PERSONALIZED VACCINE DESIGN

To create an individualized cancer vaccine, researchers must identify cancer-specific peptides called neoantigens, then use a cell-, protein-, or nucleic acid–based platform to deliver those neoantigens to patients to prime the immune system to attack the tumor.

CANCER VACCINE BASICS

Antigen-presenting cells such as dendritic cells (purple) internalize the cancer-specific peptides (bright green) selected for a personalized cancer vaccine and display them on their surface with the help of major histocompatibility complex (MHC) proteins. This triggers T cells (blue) with receptors that bind those neoantigens to differentiate into effector, or killer, T cells (green) that mobilize an immune reaction against cancer cells (orange).

NEOANTIGEN SELECTION

Before building an individualized cancer vaccine, researchers must determine which neoantigens will be included to elicit an immune response against the tumor cells. In collaboration with scientists around the world, our group has developed a computational pipeline for selecting those cancer-specific peptides that are most likely to drive a robust immune response against the tumor.

DNA SEQUENCING, ALIGNMENT, AND VARIANT CALLING

Next-generation sequencing data from tumor and normal DNA are aligned and compared to the human reference genome and then to each other to identify tumor-specific alterations. These variants are then evaluated for their resultant changes to the amino acid sequences of the encoded proteins.

CANDIDATE NEOANTIGENS

FILTER #1

RNAseq data from tumor RNA are evaluated to ensure the predicted alterations are being made into RNA transcripts, and we can further cull the list for other reasons, such as lack of sequence coverage of that region or gene.

FILTER #2

Researchers isolate MHC proteins from patients and evaluate their bound peptides by mass spectrometry to validate that these peptides are being presented by MHC. In aggregate, such data can be used to improve the computer models that predict neoantigens.

EPITOPE PREDICTION

The selected sequences are evaluated by computer models that predict the binding of the neoantigens to the major histocompatibility complex (MHC) proteins that would present them on the surface of cells.