New Immune System Understanding May Help Doctors Target Cancer

The research focuses on natural killer cells, which recognize and attack cells affected by cancer, and genes that help target invaders.

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Your immune system's natural killer cells recognize and attack two major kinds of danger — cells infected by viruses and cells affected by cancer. When natural killer (NK) cells see a cancer cell, they kill it (naturally…). And a major research focus has been to define how NK cells do this "seeing." One way NK cells see cancer is by recognizing bits of mutated DNA displayed on "silver platters" made by human leukocyte antigen (HLA) genes.

In fact, there are two classes of HLA genes. HLA class 1 genes do exactly this task of making proteins that display a cell's DNA for examination and evaluation. But while HLA class 1 genes help to identify bad actors among the body's own cells, HLA class 2 genes help the body mark and target invaders from outside the body, rallying antibodies against things like bacteria.

So why has recent research shown that patients whose cancer cells are marked by high counts of HLA class 2 proteins have better outcomes? Sure, HLA class 1 brings NK cells to attack tumor tissue, but it's not like HLA class 2 interacts with NK cells, right?

Wrong.

A University of Colorado Cancer Center study recently published in the journal >Nature Immunology shows that NK cells do, in fact, interact with HLA class 2. The implications may help researchers better harness the immune system to fight cancer, and, on the other side of the coin, may also help to calm the immune system's attack of healthy tissues in some autoimmune conditions.

"The understanding has been that NK cells interact with HLA class 1 but not class 2. The identification of a mechanism that class 2 uses to interact with NK cells changes our perception of NK cell biology," says study co-author Paul Norman, PhD, CU Cancer Center investigator and associate professor in the CU School of Medicine Division of Personalized Medicine, and Department of Microbiology and Immunology.

Basically, collaborators at the German Center for Infection Research screened many types of

proteins created by HLA class 2 genes to see if any would activate NK cells.

“This is called ligand screening — test lots of potential ligands and see what sticks. But because it was established fact that HLA class 2 didn’t interact with NK, nobody looked. They were smart enough to look when nobody else did,” Norman says.

Specifically, the team found that a kind of HLA class 2 called HLA-DP401 does indeed activate NK cells — and HLA-DP401 is one of the most common variations (called alleles) found in Europeans.

“The problem is that not every one of these HLA class 2 molecules is recognized by NK cells. HLA is polymorphic and different individuals have different kinds. The next step is to identify which patients have the right combinations of HLA class 2 and NK cells — like we recently published for HLA class 1 in leukemia protection — and then we could potentially learn to engineer NK cells to interact with HLA class 2 alleles they don’t interact with now,” Norman says.

Norman’s ongoing research hopes to further define the mechanism of interaction between the proteins created by HLA class 2 genes and NK cells.

“Eventually, this could be another way to direct the immune system toward cancer and away from healthy tissues,” Norman says.

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