



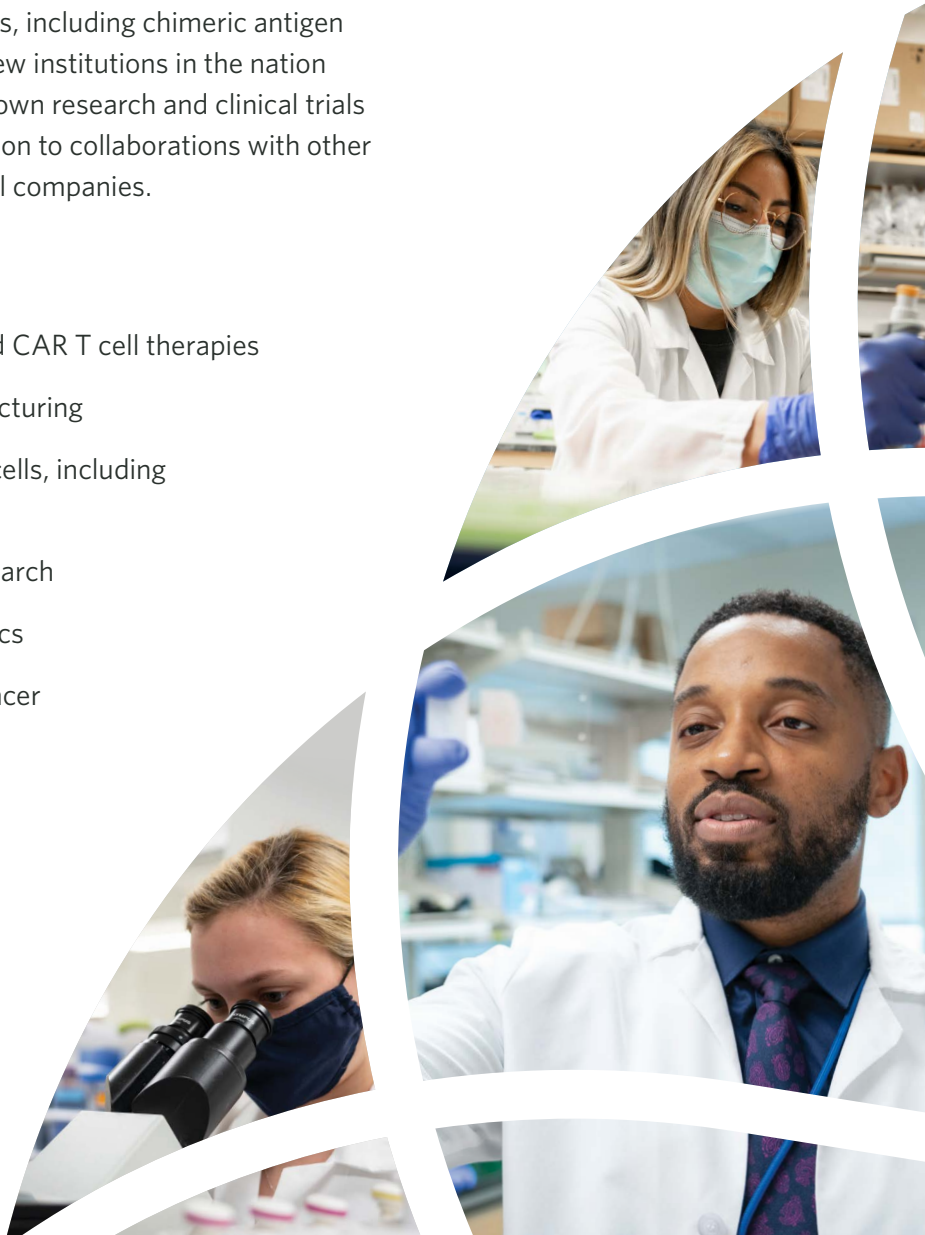
Cellular Immunotherapy

We are harnessing the immune system in ways never thought possible.

City of Hope is a leader in cellular immunotherapies, including chimeric antigen receptor (CAR) T cell therapy. We are one of the few institutions in the nation that innovates CAR T cell technology through our own research and clinical trials for hematologic cancers and solid tumors, in addition to collaborations with other academic researchers and global biopharmaceutical companies.

At the forefront of cellular immunotherapy we:

- Offer all Food and Drug Administration-approved CAR T cell therapies
- Offer on-site CAR T cell engineering and manufacturing
- Treat over 1,000 patients with immune effector cells, including CAR T cell therapy
- Conduct groundbreaking bispecific antibody research
- Develop natural killer (NK) cell-based therapeutics
- Explore oncolytic viruses for the treatment of cancer



CAR T CELL THERAPY

In **CAR T cell therapy**, a patient's own immune cells are collected, genetically modified to target the cancer cells and reintroduced to the patient. CAR T cell therapy has demonstrated promise in directing anti-tumor immune responses and has been successfully used in the treatment of B cells malignancies, such as chronic lymphocytic leukemia and acute lymphocytic leukemia. The success with hematologic malignancies has paved the way for the development of CAR T cells for other cancer types, including brain tumors and other solid tumors. City of Hope is leading the way in advancing CAR T therapies by applying our proprietary CAR T technology in active preclinical and clinical programs across a range of hematologic cancers and solid tumors. Among the diseases that City of Hope physicians and scientists are targeting with CAR T cell therapy are lymphoma, leukemia, glioblastoma and prostate cancer.

NATURAL KILLER CELLS

Natural killer (NK) cells are lymphocytes that "naturally" target and destroy any abnormal cells they find in the body, including cells infected with viruses. In those with cancer, however, tumors have developed mechanisms to circumvent NK cells. **Currently, efforts are being made to harness the potential of NK cells as a tool against cancer.** CAR-engineered NK (CAR-NK) cells are gaining ground on CAR T cells because of better safety, cell-killing ability and high feasibility for "off-the-shelf" manufacturing, as well as potentially better effectiveness against solid tumors.

In 2021, City of Hope and CytolImmune Therapeutics Inc. announced that they had entered into worldwide exclusive license agreements to develop several patent applications related to developing CAR-NK cell therapies, including a prostate stem cell antigen CAR to treat pancreatic, gastric, bladder, prostate and some lung cancers, a programmed death-ligand 1 (PD-L1)+ NK cell for use in treating lung cancer, and fms-like tyrosine kinase 3 (FLT3) CAR-NK cell therapy for use in treating acute myeloid leukemia.

ONCOLYTIC VIRUSES

An oncolytic virus is a virus that infects and kills cancer cells. As the infected cancer cells are destroyed, they release new infectious virus particles, or virions, which help destroy the remaining tumor. Oncolytic viruses can also be genetically engineered to encode transgenes for targeted delivery to tumor cells. A bonus of this approach is that the person's immune system can subsequently form a "memory response" to tumor cells, preventing recurrence. **City of Hope is studying the use of oncolytic viruses to treat breast, pancreatic, stomach, lung, ovarian and colorectal cancer.** Researchers are also studying combining oncolytic viruses with CAR T cell therapy for a more potent punch against solid tumors, which typically do not respond as well to CAR T cell therapy as blood cancers. This approach was licensed to Immugene Ltd. in 2021.

BISPECIFIC ANTIBODIES

Standard antibody drugs are designed to specifically target a single antigen. However, many complex diseases, such as cancer, are driven by multiple factors, so inhibiting a single target may not be an effective enough treatment. **Bispecific antibodies are engineered in the lab to treat multifaceted, complex diseases by engaging two disease targets using a single molecule, unlike natural antibodies, which target just one antigen.** This therapy enables the body's T cells to recognize, attack and destroy cancer cells. City of Hope is studying their efficacy in treating blood cancers, such as leukemia, lymphoma and multiple myeloma. Research by Elizabeth Budde, M.D., Ph.D., associate professor in City of Hope's Division of Lymphoma, Department of Hematology & Hematopoietic Cell Transplantation, has shown that a bispecific antibody called mosunetuzumab has paradigm-changing potential as a new treatment option for people with follicular lymphoma, a type of blood cancer and the most common indolent form of non-Hodgkin lymphoma, with 80% of patients responding positively to the treatment.

REFER A PATIENT

Call **800-COH-4DRS (264-4377)**, Monday through Friday, 8 a.m. to 6 p.m., to speak with a patient referral specialist.

