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Dana-Farber Cancer Institute

The Perry S. Levy Endowed Fellowship

Fall 2020 Progress Update

Supporting young scientists

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As a globally recognized leader in gastrointestinal (GI) oncology, Dana-Farber Cancer Institute routinely attracts early career **physician scientists dedicated to furthering our understanding of what drives these cancers.** Innovative research projects led by talented young scientists often depend on philanthropic support, given the scarcity of government funding available for scientists just beginning their careers.

The **Perry S. Levy Endowed Fellowship** provides powerful support for the Institute's most promising young investigators, allowing them to pursue research with field-altering potential while receiving valuable mentorship from established physician-scientists.

This year's update highlights the research of the 2019-2020 Levy Fellow, **Kelly Burke, MD, PhD,** who studies how **immunotherapies—drugs that harness the immune system to fight cancer—**help the body recognize and attack tumors. She is also exploring ways to minimize the side effects of these drugs so more patients can benefit from immunotherapy. Thank you for your generous partnership in this important work.

Advancing immunotherapy for gastrointestinal cancers

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Kelly Burke, MD, PhD

Born in South Korea and raised in Minnesota, Burke earned her medical degree and a doctorate in immunology at Johns Hopkins School of Medicine. She was drawn to oncology by her desire to build long-term relationships with patients.

Burke conducts research in the lab of **Arlene Sharpe, MD, PhD,** whose work studying immune checkpoints such as the PD-1/PD-L1 pathway helped pave the way for the promising new field of immuno-oncology, **changing the paradigm of cancer treatment.** Checkpoints are on/off switches on cells that control the immune system. Many cancers are known to overproduce certain proteins, such as PD-1, that "switch off" the immune system's ability to recognize them as dangerous. This allows cancer cells to evade elimination by the immune system.

Drugs that target the PD-1/PD-L1 pathway, known as immune checkpoint inhibitors, have been approved by the Food and Drug Administration for at least 20 types of cancer. While immune checkpoint inhibitors have revolutionized care for many cancers, to date they have not been as effective at treating GI malignancies, particularly colon cancers. By studying the effects that these drugs have on immune cells, **Burke hopes to one day expand the impact of immunotherapy agents** to diseases with considerable need for new therapy options.

How does PD-1 affect immune cell production?

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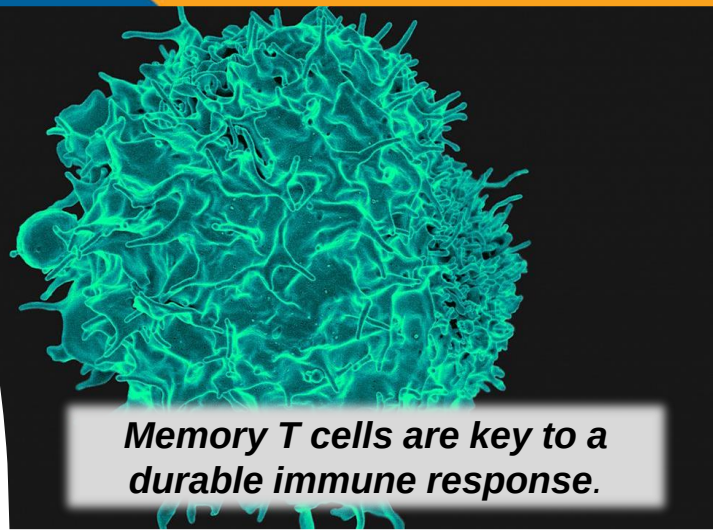
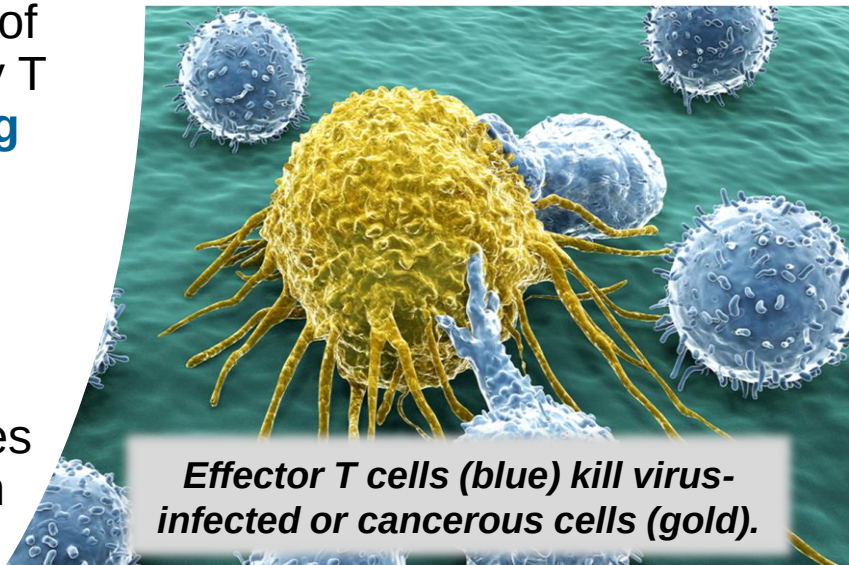
Recently, **Burke examined the role of the PD-1/PDL-1 pathway in the production of two types of immune cells**—effector T cells, those that kill virus-infected or cancerous cells, and memory T cells, those that remain in the body long term, conduct surveillance in the blood, and give rise to more effector cells upon re-exposure to pathogens.



Memory T cells are key to a durable immune response.

In a study of mice with viral infections, Burke contributed to evidence indicating that the timing of PD-1 inhibition impacts the production of memory T cells. **Therapeutically, this suggests that giving a checkpoint inhibitor after a vaccine for metastatic colon and rectal cancer may promote the production of memory T cells more effectively than giving it before, thus preventing recurrence.** These findings were shared in the June 2020 *Cell Reports*. Burke notes that these findings are very preliminary and much more work remains to be done in cancer models.



Effector T cells (blue) kill virus-infected or cancerous cells (gold).

The Power of Your Philanthropy

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Your generosity makes a world of difference. In the words of this year's Levy Fellow:

"I am extremely grateful for the opportunity to work in the lab on fundamental discoveries, to think broadly about oncology, and improve cancer care. This funding has given me the financial flexibility to focus on my research at a critical time in my career."

Kelly Burke, MD, PhD

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From all of us at Dana-Farber, thank you for your steadfast partnership in our mission to defeat cancer.

Report written by Justin Kaplan