Immunotherapy 101

New types of treatment can help the immune system recognize and fight cancer.

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Unlike chemotherapy and radiation, which directly kill cancer cells, immunotherapy helps the immune system hunt down and attack malignant cells.

Many types of immunotherapy work by boosting killer T cells, the main soldiers in the immune response against cancer. Some promote the activity of natural killer (NK) cells. Immune cells continuously patrol the body looking for abnormalities, but cancer can sometimes hide from the immune system or disable normal immune responses.

Immune checkpoint inhibitors—the most widely used immunotherapy—are monoclonal antibodies that boost T cells' ability to fight malignant cells. Several approved checkpoint inhibitors block the PD-1 receptor, which acts as a brake on T-cell activity, or its binding partner PD-L1. Drugs that interfere with the interaction between PD-1 and PD-L1 can release the brakes and restore a robust immune response. Other checkpoint inhibitors block CTLA-4 and LAG-3 proteins. Checkpoint inhibitors work best against "hot" tumors, such as melanoma, which attract many immune cells; they don't work as well against "cold" tumors, like pancreatic and prostate cancer.

Adoptive cell transfer therapies involve direct administration of immune cells. In an autologous transfer, cells are removed from a patient, multiplied and sometimes modified in a lab and returned to the body. One approach collects immune cells from a patient's tumor, known as tumor-infiltrating lymphocytes, that have proven cancer-fighting ability. An allogeneic transfer uses immune cells from someone else—for example, a stem cell transplant from a matched donor.

Chimeric antigen receptor T-cell therapy—better known as CAR-T—reprograms T cells by inserting artificial receptors that recognize cancer. T cells are collected from a patient and genetically modified to create a customized "living drug." Current CAR-T therapies work best against blood cancers, but researchers are testing new options to treat solid tumors. CAR-NK therapies are also now in development.

Cancer vaccines are one of the most promising areas of immunotherapy research. Therapeutic vaccines used for cancer treatment work differently than preventive vaccines that protect against cancer-causing hepatitis B virus or human papillomavirus.

Personalized messenger RNA (mRNA) vaccines train T cells to recognize mutated proteins called neoantigens collected from a patient's tumor after surgery. They are showing promise against melanoma, pancreatic cancer and other malignancies. Researchers are also working on off-the shelf vaccines that don't need to be custom-made for each patient. Cancer vaccines are often combined with checkpoint inhibitors, which has the effect of releasing the brakes and stepping on the accelerator at the same time.

Other types of immunotherapy include cytokines (chemical messengers that regulate immune response), immunomodulatory drugs (used to treat multiple myeloma), the IL-15 receptor superagonist Anktiva, which activates NK cells and killer T cells (approved for bladder cancer), and bispecific T-cell engagers, dual antibodies that create a bridge to bring T cells close enough to attack cancer cells.

Immunotherapy can lead to long-term remission—and potentially a cure—for some patients, but it doesn't work for everyone or for all types of cancer. Combining different approaches may yield the best outcomes. Hundreds of immunotherapy clinical trials are underway, and this can be a good way to gain access to promising experimental therapies.
