Accelerating Innovation in Immunotherapy

Geisel School of Medicine at Dartmouth
Norris Cotton Cancer Center

A strategic vision for philanthropic support

Dartmouth GEISEL SCHOOL OF MEDICINE | interaction
THE CAMPAIGN FOR DARTMOUTH MEDICINE

Background

Long before immunotherapy became the most promising breakthrough in cancer treatment, Dartmouth immunologists saw the potential of harnessing the immune system. Since the 1980s, immunologists from Dartmouth's medical school and Norris Cotton Cancer Center have been discovering important regulators of the immune system and laying the scientific foundation for revolutionary cancer treatments. In fact, scientists and physicians at Dartmouth led some of the first modern immunotherapy clinical trials. Today, Dartmouth researchers continue to advance the frontiers of immunotherapy, discovering and developing novel treatments for cancer and neurological and autoimmune diseases.

Our Vision

We will lead the nation in the development of innovative, less-toxic, and more affordable immunotherapies, drawing on Dartmouth's biomedical, engineering, and entrepreneurial expertise. In addition, we will build models of immune response to provide patients with more personalized treatment regimens that minimize unnecessary, ineffective, and potentially detrimental therapies.

Only at Dartmouth

Dartmouth's leading role in immunotherapy research and innovation speaks to the nimble, highly collaborative, and cross-disciplinary research culture at Dartmouth College, the Geisel School of Medicine, Norris Cotton Cancer Center, and Dartmouth-Hitchcock Medical Center. Physicians, basic scientists, biomedical engineers, computational scientists, and biotech entrepreneurs—many of whom are co-located on the Dartmouth-Hitchcock and Dartmouth College campuses—interact freely, without organizational barriers. The ease of interaction between physicians, scientists, and engineers enables a level of collaboration that is hard to achieve in larger medical enterprises.

This community is anchored by Geisel's Department of Microbiology and Immunology—which consistently ranks in the top 15 departments of its kind, nationally, for total federal grant funding—and by Dartmouth's Norris Cotton Cancer Center, a National Cancer Institute-designated Comprehensive Cancer Center. Among the community's successes are the creation of several promising immunotherapies and the formation of multiple biotech start-ups—including Medarex, Celdara Medical, and ImmuNext.

Opportunity for Impact

With targeted philanthropic support, Dartmouth will invest in the people and resources needed to move novel immunotherapies quickly into clinical trials for the benefit of patients at Dartmouth and beyond. We will grow Dartmouth's already strong immunotherapy research pipeline, make discoveries that reveal new opportunities for modulating the immune system,

and scale-up our early phase clinical trial capacity. Dartmouth and its primary clinical partner, Dartmouth-Hitchcock, will become a preferred partner for early phase immunotherapy clinical development and a place known for the rapid cycle of innovation between scientists and physicians.

Outcomes

The impact of your generosity and that of others will be seen in the following:

- New therapeutic approaches devised at Dartmouth will undergo rapid testing and clinical translation to patient care.
- Expanded treatment options will benefit patients facing life-threatening cancers and debilitating neurological and auto-immune diseases.
- Dartmouth's immunology labs will benefit from an increase in partnerships with biotech companies and in new, successful biotech start-ups—both of which are essential to advancing new therapies and sustaining pioneering scientific research.
- Dartmouth will become a preferred partner for pre-clinical and early phase clinical trials, thereby accelerating the testing and development of Dartmouth-created therapies.
- More Dartmouth students will learn from and contribute to the nimble, highly productive immunotherapy research community at Dartmouth and be inspired to pursue careers in biomedical fields.

Gift Opportunities

Clinical Trials Accelerator Fund | $6,000,000 (current use)

Gifts totaling $6,000,000 will provide the immediate resources needed to scale up our early phase clinical trials capacity. While Dartmouth's preclinical immunotherapy research pipeline is world class, its capacity for early phase clinical studies has been limited. This fund will fuel the recruitment of two additional physician-researchers with expertise in running clinical trials, as well as the essential staff and specialized technology needed to support early phase clinical testing of therapies discovered at Dartmouth and other institutions.

Immunotherapy Research Resources Fund | $1,000,000 (current use)

This fund will support a variety of activities essential to scaling up Dartmouth's clinical trial infrastructure. Activities include the creation of a cell therapy suite that meets the regulatory standards for pharmaceutical manufacturing, as required by the Food and Drug Administration; the purchase of specialized equipment; and applications for Investigational New Drug (IND) approval, which allows a new therapy to be tested in humans. These advances will speed the testing and development of new therapies, bringing life-changing treatments to patients at Dartmouth and beyond.

Named Clinician-Scientist Fellowships | $1,000,000 each (endowment)

Endowed fellowships provide critical support to both junior and senior faculty, especially physicians who have busy clinical schedules. Fellowships provide faculty with protected

time to advance new lines of research, clinical treatments, and/or entrepreneurial ideas, and aid in the recruitment of young investigators from high-demand fields.

Named Graduate Student Fellowship | $500,000 each (endowment)

A named endowment of $500,000 will provide support for one graduate student per year to work and learn as part of our distinctive immunotherapy research group. Graduate students are critical members of a research team, contributing both to the science and the mentoring of less-experienced lab members. Fellowships are especially important for international graduate students who do not have access to federal training grants.

Named Student Research Opportunity in Immunology | $100,000 each (endowment)

A named endowment of $100,000 will provide support for one undergraduate student per year to work and learn in an immunotherapy lab at Geisel. Dartmouth students have unparalleled access to leading investigators and contribute broadly to biomedical research across Geisel. Our faculty welcome undergraduate students into their labs as research partners, helping to prepare them for roles as future leaders in science and medicine. Faculty often remark on the energy, creativity, and commitment that Dartmouth students bring to their teams.

Appendix I: Immunotherapy Innovation and Entrepreneurship at Dartmouth

Three biotech companies founded by immunologists at Geisel and Norris Cotton Cancer Center have translated groundbreaking scientific discoveries made at Dartmouth into remarkable treatments for patients.

"Medarex survived in the early days because our clinical colleagues made time to work with us and lead clinical trials with Medarex antibodies, right here, at Dartmouth."

—Paul Guyre, PhD, Medarex Co-Founder

Medarex (est. 1987)

FOUNDED: By three immunologists at Dartmouth's medical school and Norris Cotton Cancer Center: Mike Fanger, PhD, Paul Guyre, PhD, and Edward Ball, MD.

INNOVATION: At a time when most of biotech shied away from cancer immunotherapy, Medarex invested in two promising antibodies—anti-CTLA-4 and anti-PD-1—designed to essentially take the brakes off immune cells so they can attack tumors.

IMPACT: The therapies became the blockbuster, life-saving cancer drugs ipilimumab (Yervoy) and nivolumab (Opdivo) and led to the 2018 Nobel Prize in Physiology and Medicine being awarded to the scientists who brought anti-CTLA-4 and anti-PD-1 to Medarex.

Bristol-Myers Squibb purchased Medarex in 2009 for $2.4 billion; a portion of those profits fund translational research at Geisel.

Celdara (est. 2008)

FOUNDED: By Dartmouth immunologist and Norris Cotton Cancer Center researcher Mike Fanger, PhD, and Jake Reder, PhD, director of the New Ventures Office at Dartmouth's medical school.

INNOVATION: Celdara partnered with Dartmouth immunologist Charles Sentman, PhD, who created a unique form of CAR T-cells based on a natural receptor. Unlike other CAR T-cells on the market, these engineered immune cells can target up to 80%-90% of human cancers and can be allogeneic—compatible with any patient.

IMPACT: Celdara and Sentman's CAR T-cells—now in clinical trials in the U.S. and Europe against seven types of cancer—will revolutionize CAR T-cell therapy, making it widely effective, efficient, and affordable.

ImmuNext (est. 2010)

FOUNDED: By Dartmouth immunologist and Norris Cotton Cancer Center researcher Randy Noelle, PhD, to develop two therapies based on Noelle's discoveries.

INNOVATION: Known as immune checkpoint inhibitors, the ImmuNext therapies target immune system proteins VISTA and CD154—both of which regulate immune cells and play important roles in cancer and a range of autoimmune diseases, such as lupus and multiple sclerosis.

IMPACT: Both therapies have been licensed to large pharmaceutical companies and are in multicenter, Phase I clinical trials in cancer and autoimmunity. Early results are promising.

Appendix II: A Timeline of Immunotherapy

Medarex and Early Immunotherapies

1987	Three immunologists at Dartmouth's medical school and Norris Cotton Cancer Center—Mike Fanger, PhD, Paul Guyre, PhD, and Edward Ball, MD—found the company Medarex to develop cancer immunotherapies based in part on discoveries made in their labs with the support of basic science and clinical colleagues.
1999	Medarex acquires the rights to two antibodies—anti-CTLA-4 and anti-PD-1—and later develops them into two of the top immunotherapies in use today: ipilimumab (Yervoy) and nivolumab (Opdivo). Most pharmaceutical companies considered immunotherapy too risky at that time.
2009	Bristol-Myers Squibb purchases Medarex for $2.4 billion. A portion of the profits support the annual Munck-Pfefferkorn Awards, which fund new biomedical research projects at the Geisel School of Medicine that have high potential to benefit patients and to generate future revenue through grants or entrepreneurial endeavors.
2011	The Food and Drug Administration approves ipilimumab (Yervoy) for late-stage melanoma. The approved uses of Yervoy expand over subsequent years.
2013	*Science* names cancer immunotherapy the "breakthrough of the year," noting results from several recent clinical trials and declaring immunotherapy a "turning point in cancer."
2014	The Food and Drug Administration approves nivolumab (Opdivo) for advanced melanoma. The approved uses of Opdivo expand over subsequent years, including combination treatment with Yervoy and Opdivo for certain cancers.
2018	Nobel Prize in Physiology and Medicine is awarded to two scientists who brought anti-CTLA-4 and anti-PD-1 technology to Medarex—the antibodies that became Yervoy and Opdivo.

ImmuNext and Immune Checkpoints Inhibitors

1991	Dartmouth immunologist and Norris Cotton Cancer Center researcher Randy Noelle, PhD, and his team of students and postdocs discover the protein CD154 and its receptor CD40, which together play a central role in controlling the immune system. Noelle predicts that targeting CD154-CD40 interactions could yield therapies for cancer, transplant rejection, and autoimmune diseases.
2010	The Noelle lab discovers a new immune system protein, called VISTA, which functions as a negative checkpoint regulator, preventing immune cells from attacking tumors.

	Noelle founds ImmuNext, embedded within Norris Cotton Cancer Center, to develop therapies to block VISTA and to target CD154-CD40 interactions, thereby enhancing the body's own immune responses to cancer.
2012	ImmuNext teams up with Janssen Biotech, a Johnson & Johnson subsidiary, to develop anti-VISTA therapies and subsequent clinical trials.
2016	ImmuNext grants Roche a worldwide, exclusive license to develop and commercialize therapeutics that target the VISTA immune system pathway.
2017	ImmuNext grants Sanofi an exclusive, worldwide license to develop and commercialize INX-021, a CD40L monoclonal antibody. Preclinical studies indicate a high potential for the medication to treat a range of autoimmune diseases, including lupus and multiple sclerosis.

Celdara and Natural Receptor CAR T-cells

2005	Dartmouth immunologist and Norris Cotton Cancer Center researcher Charles Sentman, PhD, demonstrates for the first time the feasibility of engineering immune cells using a naturally occurring receptor. Subsequent studies show that Sentman's chimeric antigen receptor T-cells (CAR T-cells) could be used to treat up to 80%-90% of human cancers.
2008	Dartmouth immunologist Mike Fanger, PhD, and Jake Reder, PhD, director of the New Ventures Office at Dartmouth's medical school, found Celdara Medical, a company dedicated to helping investigators secure the funding and partners needed to translate biomedical discoveries into medicines. (Another Dartmouth immunologist and Medarex co-founder, Paul Guyre, PhD, later joins Celdara as vice president for research and discovery.)
2009	Charles Sentman, PhD, develops the design and use of TCR-defective T-cells as the basis for allogeneic CAR T-cell therapy. This approach turns a gene therapy process into a cell product that could be made available to any patient.
2015	Celdara partners with Celyad to run Phase I clinical trials testing the safety, feasibility, and dosing of CAR T-cell therapies based on research by Dartmouth immunologist Charles Sentman, PhD, and his lab.
2018	The NKG2D CAR (CYAD-01) is in multiple ongoing Phase I/II clinical testing against seven types of cancer. The allogeneic NKG2D CAR (CYAD-101) enters Phase I clinical testing.