagues took metastatic melanoma samples from 59 patients, five established melanoma cell lines, and 31 normal tissue samples to profile the excessively expressed genes using NanoString. The researchers identified 67 genes that can be recognized by immune cells as targets on melanoma cells. They subsequently short-listed seven of these genes as ideal candidates because these genes fit the criteria: they were excessively expressed in melanoma tumors and were absent or at low levels in normal tissues, thus targeting them should cause no or minimal toxicity to nontarget organs.

Of these seven genes, five of them, CSAG2, IL13RA2, MAGEA3, MAGEC2, and PRAME, belong to a family called the cancer-testis genes, and the remaining two, CSPG4 and SOX10, are melanoma-related genes. Further investigation is needed before immune cells engineered to target these markers can be used in patients, according to Morgan.

"This is a good example of how newer technologies like NanoString arm cancer researchers and clinicians with the best gear to make tremendous advancements in cancer research and treatment," said Morgan. His team is currently using this technology to identify immunotherapy targets for

pancreatic cancer.

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