

# Scientists identify critical cancer immunity genes using new genetic barcoding technology

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Scientists at Mount Sinai have developed a novel technology for simultaneously analyzing the functions of hundreds of genes with resolution reaching the single cell level. The technology relies on a barcoding approach using a novel protein described in a paper published in the journal *Cell*.

Since the sequencing of the first human genome in the early 2000s revealed a set of more than 20,000 protein-coding genes, scientists have not yet been able to characterize the many functions of individual gene. Without that information, our understanding of how the human genome works—and how to use that knowledge to predict, prevent, treat and even cure disease—is limited. In 2012 and 2013, scientists established a powerful new approach for editing genes, called CRISPR, which can be used to determine gene functions. CRISPR has taken the scientific world by storm, but researchers have still been challenged with using CRISPR to study the many thousands of genes and their numerous possible roles.

A new technology developed by scientists at the Icahn School of Medicine at Mount Sinai helps address the genomics challenge of analyzing the genome at an unprecedented scale. The research, led by postdoctoral fellows Aleksandra Wroblewska, Ph.D. and Maxime Dhainaut, Ph.D., is novel tool to barcode and track different CRISPRs using synthetic proteins called epitopes. The protein barcodes referred to as Pro-codes, enables hundreds of CRISPRs to be used together to knockout a multitude of genes.

While there are existing technologies for pooling CRISPRs, these approaches rely heavily on DNA as a barcode and permit only a low resolution look into gene function. Through the Pro-Code technique, Mount Sinai researchers were able to demonstrate a way for scientists to more comprehensively characterize the biological effects of a gene.,

In the study, the researchers used the Pro-Code technology to search for genes required for the immune system to protect from cancer. They generated CRISPRs to target the deletion of suspected immune regulatory genes, and paired them with the Pro-Codes. Pro-Code/CRISPR libraries were then introduced to breast [cancer cells](#), and the tumors were challenged with killer T [cells](#) that had been engineered to recognize the cancer cells. Most of the cancer cells were rapidly

eliminated by the T cells but there were some cells that completed resisted death. The Pro-Code technology helped determine which genes were lost in the resistant cells some with unrecognized roles in sensitizing cancer cells in the immune system. The studies also identified a negative regulator of the immune checkpoint PD-L1, a major clinical target of cancer immunotherapy.

"There is still a great deal of work to be done to fully understand the human genome. We still don't know what most genes do and how they are connected," said Brian Brown, Ph.D., Associate Professor of Genetics and Genomic Sciences and Associate Director of the Immunology Institute at the Icahn Institute at Mount Sinai and senior author of the publication. "The Pro-Code technology could greatly accelerate one of the major goals of the post-genome era: annotation of the [human genome](#). This discovery will be key to discover disease-causing [genes](#) that could lead to novel drug targets. It's already given us new insights in [cancer](#) immunology."

**More information:** Aleksandra Wroblewska et al, Protein Barcodes Enable High-Dimensional Single-Cell CRISPR Screens, *Cell* (2018). [DOI: 10.1016/j.cell.2018.09.022](https://doi.org/10.1016/j.cell.2018.09.022)

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