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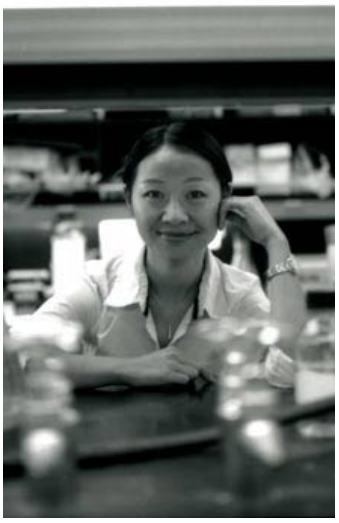

Credit: Daniel Chavkin

Lili Yang, 32

Engineering immunity

Caltech

The immune system is a sophisticated machine, designed to fend off a constant barrage of disease-causing microbes. Unfortunately, it's not as good at fighting cancer, which disguises itself as normal tissue. Using gene therapy, Lili Yang is reprogramming the immune system to recognize and kill cancer cells.

Stimulating the immune system to fight cancer is one of today's hottest research areas. Some scientists hope to genetically modify patients' white blood cells to do the job, but Yang is altering the body's blood-forming stem cells, a technique that could prove much more powerful. Because stem cells are self-renewing, they could generate a lifelong supply of immune cells programmed to combat, or even prevent, the disease.

A project manager and lead scientist in Caltech's Engineering Immunity Program, Yang created a viral "vector" that simultaneously delivers two genes to the stem cells: the genes encode the T-cell receptor protein, which enables white blood cells called T cells to recognize and kill cancer cells. The modified stem cells then give rise to T cells that bear the receptor. The technique has so successfully suppressed tumors in mice that Yang plans to begin trials this spring in melanoma patients.

In order to treat patients, Yang will have to isolate and modify their blood-forming stem cells in the lab and then reinject them--a laborious, costly process. So she is collaborating with her husband, Pin Wang of the University of Southern California, to design viral vectors that can deliver therapeutic genes to only one cell type. They have succeeded in mice, a significant advance in gene therapy.

In the future, says Yang, treating cancer could be as simple as injecting patients with such targeted vectors. Gene therapy has yet to live up to its huge potential, but "Lili has the ability to make it a part of modern medicine," says Caltech biologist and Nobel Prize winner David - Baltimore, Yang's supervisor. Indeed, Yang is also creating vectors to stimulate specific immune cells to make antibodies against HIV. If successful, that project could at last lead to an AIDS vaccine.

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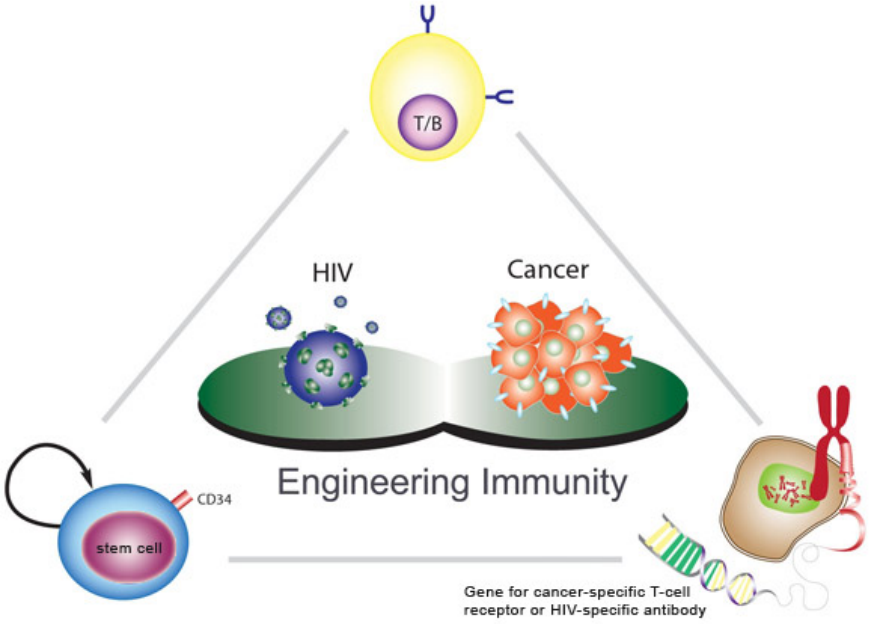

Credit: Lili Yang, Steven Lee, and Sungjin Park

Engineering immunity: *Caltech's Engineering Immunity project, which Lili Yang heads, aims to combine immunotherapy, gene therapy, and stem cell therapy to treat diseases such as HIV and cancer. The lower-right image shows that, first, cancer-specific T cell receptor genes or HIV-specific antibody genes are extracted from disease-specific white blood cells. At left, these genes are delivered to the blood-forming stem cells found in bone marrow. In the top image, the genes program the stem cells to develop into disease-battling white blood cells called T lymphocytes (for cancer) or B lymphocytes (for HIV). Since the blood-forming stem cells can survive throughout the lifetime of a person, such gene therapy could potentially provide lifelong protection against cancer or HIV.*

--Alexandra Goho

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