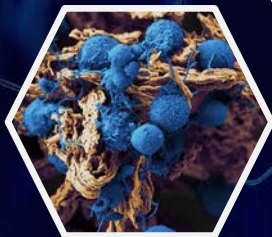


WYSS INSTITUTE AT HARVARD UNIVERSITY

Impact Through Collaboration

IMPACT REPORT | JULY 2021



Breakthrough discoveries cannot change the world if they do not leave the lab

A LETTER FROM THE FOUNDING DIRECTOR



Donald Ingber, M.D., Ph.D.

Founding Director and Core Faculty, Wyss Institute | Judah Folkman
Professor of Vascular Biology, Harvard Medical School & Boston
Children's Hospital | Professor of Bioengineering, Harvard John A.
Paulson School of Engineering & Applied Sciences

During the past year and in the midst of the COVID-19 crisis, we at Harvard University's Wyss Institute for Biologically Inspired Engineering continued to live up to our central credo that **"breakthrough technologies cannot change the world if they do not leave the lab."** We have made remarkable strides in bringing transformative technologies to the people whose lives we intended to impact.

In a year that was challenging in so many ways, we provided instrumental solutions for curbing the COVID-19 pandemic. Technologies developed in our laboratories, many of which in record time, were **quickly licensed to industry partners under Harvard's COVID-19 Technology Access Framework** and are now the foundation for commercially available products. This success is first and foremost owed to our extraordinary community of gifted researchers, technology and business development experts, and entrepreneurs, who pivoted almost instantaneously to find those solutions, often in multi-disciplinary collaborations and with our partnering hospitals and research institutions — all of which were supported by an equally entrepreneurial Administrative Team that made the impossible possible, steering the Institute through COVID-19 restrictions, supply chain hurdles, and many other less visible challenges.

In the Wyss' grander scheme, over the past decade **we have innovated a unique and highly effective technology translation model within the Boston-Cambridge ecosystem** that enables us to devise and validate an extraordinarily broad range of solutions for pressing diagnostic, therapeutic, and MedTech challenges, as well as to enhance environmental sustainability. At the same time, we realized that to confront some these problems on a grand scale, we also needed to innovate **new collaboration models**.

We injected into these collaborations the same level of **creativity that drives our science and engineering to harness the unique strengths of new partners** from the venture capital world, industry, and other academic clinical research institutions. In addition to these larger efforts, the Wyss has produced a steady flow of discoveries and bioinspired technology innovations that have enormous potential in many other areas in healthcare and sustainability, many of which are reaching **prime time for becoming high-value assets in the hands of new startups and industrial licensees**. This report is just a single-year snapshot, and I am confident that now with the end of the COVID-19 pandemic in sight, there will be even more impactful progress in the year to come.

DI



COVID-19: One Year Later

Our 2020 Impact Report highlighted the many ways that Wyss Institute researchers rose to the challenge to combat the novel coronavirus. Several of these projects, including new types of personal protective equipment, medical devices, diagnostics, and therapeutics, have had a significant impact in the ongoing fight against COVID-19.

SELECT COVID-19 PUBLICATIONS

Face masks that diagnose COVID-19

WYSS LEAD

James Collins, Ph.D., Core Faculty

PLATFORM

Living Cellular Devices

Wyss engineers were working on developing flexible, wearable biosensors when the pandemic struck, and they quickly pivoted to focus their work on COVID-19. They integrated their paper-based diagnostic technology into standard face masks to create a wearable device that uses synthetic biology-based reactions to identify the presence of SARS-CoV-2 particles in a patient's breath within 90 minutes – without the need for nasal swab samples. In June 2021 the team published an article about their accomplishment in ***Nature Biotechnology*** and is now actively looking for manufacturing partners to bring this innovation to the market.

Diagnosing down to the molecule

WYSS LEAD

David Walt, Ph.D., Core Faculty

INITIATIVE

Diagnostics Accelerator

In a series of three papers published in ***Clinical Chemistry***, ***Nature Biomedical Engineering***, and ***Analytical Chemistry***, the Wyss team used single molecule array (Simoa) technology to develop ultrasensitive diagnostic tests that can detect multiple SARS-CoV-2 antigens in blood plasma, the presence of SARS-CoV-2 antibodies in blood, and SARS-CoV-2 viral RNA and antibodies in the saliva of COVID-19 patients. Some of these assays were **licensed by Brigham and Women's Hospital to Quanterix Corporation** for commercialization.

Organ Chips identify existing drug that could treat COVID-19

WYSS LEAD

Donald Ingber, M.D., Ph.D., Founding Director

PLATFORM

Bioinspired Therapeutics & Diagnostics

In April 2020, the Wyss team and collaborators from two other research universities set up a drug discovery pipeline to quickly identify and test existing drugs that could be repurposed for COVID-19. By May 2021, the team published an article in ***Nature Biomedical Engineering*** reporting that amodiaquine, an antimalarial drug, significantly reduced SARS-CoV-2's ability to enter and infect living lung cells in human Airway Chips and small animal models. This research led to the inclusion of amodiaquine in human clinical trials across 20 sites in Africa, which aims to identify a much-needed low-cost treatment option for millions of people who lack access to vaccines.



COVID-19: Technology Licensing

Over the past year, 14 startups and established companies working to curb the global pandemic licensed Wyss-developed technologies through Harvard's Office of Technology Development (OTD) and in accordance with the University's commitment to the COVID-19 Technology Access Framework. Created in April 2020, the Framework incentivizes the broad and equitable adoption of potentially life-saving technologies to prevent, diagnose, or treat COVID-19 by offering rapidly executable, non-exclusive, royalty-free licenses for the use of these technologies during the pandemic. Many of these innovations also have enormous potential beyond COVID-19.



SELECT COVID-19 LICENSES

Nasal Swabs

Our nasopharyngeal swab technology uses a new design and manufacturing process that allows for cost-effective mass-production.

WYSS LEADS

Richard Novak, Ph.D., Senior Staff Engineer
Donald Ingber, M.D., Ph.D., Founding Director

COLLABORATION

After the initial design work, the Wyss team then collaborated with Michael Springer, Ph.D., Associate Professor of Systems Biology at Harvard Medical School, who had explored ways to increase the throughput of centralized rRT-PCR assays to diagnose COVID-19, while decreasing labor and costs. Together, they modified the original swab design to make it compatible with automated multiplexing technologies, which is expected to help significantly accelerate the speed of COVID-19 testing.

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COVID-19
TECHNOLOGIES
LICENSED



IMPACT

Our nasal swab technology has been licensed to multiple companies to facilitate SARS-CoV-2 testing in clinical and environmental settings.

One company, Rhinostics, a startup co-founded by Novak and Springer, is now developing and commercializing multiplexed solutions for processing nasal samples from people suspected to have COVID-19 and other respiratory infectious diseases.

Toehold Switches

WYSS LEADS

Jim Collins, Ph.D., Core Faculty
Peng Yin, Ph.D., Core Faculty

Synthetic nucleic acid-based devices that can function as sensors for RNA molecules produced by viruses including SARS-CoV-2, and may enable COVID-19-detection assays with improved readouts.

IMPACT

Our toehold switch technology was licensed to several parties for applications in new, highly specific and sensitive diagnostic tests for SARS-CoV-2 that can be used in the clinic and various other environments.

eRapid

WYSS LEADS

Pawan Jolly, Ph.D., Senior Staff Scientist
Donald Ingber, M.D., Ph.D., Founding Director

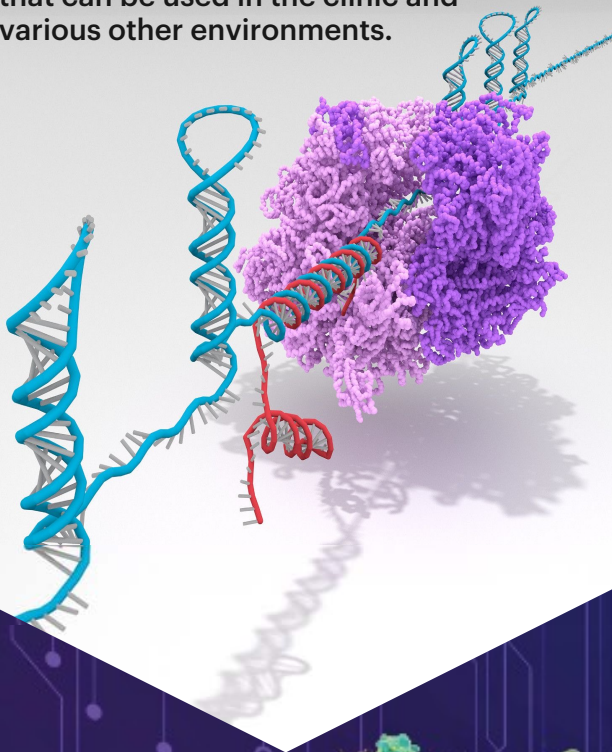
This low-cost, affinity-based electrochemical sensing platform can simultaneously detect and quantify a broad range of biomarkers, with high sensitivity and selectivity, from a small volume of saliva or blood. The technology has been adapted to detect SARS-CoV-2 antibodies by employing a novel, low-cost, antifouling nanocomposite coating to which SARS-CoV-2-specific ligands may be attached to capture viral molecules, host antibodies, and proteins produced by infected individuals in response to the virus. Each capturing event generates an electrical signal whose strength correlates with the level of detected target molecules.

COLLABORATION

eRapid's development is being adapted to function as a COVID-19 diagnostic point-of-care device through a collaboration between the Wyss Institute and The iQ Group Global's portfolio company GBS Inc., using the company's signal-enhancing SARS-CoV-2 Antibody Biosensor.

IMPACT

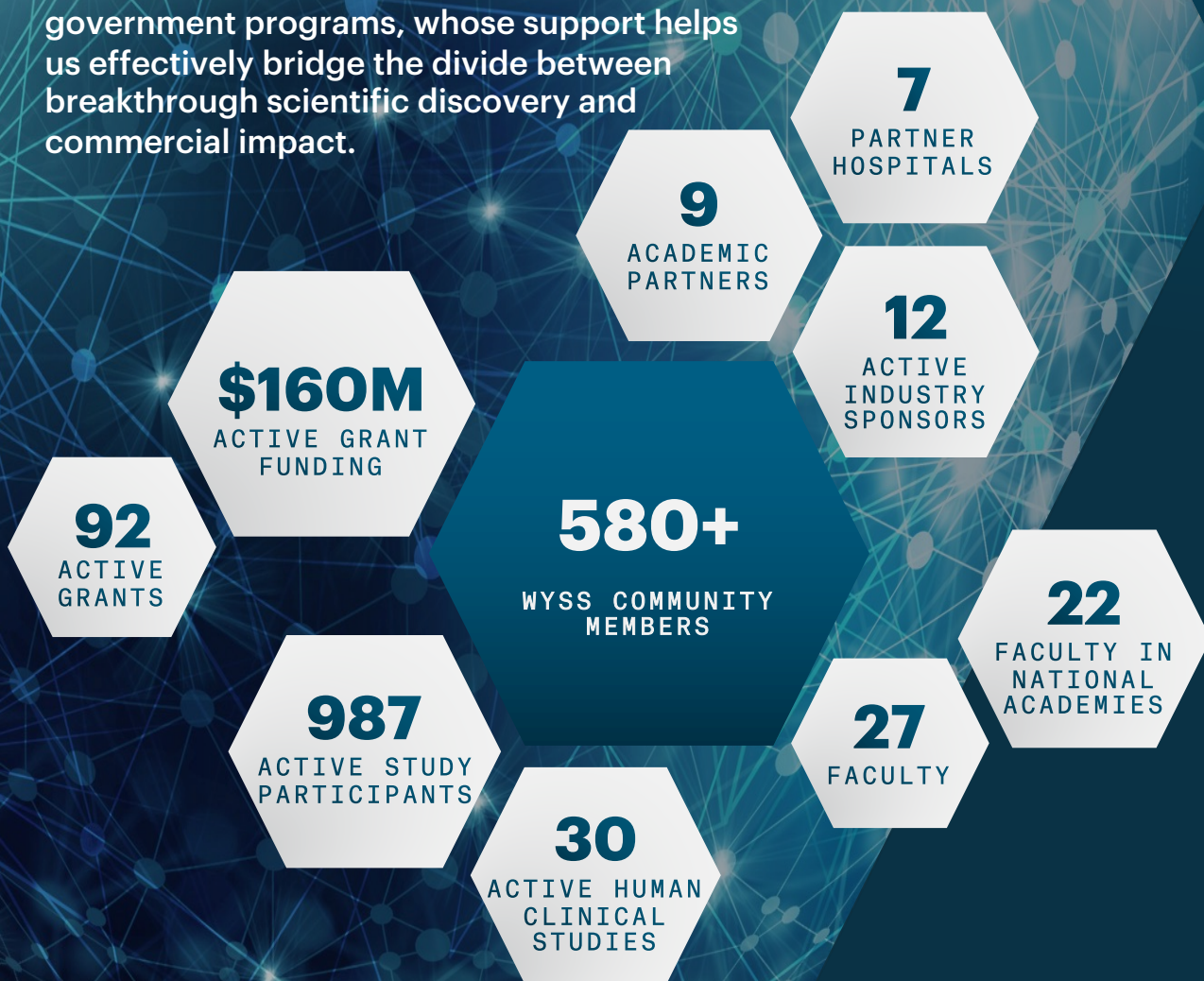
Recently, the Wyss team's integrated electrochemical assay received IRB approval to perform a clinical study with patient samples with the GBS Inc. SARS-CoV-2 Antibody Biosensor that will be performed by the Wyss team.



Collaboration at a Higher Level

Our mission is to engineer transformative solutions to some of the world's most urgent problems in healthcare and sustainability. It is not enough for a technology to simply work, it must work outside of the lab, robustly, and at scale.

To achieve this goal, we strengthen technology innovation and product development capabilities by creatively forging alliances with industry partners, investors, foundations, philanthropic organizations, and government programs, whose support helps us effectively bridge the divide between breakthrough scientific discovery and commercial impact.



Northpond Labs Alliance

STRATEGIC ALLIANCE

R&D affiliate of Northpond Ventures commits \$12M to create the *Laboratory for Bioengineering Research and Innovation* at the Wyss Institute

ALLIANCE LEADS

*Andrea Jackson, Northpond Ventures Director
Samuel Inverso, Ph.D., Wyss Institute Director of Business Development*

We established a new, first-of-its-kind alliance by joining forces with Northpond Labs, the research and development-focused affiliate of Northpond Ventures, with the goal to support research with strong technology translation potential.

Through a separate arrangement with Harvard and the Wyss Institute, Northpond is providing an additional \$3 million in funding to the Institute to create and fund the *Northpond Director's Innovation Fund*. The fund bolsters the pursuit of Wyss projects with promise to solve important unmet problems, even when the path to commercialization has not yet been mapped out.

Additionally, members of the Northpond team routinely work with Wyss researchers, enhancing our culture of entrepreneurship through information sessions, roundtables, and one-on-one meetings. This first strategic alliance embodies an impactful collaboration model that spans academia and industry for supporting innovation and empowers entrepreneurial teams to translate their discoveries into commercial opportunities.



Brain-Targeting Program

INDUSTRIAL PARTNERSHIP

Pre-competitive, multi-partner collaboration with pharmaceutical companies launched to solve complex challenge of effective therapeutic drug delivery to the brain

WYSS LEADS

*James Gorman, M.D., Ph.D., Lead Scientist
Donald Ingber, M.D., Ph.D., Founding Director*

This industry collaboration with Bristol-Myers Squibb Company, Eisai Inc., and H. Lundbeck A/S, aims to discover protein targets that will enable delivery of therapeutics across the blood-brain barrier. All partners equally support this research effort and will collectively use the program's findings to inform their own drug development activities.

In additional agreements, the Wyss Institute team initiated collaborations with Cell Signaling Technologies, Inc., and with Lundbeck and FairJourney Biologics, to co-develop antibody compounds that will shuttle drugs to the brain via known and novel targets identified in the broader program.

Want to join the Brain Targeting Program?

We seek to collaborate with biopharmaceutical partners to discover more effective approaches to deliver therapeutics across the blood-brain barrier. Contact James Gorman at james.gorman@wyss.harvard.edu to learn more.



COLLABORATION AT A HIGHER LEVEL

Wyss Diagnostic Accelerator (DxA)

CLINICAL RESEARCH COLLABORATION

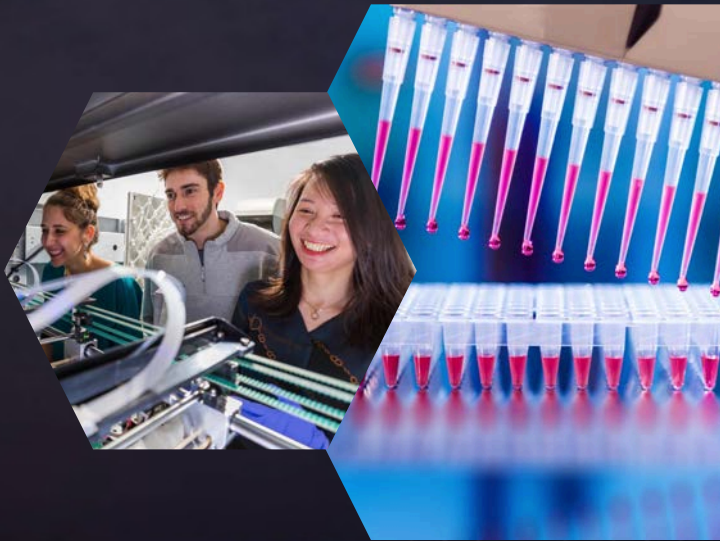
The Wyss DxA aims to solve high-value clinical problems through deep collaborations driven by physicians' needs for improved diagnostic tools and methods

WYSS LEADS

Rushdy Ahmad, Ph.D., Staff Scientist
David Walt, Ph.D., Core Faculty

As a multifaceted collaboration between clinicians, researchers, engineers, philanthropists, government agencies and industry partners, the Wyss DxA develops diagnostic technologies in direct response to real-world clinical needs.

In a newly announced cross-institutional agreement with the Brigham and Women's Hospital (BWH), hospital clinicians will identify unmet diagnostic needs and work alongside Wyss scientists and engineers to develop specifically tailored technologies. These technologies are then brought to BWH's CLIA-certified lab to be tested with real patient samples and optimized in an iterative process with continuous feedback between clinicians and engineers. CLIA designation is granted by the FDA, so our diagnostic technologies are validated under standards matching those required for regulatory approval and accelerated into the market.



INDUSTRIAL PARTICIPANT PROGRAM

The Wyss DxA pilot Industrial Participant Program serves as a collaboration hub between healthcare testing companies and the scientific and clinical community, as well as our affiliated institutions and the broader Harvard ecosystem

LAUNCHING FALL 2021

Participants build relationships and explore pre-competitive collaboration opportunities, connect with thought leaders and subject matter experts, identify key opportunities and challenges within the industry, and align on a vision to transform the future of diagnostic and healthcare testing, all driven by the passion to solve unmet diagnostic needs.



Want to join the DxA Industrial Participant Program?

Get in touch with Rushdy Ahmad at rushdy.ahmad@wyss.harvard.edu to get involved.

COLLABORATION AT A HIGHER LEVEL

i3 Center

RESEARCH COLLABORATION

World-leading cancer immunologists and bioengineers launch the Immuno-Engineering to Improve Immunotherapy (i3) Center to create biomaterial-based approaches to improve T cell immunity

PROGRAM LEADS

David Mooney, Ph.D., Wyss Core Faculty
F. Steven Hodi, M.D., Director, Dana-Farber
Melanoma Center & Center for Immuno-Oncology

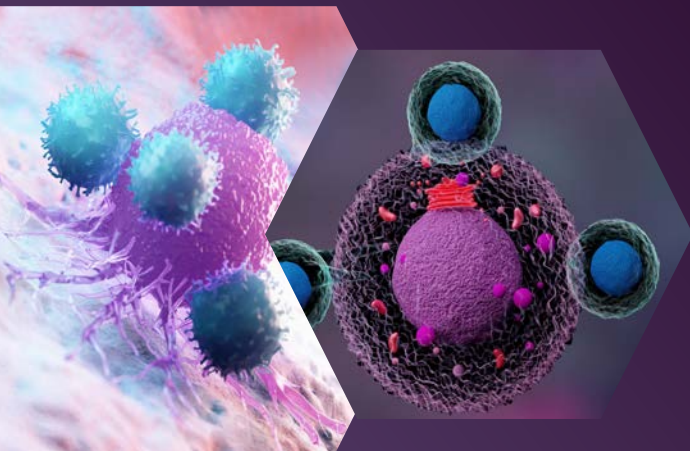
COLLABORATION

Wyss Institute	Dana-Farber Cancer Institute
Harvard John A. Paulson School of Engineering and Applied Sciences	Harvard Stem Cell Institute
	Mass General Hospital

Funded by the NIH, the cross-institutional and cross-disciplinary i3 Center is creating new biomaterials-based approaches to enable anti-cancer immunotherapies in settings where their use is currently limited, such as in myeloid malignancies and solid tumors.

IMPACT

In support of this goal, the collaborators are bundling their diverse expertise in the development of checkpoint blockade therapy, neoantigen vaccines, cellular therapies, DNA nanotechnologies, and therapeutic biomaterials to enable major scientific and translational advances.



Drug Testing in Human Bone Marrow Chip

RESEARCH COLLABORATION

Human Bone Marrow Chip supports blood formation and replicates defects in particular blood cells, as well as drug- and radiation-induced toxicity responses observed in human patients

WYSS LEADS

David Chou, M.D., Ph.D., Clinical Fellow
Donald Ingber, M.D., Ph.D., Founding Director

COLLABORATION

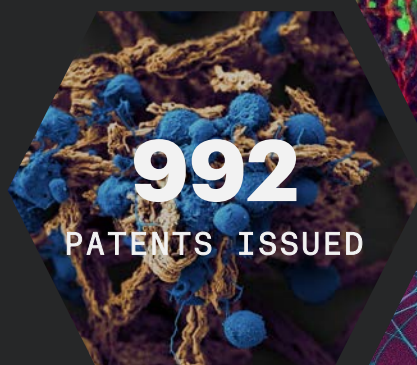
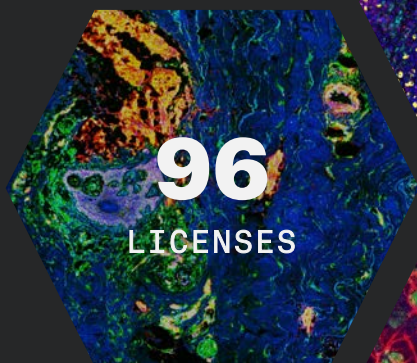
In a collaboration with Fulcrum Therapeutics, a clinical-stage biopharmaceutical company, the team is now testing a small molecule drug developed by the company to increase fetal hemoglobin in red blood cells as a potential treatment for sickle cell disease. The researchers are investigating in the microfluidic chip how the drug affects the hemoglobinization of newly generated red blood cells, and whether it alters the development of other lineages of the hematopoietic system, such as neutrophil cells, which are white blood cells that are an essential part of the innate immune system.

IMPACT

Success in this study would provide insight into the effects of this novel therapeutic on the bone marrow that could guide its continued clinical development as well as further validate the utility of the Human Bone Marrow Chip in drug development for blood disorders.

SINCE 2009

Disruptive Innovation Inspired by Nature



New Directions for Technology Advancement

A LETTER FROM THE COO



Angelika Fretzen, Ph.D., M.B.A.
Chief Operations Officer
Wyss Institute at Harvard University

The past 16 months have made it clear that organizations, more so than ever before, must be nimble, creative, and willing to take risks to adapt and succeed in unpredictably changing and challenging conditions.

The Wyss Institute was created with these principles in mind more than a decade ago, and our structure has continually evolved to enable many diverse types of projects and partnerships. My own role is evolving this coming year as I take on the responsibilities of Chief Operating Officer in response to the Institute's continued need to streamline our collaborative approach to technology development, strategic engagement, and administration and operations. We continue to strive towards a **nimble innovative organization** on all levels, without silos, and ready to provide impactful solutions to the many challenges the future brings.

We continue to raise our own bar: in the last year we have spun out eight startups, through Harvard's Office of Technology Development have signed 29 licensing agreements, welcomed 14 technology efforts as Wyss Institute Validation Projects, and hired four new members to our Business Development team.

Recognizing the value that we can provide to impact-oriented partners, we launched a new

Strategic Engagement initiative to connect directly with family foundations and other philanthropic organizations that want to support groundbreaking scientific research and technology innovation. We started hosting meetings and roundtables to create opportunities that will give us invaluable avenues to learn about which impact areas are of interest to this community, and how we can create the most meaningful solutions in health and sustainability.

We also created our **Lumineers program**, which recognizes Wyss members who have taken on the enormous challenge of launching their own startup companies from the Wyss Institute to commercialize their technologies. These invaluable mentors are "lighting the way" for other community members who also want to make the leap from research to entrepreneurship.

The past year under COVID-19 restrictions has taught us how invaluable our community and our broader research and innovation ecosystems are to us. While we have accomplished a lot in the past year, **we cannot wait to deepen our current collaborations and initiate new strong alliances and partnerships.** We hope to meet many of you in person at the Wyss Institute to discuss current challenges that need impactful solutions and a shared vision for the future.

VENTURE CAPITAL CONNECT

In 2021, we also launched our Venture Capital Connect event series in collaboration with some of the nation's leading VC firms. Virtual for now, these events offer our entrepreneurial researchers the opportunity to engage directly with top venture capital professionals to gain valuable insights and build relationships. Each event focuses on a different topic within the VC space and includes a breakout session for selected teams to pitch their ideas to the presenters and receive feedback. We have so far hosted members of Northpond Ventures, XFund, 8VC, and Wireframe Ventures, and look forward to introducing more to our community over time.



Startup Spotlights

Growing a fledgling startup company is hard – doing so during a global pandemic is even harder. Despite the past year's challenges, companies that licensed technologies developed at the Wyss Institute have made great strides toward bringing these impactful products to patients who need them.

Rejuvenate Bio.

NOVEL GENE THERAPIES FOR DOGS

Rejuvenate Bio licensed technology developed by a Wyss Institute team led by George Church, Ph.D., in early 2020, as COVID-19 was beginning to sweep the globe. Rejuvenate's combination gene therapy treatment targets multiple age-related diseases to increase overall healthspan with a single injection.

In April 2021, Rejuvenate closed a **\$13.5M Series A** funding round to support its development of this therapy. The company is currently running a clinical trial with the Cummings School of Veterinary Medicine at Tufts University to evaluate the treatment's efficacy against mitral valve disease in dogs. Preliminary data from that trial suggest that Rejuvenate's therapy is effectively treating the disease in multiple dogs with no adverse side effects. The company plans to submit its therapy to the FDA for approval in the near future and aims to bring it to market in 2023. The data from the dog trial will also serve as preclinical data to inform the treatment's applicability to humans.

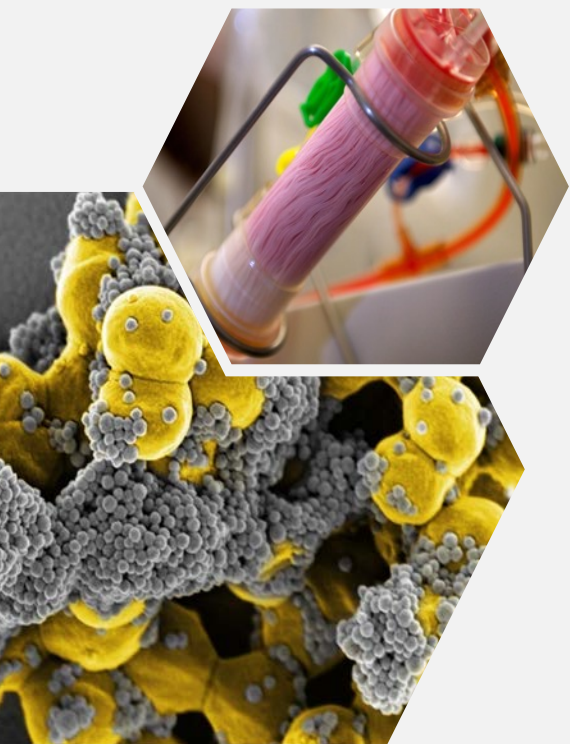


BOA Biomedical

SEPSIS DIAGNOSTIC & TREATMENT

The Wyss Institute's FcMBL pathogen capture technology was licensed in 2018 to BOA Biomedical (BOA), a Miraki Innovation company, to develop it into diagnostics and treatments for patients with bloodstream infections and to prevent sepsis. BOA retains close ties to the Wyss Institute, with Donald Ingber, M.D., Ph.D., BOA Scientific Founder and Board Member and Lead Senior Staff Scientist Michael Super, Ph.D., BOA Scientific Founder.

In March 2021, BOA announced that its GARNET™ extracorporeal therapeutic had obtained approval from the U.S. FDA to conduct an Early Feasibility Study under an Investigational Device Exemption in patients with confirmed or suspected bloodstream infections, including SARS-CoV-2. GARNET™ was also made available for compassionate use in seriously ill patients if ordered by a physician. The company has initiated First In Human clinical trials at several clinical sites, including Beth Israel Deaconess Medical Center, one of the Wyss Institute's collaborating hospitals, which has already enrolled the first study subjects.



Featured News from Wyss-enabled Startups & Technology Licensers

8

STARTUPS
LAUNCHED
THIS YEAR

MEDTECH

PionEar
Pristine Surgical
Imago Rehab

DIAGNOSTICS

Rhinostics

THERAPEUTICS

Manifold Bio
Trestle Bio

SUSTAINABILITY

Boston Meats
Metalmark

\$27.9M

VENTURE FUNDING RAISED
BY NEW STARTUPS THIS YEAR

29

TECHNOLOGIES
LICENSED
THIS YEAR

ReadCoor

Acquired by 10x Genomics for \$350M

Dyno Therapeutics

Entered a \$1.8B collaboration and license agreement with Spark Therapeutics, Inc., a member of the Roche Group

Raised \$100M Series A

Ultivue

Raised \$50M Series D

Kula Bio

Raised \$10M for sustainable agriculture

FitBiomics

Launched first product, Nella

NuProbe

Raised \$42M

Torus Biosystems

Raised \$25M Series A

64x Bio

Emerged from stealth

Manifold Bio

Raised \$5.4M

Awarded \$75K as grand prize winner of Harvard President's Innovation Challenge

Prapela

Awarded \$2.5M from NIH to treat newborns diagnosed with Neonatal Abstinence Syndrome

Editas

Received Rare Pediatric Disease (RPD) designation for EDIT-301 for the treatment of sickle cell disease

FDA cleared initiation of EDIT-301 clinical trial for sickle cell disease

eGenesis

Raised \$125M Series C

Announced research collaboration with Duke University School of Medicine to evaluate gene-edited pancreatic cells

Sherlock Biosciences

Awarded \$5M from Bill & Melinda Gates Foundation for COVID Diagnostics

Named one of *Fast Company's* "World's Most Innovative Companies"

Emulate

U.S. Army used Lung Chip technology to study the effects of COVID-19

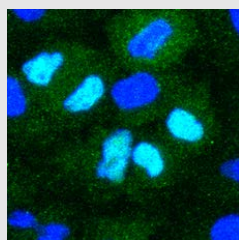
Signed collaboration agreement with FDA to use Lung Chip to evaluate safety of COVID-19 vaccines and immunity against SARS-CoV-2

Future Impact

LICENSING OPPORTUNITIES

In our pursuit of new tests, treatments, and technologies that have the potential to address some of the world's most pressing unmet needs, we are constantly looking for partners and collaborators to help us advance them into real-world settings.

HEALTHCARE



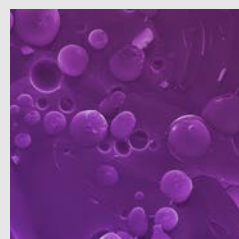
Broad-Spectrum RNA Therapeutic for COVID-19 and Influenza

Immunostimulatory RNAs inhibit infection of multiple types of respiratory viruses, including SARS-CoV-2.



eRNA: Controlled Enzymatic RNA Oligonucleotide Synthesis

Versatile and inexpensive enzymatic RNA oligonucleotide synthesis approach with the potential to greatly facilitate the development of novel RNA therapeutics.



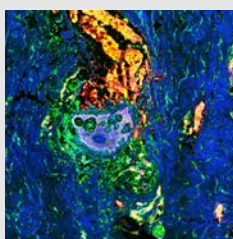
Rapid Metabolite-Sensing System for Blood Lactate

Enzyme-driven fluorescent biosensing system rapidly measures the levels of blood lactate and other metabolites, with potential to provide fast diagnostics at the point-of-care.



Microrobotic Laser-Steering Medical Device for Minimally Invasive Surgery

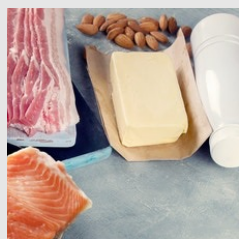
A compact, highly precise, and controllable laser-steering end-effector to enhance endoscopic and minimally invasive surgeries.



MRBL: Next-Generation Gene Therapy for Molecular Skin Rejuvenation

Comprehensive gene prediction and therapy platform for local, skin-specific, and safe delivery of therapies to treat rare monogenetic skin diseases and aging.

SUSTAINABILITY



Circe: Tailored Fats for Food Applications

A fermentation-based platform that uses greenhouse gases to produce food-grade fats without the use of plants or animals.



cold-SNAP: Eco-Friendly Air Conditioning

Evaporative-cooling-based system that uses a specially coated ceramic to cool air without adding humidity.

COLLABORATE WITH US

Email Angelika Fretzen at a.fretzen@wyss.harvard.edu to learn how you can get involved.

[EXPLORE ALL TECHNOLOGIES ON OUR WEBSITE](#)

**Breakthrough discoveries
cannot change the world if they
do not leave the lab**

