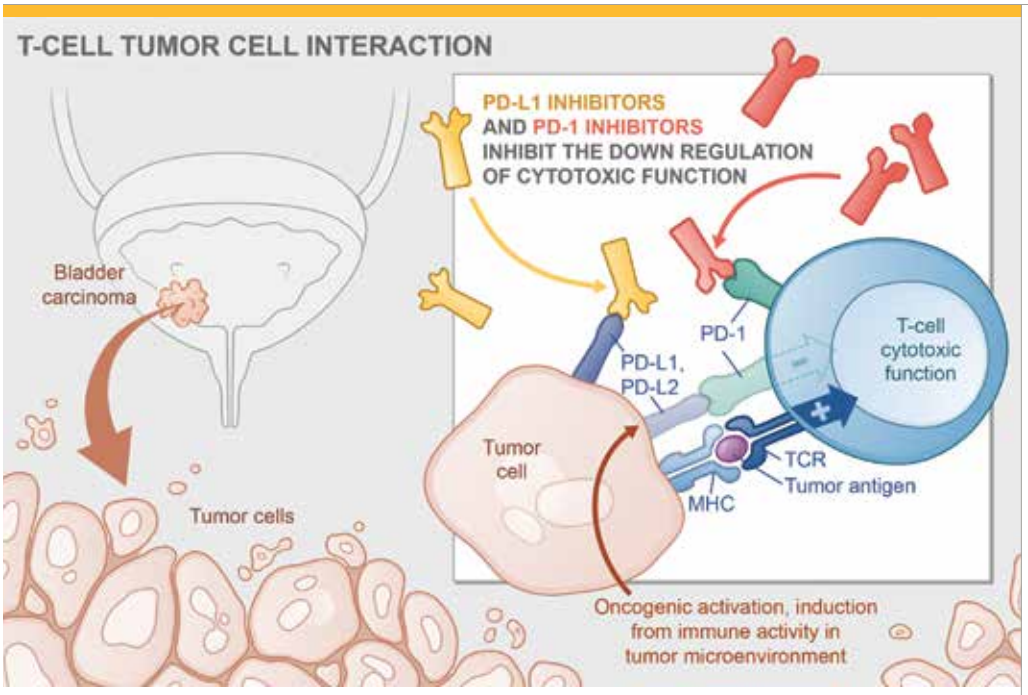
UCLA Health

UCLA researchers advance immunotherapy approaches for genitourinary cancers



The programmed cell death 1 receptor (PD-1) and its ligands, PD-L1 and PD-L2, play key roles in the suppression of T-cell activity. Checkpoint-inhibiting drugs block this receptor/ligand interaction and enhance T-cell-mediated tumor destruction.

Breakthroughs in immunotherapy are revolutionizing the treatment of genitourinary cancer, with new treatment options available or imminent for patients with kidney, bladder and prostate cancer.

UCLA was an early innovator in treatments that bring the patient's immune system to bear against cancer. With more than 25 years of experience, the UCLA Institute of Urologic Oncology maintains one of the nation's largest immunotherapy treatment and research programs, offering patients every new clinical protocol that becomes available and with multiple clinical trials currently under way or slated to begin.

The Institute of Urologic Oncology houses separate clinics for kidney, bladder and prostate cancers. A team of urologists, medical oncologists and radiation therapists collaborate to review challenging cases and make treatment recommendations.

Early successes in immunotherapy

Urologists were among the first specialists to employ immunotherapy in the fight against cancer, with introduction in the mid-1970s of the Bacillus Calmette-Guérin (BCG) vaccine for superficial bladder cancer. In 1985, immunotherapy produced another success when interleukin-2 (IL-2) — a protein that regulates white blood

Immunotherapy will play major role in future cancer therapy

Immunotherapy has been called one of today's most promising frontiers in cancer therapy. Among developments just on the horizon, researchers are looking into ways to "turbocharge" T-cells by injecting them with genes that make them work even faster, a process called target-specific immune activation.

Arie Belldegrun, MD, FACS, director of the UCLA Institute of Urologic Oncology and professor of urology, calls this and other developments "the future landscape of immunotherapy."

In the next five years, at least half of all oncologic cases will be managed by immunotherapy alone or in combination with other therapies, as immunotherapy replaces many existing treatments, says Dr. Bellegrun. He envisions a day when immunotherapy, targeted therapy and hormonal treatment will be the "gold standard" for cancer care, while chemotherapy will be limited and surgery integrated with other therapies.

"After many years of basic and molecular research, we are finally equipped with all the right tools to create new therapies," he says, "and for the first time, we are starting to talk about cancer cures rather than just persistent long remission."

cells responsible for immunity — won approval from the U.S. Food and Drug Administration (FDA). Seven years later, IL-2 would be deployed to treat metastatic kidney cancer. Then in 2010, a cancer vaccine, sipuleucel-T, was FDA approved to treat hormone-refractory metastatic prostate cancer.

Over the past few years, development of immunotherapy treatments has accelerated. One significant area of advancement involves a new class of drugs called checkpoint inhibitors. To block the immune system from waging an attack, cancers create a shield, using receptor proteins found on the surface of T-cells, such as CTLA-4 (Cytotoxic T-lymphocyte–associated antigen 4) or PD-L1 (programmed cell death ligand). Checkpoint inhibitors counter these immune system deterrents.

In a major step forward, checkpoint inhibitors — unlike most cancer drugs — appear to work across tumor types, showing effectiveness in melanoma, kidney and lung cancer, and strong early evidence of a pivotal role in urothelial cancer.

UCLA genitourinary specialists are also investigating the following approaches:

- Cancer vaccines designed to trigger an immune response against tumor cells
- Monoclonal antibodies — molecules engineered to cause cancer-cell death in various ways, such as by blocking signaling pathways needed for tumor growth
- Cytokines — proteins that stimulate a broad-based immune response
- Viruses engineered to destroy tumors and prime the immune system to continue fighting off cancer
- Novel genes (non-coding RNAs) that serve as potential therapeutic targets and immune-system regulators

Specificity, durability and memory

Among immunotherapy's chief advantages are its specificity — it attacks cancer cells while sparing normal cells — and its durability. Studies show some T-cells become long-lasting memory cells, which circulate in the blood for many years, able to identify and attack new cancer cells, even when cancers mutate over time.

At the UCLA Institute of Urologic Oncology, clinical trials are no longer limited to metastatic cancers or patients who have failed other therapies. Doctors are able to provide access to new therapies at earlier stages of the disease. Work is under way on a targeted vaccine for kidney cancer, in development for the past decade, as well as a vaccine for bladder cancer. Among other questions, researchers are examining why immunotherapy works for some patients and not others and whether some immunotherapy approaches are more effective when combined with other treatments.

A first-of-its-kind clinical trial involving bladder cancer, now open and enrolling patients, is exploring the ideal treatment sequence — which patients should receive immunotherapy as a first-line therapy and which should get the treatment after chemotherapy or surgery. Other basic research at UCLA seeks to identify the proteins or antigens present in prostate cancer that the immune system recognizes, a precursor to developing potential T-cell therapies.

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Participating Physicians

Arie Belldegrun, MD, FACS
Director, UCLA Institute of Urologic Oncology
Professor of Urology
Chief, Division of Urologic Oncology
Roy and Carol Doumani Chair in Urologic Oncology

Karim Chamie, MD, MSHS
Assistant Professor-in-Residence of Urology

Alexandra Drakaki, MD, PhD
Assistant Clinical Professor of Hematology/Oncology
Medical Director of Bladder Cancer Research Program

Stuart Holden, MD
Clinical Professor of Urology
Spielberg Family Chair in Urologic Oncology
Associate Director, Institute of Urologic Oncology

Fairooz Kabbinavar MD, FACP
Professor of Medicine and Urologic Oncology
Henry Alvin and Carrie L. Meinhardt Endowed Chair in Kidney Cancer Research
Medical Director, Genitourinary Oncology Program

Allan Pantuck, MD, MS, FACS
Professor of Urology

Robert Reiter, MD, MBA
Professor of Urology, Molecular Biology
Director, Prostate Cancer Program
Director of Urologic Research

Contact Information

UCLA Institute of Urologic Oncology
Wasserman Building
300 Stein Plaza
Los Angeles, CA 90095-7383

(310) 794-7700 Appointments and referrals

iuo.ucla.edu