The Future of Therapeutics

Dave Mooney, Ph.D.
Wyss Institute Founding Core Faculty

There’s no denying that humans greatly value therapies that can treat injury and disease. Healers, shamans, and medicine-makers held places of high regard in ancient civilizations across the globe, and today, the pharmaceutical and biomedical industries are some of the largest and most heavily financed in the world.

But the methods we use to develop medicines have changed drastically over human history as our understanding of biology has advanced. The development of germ theory led to the first antibiotics. Genetics led to the first gene therapies. And our ongoing exploration of the immune system has produced immunotherapies whose focus is not pathogens themselves, but our own bodies. Personalized medicines are increasingly playing a major role, and advances in bioengineering, synthetic biology and AI are underpinning many recent advances.

As Ed Yong put it succinctly, “The immune system is very complicated.” We are still at the early stages of understanding and harnessing it to fight diseases, and figuring out how to rein it in when it inadvertently causes autoimmune conditions. And the immune system’s complexity means that solutions can take unexpected forms, like the biomaterials that Wyss labs are developing to influence the behavior of T cells and macrophages.

I am confident that the next few years will see the further expansion and refinement of therapeutic tools that nudge the well-oiled machine that is the human body to more effectively heal and protect itself from threats.

I hope you enjoy reading about how my Wyss colleagues and I are leading that charge in this latest issue of the Business Insider.

GET IN TOUCH WITH OUR BUSINESS DEVELOPMENT TEAM

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Prior to the 1990s, the treatment options available to cancer patients were so disfiguring, toxic, or ineffective that many chose to forego therapy altogether. That changed with the approval of the first immunotherapies: Rituxan for lymphoma and Herceptin for breast cancer. These drugs consist of antibodies that bind to molecules on their target cancer cells’ membranes, which activates a patient’s immune system to attack them. This approach has sparked a revolution not only in cancer treatment, but in using immune-targeted strategies to address a variety of inflammatory diseases. Several Wyss Institute labs are working to overcome roadblocks in the field and develop the next generation of immunotherapies through the Institute’s Validation Project program.

**T-cell therapy for all tumors**

Instead of delivering antibodies, another type of immunotherapy called adoptive T-cell therapies involves extracting T cells from patients, engineering them to target the patient’s particular form of cancer, and delivering them back into the blood to enhance the immune response. These therapies are remarkably effective against blood cancers, but so far have shown limited success against solid tumors.

A team in Core Faculty member Dave Mooney’s lab has developed a technique that allows them to metabolically “tag” the surface of T cells with cytokines, which enhance the anti-tumor activity of immune cells. This technique avoids the negative side effects that prevent cytokines from being delivered systemically, and effectively treated both solid and liquid tumors in mice as an add-on to CAR-T cell therapy. This technology could boost the efficacy of multiple forms of cellular therapies, and is currently being de-risked.

**“Waking up” deactivated macrophages**

T cells aren’t the only immune cells involved in fighting off invaders - macrophages, or white blood cells, constantly patrol the body for threats, and are often the first cells to flock to a tumor. However, tumors secrete molecules that deactivate macrophages upon arrival, to the point that as much as 50% of a tumor’s mass is made of macrophages.
A Wyss team led by Core Faculty member Samir Mitragotri is solving this problem by attaching tiny “backpacks” - disc-shaped nanoparticles loaded with pro-inflammatory cytokines - to macrophages.

When infused into the body, these macrophages can switch those inside a tumor from an “off” state to an “on” state, reactivating them against the cancer. The team is now investigating this technology for use in treating glioblastoma, as macrophages are able to penetrate the infamously tough blood-brain barrier that prevents most drugs from reaching the brain.

**Deliberately designing vaccines with DNA**

Although immunotherapies are a relatively new technology, a much older technique also works by stimulating the body’s immune response: vaccines. Many labs and companies are developing personalized cancer vaccines that preemptively train the immune system to recognize and kill cancer, but so far none are on the market.

These vaccines typically contain an antigen (a protein fragment taken from a patient’s cancer cells that activates antigen-presenting cells [APCs]) and an adjuvant (a molecule that enhances the immune-stimulating response of APCs). Both an antigen and an adjuvant are required for an effective tumor-specific response, but little is known about the optimal method of presenting these components to APCs. Core Faculty member William Shih and his lab have created a solution composed of the stuff of life itself: DNA.

Their DoriVac technology consists of folded sheets of DNA origami whose configuration can be controlled down to the nanoscale. This precision has allowed them to experiment with different arrangements of antigens and adjuvants in cancer vaccines, and they have identified patterns that produced strong tumor-inhibiting responses in mice and could be combined with other cancer treatments for better outcomes. The team is de-risking their innovation for commercialization.

**SWEET PARTNERSHIPS**

**Making sugar healthier, together with Kraft Heinz**

The Kraft Heinz Company had set itself a seemingly impossible challenge:
Reduce the total amount of sugar in its products by more than 60 million pounds by 2025, but find a way to replicate sugar’s uniquely beneficial properties like browning and thickening.

They brought that challenge to the Wyss Institute, who turned it on its head:

Rather than trying to find a healthier replacement for sugar, why not figure out a way to use the real thing but reduce its harmful effects on human health?

That collaboration spawned a novel sugar-to-fiber technology that is now on track to be spun out into a startup.

[Read the full story online.](#)
Wyss Associate Faculty members Chris Chen and Sangeeta Bhatia are long-time friends and colleagues. They met as graduate students in the Harvard–MIT Program in Health Sciences and Technology, got their M.D.s together at Harvard Medical School, and collaborated on projects once they started their own labs - Chen working on angiogenesis at the Johns Hopkins University and Bhatia working on liver cells at UC San Diego. Once their respective careers brought them back to Boston, their interactions grew exponentially, as they are both interested in bridging the gap between interesting science projects and innovations that help patients in the real world.

Chen and Bhatia have been working on a set of technologies to build models of tissues and organs in cell culture in the lab. Similar to the Human Organ Chips created by the Wyss Institute’s Founding Director Don Ingber, their microfluidic systems mimic the physiology of functional units of organs. Given Chen’s focus on the vascular system and Bhatia’s focus on the liver, their cells are grown in a channel vessel structure instead of the laminate layer found in Ingber’s chips. In the process of modeling vasculature within these devices, they started studying the physiology of the blood vessels themselves, including permeability, clotting, and immune cell infiltration.

This research led Chen and Bhatia to co-found Satellite Bio in 2022, a startup that selectively programs cells and then assembles them into tissue structures that can be implanted into patients to repair, restore, or even replace dysfunctional or diseased tissues or organs. The company is initially focusing on ushering in a new realm of treatment for liver diseases with its hepatocyte Satellite tissues (HepSAT) that enable hepatocyte engraftment, function and vascularization, leading to long-term repair and restoration of liver function.

The Wyss Institute’s translational infrastructure allowed us to seamlessly transition from asking fundamental science questions about how these tissues worked to working on developing therapeutic interventions that could actually be transformational for these patients who currently have no options. That kind of pivot would not have been possible if we had needed to rely on academic grants for funding.

Sangeeta Bhatia
Wyss Associate Faculty

Chen and Bhatia’s project was named an Institute Project in July 2021, and they are actively working to commercialize their new therapeutic for lymphedema, or chronic swelling caused by a buildup of lymphatic fluid. There is currently no cure for this condition, which occurs in numerous post-surgical settings and in some rare genetic disorders.

Bhatia and Chen’s project was named an Institute Project in July 2021, and they are actively working to commercialize their new therapeutic with another startup in 2023. The success of that venture will validate their lymph model, which they then plan to use as an engine to keep developing more applications in the lymphatic space.
Introducing the Wyss Lumineers class of 2022

These innovators launched startup companies from the Wyss Institute in 2022, and we are excited to watch them continue their entrepreneurial journeys this year.

Wyss Lumineers, members of our community that commit themselves to science and entrepreneurship, embody the Institute’s mission to transform healthcare and the environment by developing innovative technologies and accelerating their translation into commercial products.

These startup founders envision the positive near-term impact their scientific work can have in the world and took the risky steps of forming companies determined to make that vision a reality. In doing so, Wyss Lumineers also lead by example by lighting the way for other scientists to pursue an entrepreneurial path.

Our class of 2022 Wyss Lumineers represent six new startups based on Wyss-developed technologies and cover a breadth of fields and applications, including new approaches to therapeutic discovery and delivery, sustainable food production, and diagnostics for neurological disorders.

Daniele Foresti – AcousticaBio
Faculty Advisor: Jennifer Lewis
AcousticaBio is using its proprietary fluid processing technology to transform antibody infusions from an in-hospital IV treatment to a painless subcutaneous injection that can be administered anywhere, which could improve the clinical care of millions of patients.

Ciaran Dunn, Shannon Nangle, Marika Ziesack – Circe Bioscience
Faculty Advisor: Pam Silver
Circe Bioscience is decarbonizing food production by manufacturing food-grade fats inside proprietary microbes through a fermentation process that does not produce but rather uses carbon dioxide, with the goal of making food people want to eat in a massively scalable way without harming the planet.

Jack Jordanides, Jocelyn Kishi, Emma West – Digital Biology
Faculty Advisor: Peng Yin
Digital Biology is building DNA nanotechnology tools that allow cells in tissue samples to be imaged, then sequenced, and then imaged again.

Daniel Ahlstedt, Jonathan Rittichier, Daniel Wiegand – EnPlusOne Biosciences
Faculty Advisor: George Church
EnPlusOne is harnessing the power and flexibility of enzymes to deliver RNA-based products to the world with greater efficiency and a lower carbon footprint than existing synthesis methods.

Parastoo Khoshakhlagh, Alex Ng – GC Therapeutics
Faculty Advisor: George Church
GC Therapeutics uses synthetic biology to program stem cells into any cell type with best-in-class efficiency, speed, and scalability. Their technology dictates cells’ fates in a single step and has been validated for many applications.

Nolan Durr, Sanjay Sharma Timilsina – StataDX
Faculty Advisor: Don Ingber
StataDX is a medical diagnostics company building a near-patient diagnostic platform to provide a cost-effective solution to support biomarker-guided therapeutic strategies for patients suffering from chronic conditions including Alzheimer’s, Multiple Sclerosis, ALS, and stroke.

These innovators launched startup companies from the Wyss Institute in 2022, and we are excited to watch them continue their entrepreneurial journeys this year.
Tech Developments to Watch this Year

**STARTUP OPPORTUNITIES**

**A SPINK1-based fusion protein for treatment of pancreatitis**

Team Lead: Jeffrey Way  
Faculty Lead: Pam Silver  
Contact: Alex Li

Pancreatitis, or inflammation of the pancreas, is a common, painful, and sometimes fatal disorder with no existing treatments.

A team from Pam Silver’s lab has developed an engineered protein treatment for pancreatitis that inhibits trypsin, the disease’s primary cause. The molecule is effective in a mouse model of acute pancreatitis, is easy to manufacture, and has a clear path toward commercialization for treatment of post-ERCP pancreatitis, which frequently results from a common surgical procedure. The team is also developing a second molecule for treatment of chronic pancreatitis. This technology was named a 2022 Validation Project.

The team is currently looking to engage with investors for a potential startup opportunity.

**DNA nanoswitches for “lab-on-a-molecule” drug discovery**

Team Leads: Sylvie Bernier, Ken Carlson, Clinton Hanson, Mark Lipstein  
Faculty Lead: Wesley Wong  
Contact: Bill Bedell

There is an urgent need for low-cost, high-throughput drug screening techniques. Using DNA nanotechnology, this team has developed a platform for logic-gated, high-throughput screening to identify novel therapeutic compounds. This technology can be used to find biologic or small molecule drug candidates that modulate the function of important drug targets with high specificity. For initial proof-of-concept studies, the team is using the platform to identify compounds against disease-related proteins, unlocking the potential to treat cancer, diabetes, obesity, and autoimmune diseases.

The team is currently seeking prospective partners from pharmaceutical companies.

**COLLABORATION & LICENSING OPPORTUNITIES**

**Broad-spectrum immunostimulatory RNA therapy for infectious diseases and cancer**

Team Lead: Ken Carlson  
Faculty Lead: Don Ingber  
Contact: Paul Resnick

Wyss researchers have discovered a new class of short, immunostimulatory double-stranded RNAs (dsRNAs) that can potently induce the production of Type I/III interferons, inhibiting a wide range of infections as well as several types of cancer.

These dsRNAs effectively inhibit infection of human lung cells by many viruses including SARS-CoV-2, influenza A, and even common cold viruses. In studies with human lung Organ Chips, dsRNAs resulted in >95% inhibition of influenza infection and >99% inhibition of SARS-CoV-2 infection. They also significantly inhibited SARS-CoV-2 infection in a mouse COVID-19 model after systemic administration. They could be used both to prevent infection and to treat patients after they get sick, and can also be used to treat bacterial, fungal, and parasitic infections. Importantly, based on their ability to raise endogenous levels of interferons, they could be used for the treatment of a wide range of cancers, particularly in combination with approved immunotherapy drugs. They could also serve as adjuvants to enhance the efficacy of existing vaccines.

The Wyss Institute is currently seeking an industry partner with experience in RNA therapeutics to help rapidly commercialize this technology for multiple indications.
**SomaCode: Getting cell therapies where they need to go**

Among the biggest challenges in cell therapy is efficiently delivering cells to specific tissues in the body via the blood. **SomaCode** is a platform technology and discovery pipeline that uses high-throughput, *in vivo* pooled genetic screens to identify unique molecular disease signatures and engineer therapeutic cells that home to that signature, just like a car following directions to a specific zip code. These experiments are performed in mice, ensuring that the cells experience conditions closer to those in the human body. The platform currently uses primary T cells, but could be used with any therapeutic cell type. The team is currently seeking a Postdoctoral Fellow to join SomaCode. [Apply here.](#)

**MAGENTA: Preventing and treating muscle atrophy**

Anyone who has broken a bone and had to wear a cast knows that unused muscles quickly atrophy, losing their strength and function. The problem also occurs in patients suffering from neurological disorders and other diseases.

A Wyss team has created a solution to this problem in the form of a **wearable, mechanically active adhesive called MAGENTA**. The adhesive works like a soft robot, stretching and contracting muscles externally to rebuild them. Mice who received the treatment displayed significantly less muscle wasting after hind limb injury. The team is currently exploring commercialization options and is seeking interested collaborators.

**CogniXense for rare disease drug discovery**

Many neurological diseases, like bipolar disorder and Alzheimer's disease, have complex effects on patients’ mental and behavioral functions that are difficult to replicate in animal models.

The Wyss Institute’s **CogniXense platform** is an alternative to traditional drug development that combines predictive algorithms, a tadpole-based drug screening system, and an iterative discovery process to rapidly advance effective treatments for complex diseases through preclinical development to human clinical trials. It has been licensed by **Unravel Biosciences** for the treatment of Rett syndrome, and we are currently seeking collaborators to expand its uses to other diseases.

**Single-cell encapsulation for improved cell therapies**

Mesenchymal stromal cells (MSCs) are valued for their ability to secrete compounds that modulate the body's immune system, making them an attractive solution for problems in cell therapy like graft-vs-host disease and organ transplant rejections. However, MSCs are rapidly cleared from the body after infusion, and can draw fire from immune cells. The Wyss Institute has developed a novel single-cell encapsulation method that coats individual MSCs with a thin layer of an alginate-based hydrogel that protects MSCs from clearance and attack, and allows them to multiply to produce a stronger therapeutic effect. We are currently seeking collaborators to help develop this technology.
As we enter this exciting next chapter, we hope to expand our collaborative equipment facilities through key partnerships with industry that will ignite new breakthrough research.

We are moving quickly to secure key stakeholders as our new labs and equipment are placed to ensure that our researchers experience limited downtime during the transition.

Among the many pieces of equipment that would be transformative for our research are:

- HRAM (high-resolution accurate mass) LC-MS
- Bravo Automated Liquid Handling Platform
- NovoCyte 3000 flow cytometer system
- 1200 Series HPLC and more

Please contact Jonelle Prill-Tate to learn more about our current needs and what opportunities sponsorship could provide to your organization.

GET IN TOUCH

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**WYSS STARTUP NEWS**

**Sherlock Biosciences** signed a licensing agreement with Shanghai-based Tolo Biotech granting co-exclusive rights to Cas12 and Cas13 CRISPR diagnostic methods in markets outside of the U.S. and Greater China.

**Rejuvenate Bio** launched a new 15,500 square foot office in San Diego to support its discovery and development of gene therapies for human and animal health.

**Rhinostics** partnered with LVL technologies to launch the RHINObot™, a customized version of LVL’s decapper instrument that enables both the RHINObot™ and VERIstic™ automated collection devices to offer hands-free sample-in to result-out workflows.

**Emulate** published a landmark paper demonstrating that its human Liver-Chip was able to correctly identify 87% of drugs that caused liver injury to patients despite passing animal testing.

**Prapela** received FDA Breakthrough Device Designation to investigate the use of its vibrating mattress pad to treat apnea in premature infants, in addition to its previous designation to treat newborns with prenatal opioid exposure.

**Desktop Health** and its PhonoGraft device were featured in an award-winning documentary film called “Pathways to Invention.” Sangeeta Bhatia is also included in the film.

**Circe Bioscience** licensed proprietary microbes that consume greenhouse gasses and produce food-grade fats via gas fermentation to decarbonize food production.

**AWARDS & RECOGNITION**

14 Wyss Faculty members were named Highly Cited Researchers by Clarivate in 2022.

Natalie Artzi received the Brigham Ignite Award, honoring Brigham and Women’s Hospital Innovators.

Elizabeth Carstens and Yang Claire Zeng were selected as the third recipients of Harvard’s “Immunoneering to Improve Immunotherapy” (i3) Center award.

Christopher Chen was elected to the National Academy of Inventors.

David Walt won the prestigious Kabiller Prize in Nanoscience and Nanomedicine award and a $4.5M Open Philanthropy Grant to develop a blood test to detect early Alzheimer’s disease. Walt was also awarded the 2023 Fritz J. and Dolores H. Russ Prize from the National Academy of Engineering.

**OUT & ABOUT**

The FDA Modernization Act 2.0 was passed by the US government and signed into law by President Biden on Dec. 23, 2022. This act allows the FDA to consider data from non-animal drug testing methods when evaluating a new drug for approval, including human Organ Chips, which can more accurately mimic human organ responses to drugs.

Don Ingber was invited to speak to Congress about Organ Chips alongside conservationist Jane Goodall at a House subcommittee hearing on the new regulation in March 2021.

**LICENSING AGREEMENTS**

EnPlusOne licensed a novel, enzyme-based RNA synthesis technology to support the development of the next generation of RNA-based products with greater efficiency and a lower carbon footprint.

Gameto licensed a cell engineering platform to generate engineered ovarian cell lines that mimic the functions of human ovarian cells, with the goal of developing therapeutics for female reproductive diseases.

Every day we Reimagine

Wyss members work to reimagine a world where anything is possible. It’s a world of scientific discovery, imagination, and reality, where diseases are cured, global warming is reversed, pandemics are prevented, and lives are ultimately changed for the better. The possibilities that we are working to realize through our science and engineering are as boundless as our imaginations.

Tell us, if you could Reimagine the World, what would it look like?

Learn more