ERC for Advanced Technologies for Preservation of Biological Systems (ATP-Bio)

University of Minnesota (Lead Institution)

Dramatically advancing the field of biopreservation to achieve major societal benefits

A National Science Foundation Engineering Research Center since 2020

Partner Institutions:

- ***Massachusetts General Hospital***
- ***University of California, Berkeley***
- ***University of California, Riverside***

Vision and Mission. The ERC for Advanced Technologies for the Preservation of Biological Systems (ATP-Bio) aims to "suspend biological time" and radically extend the ability to bank and transport cells, micro-physiological systems (MPS or "organs-on-a-chip"), aquatic embryos, tissue, skin, whole organs, and even whole organisms through a team approach to building advanced biopreservation technologies. We will accomplish this by engineering technologies for application to biological systems before cooling (Thrust Area 1), during cooling and stasis at subzero temperatures (Thrust Area 2), and during rewarming to normal biological temperatures (Thrust Area 3). At each stage, our engineering will aim at eliminating or controlling ice, mitigating toxicity from cryoprotective agents, and eliminating thermal and mechanical stress—the prime causes of biological damage at subzero temperatures. We envision a world in 10 years in which a broad spectrum of biological systems are preserved in a high-throughput manner for a wide range of benefits to humankind and the natural environment (Figure 1). We also anticipate that the core technologies developed by ATP-Bio will be the foundation for advances in nanotechnology, 3D printing, genetics, and numerous other fields that we will merge to improve biopreservation.

Educational Foci. In addition to producing new convergent and transformative biopreservation technologies across multiple scales and testbed systems, we will build the workforce and industry to use it.Building a sustainable STEM workforce pipeline requires promoting a STEM workforce that reflects the demographics of our current and future. Our efforts will span students from middle school and high school to undergraduates, graduate students, and postdocs at all core institutions.

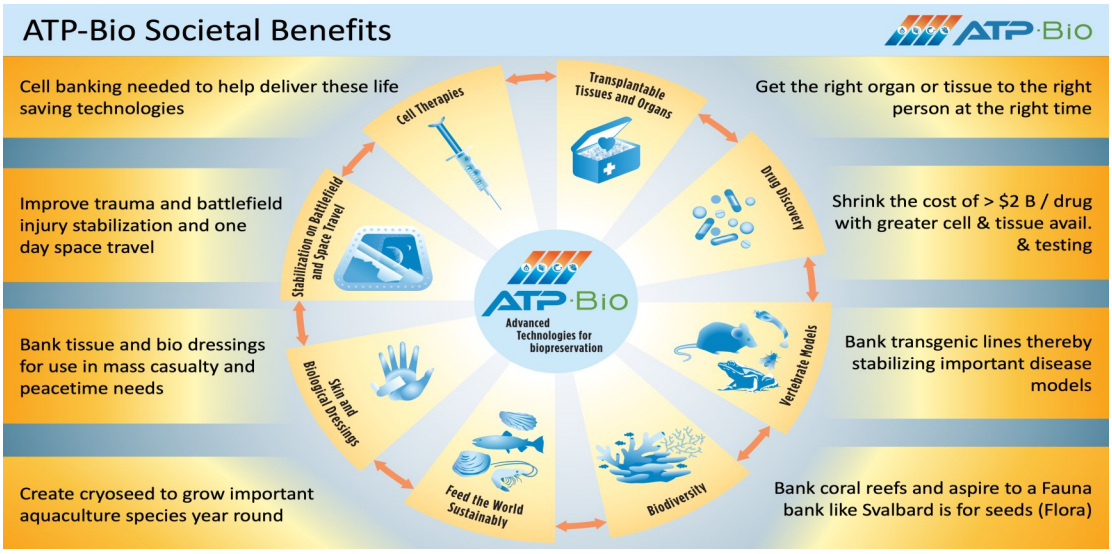

Fig. 1. ATP-Bio Research Milestones

RESEARCH

Recent consensus documents including NSF-funded roadmaps highlight that fundamental barriers to biopreservation are essentially the same for all living systems. Our research and engineering will be aimed at eliminating or controlling ice, toxicity from cryoprotective agents (CPAs), and thermal and mechanical stress—the causes of nearly all biological damage at subzero temperatures (Figure 2).

Fig. 2. Overarching biopreservation problems

Thrust Area 1: Biological Engineering attacks these at the pre-cooling stage, aiming to engineer CPAs and the biosystems themselves to prepare for subzero preservation and recover to normal function. Researchers in this Thrust Area use nature's freeze-tolerant organisms (e.g., wood frogs–seeFigure 2) to guide their bioengineering.

Thrust Area 2: Multi-scale Thermodynamics of Water focuses on preventing and/or mitigating ice crystallization during the cooling process, even in systems as cold as -140 ºC, through strategic use of CPAs and manipulating cooling conditions.

Thrust Area 3: Rapid and Uniform Warming tackles the ice that spontaneously forms as cryopreserved specimens are warmed through subzero temperatures, along with the "cracking" that destroys cells and tissues due to thermal and mechanical stress. The goal is to rewarm systems rapidly enough to "outrun" ice formation and uniformly enough to prevent thermal gradients, even in systems as large as whole human organs.

Our research testbeds represent the key products that ATP-Bio will enable:

- **Cells.** Cells have become modern workhorses for therapy (e.g., CAR T cells); in vitro models for drug testing and understanding disease; and micro-factories for proteins, viral vaccines, and antibodies. The ability to preserve, store, and ship cells for therapeutic and research purposes will be crucial for them to have maximum societal benefit across global and economic boundaries.
- **Microphysiological Systems (MPS).** The ability to use human induced-pluripotent stem cells (hiPSCs) has led to the development of powerful in vitro tissue models known as microphysiological systems (MPS) or "organs-on-a-chip." Advances in the preservation of MPS will enable us to efficiently produce high-quality MPS for high-throughput testing on a wide variety of human tissues for pharmacological studies and preparation for whole organ preservation.
- **Whole Organs.** A key long-term objective of ATP-Bio is to store whole human organs and a wide range of human tissues at subzero temperatures for long periods of time. In the first period of the ERC, we aim to establish protocols for preserving livers, hearts, and multiple tissues at subzero temperatures, with other organs following in Years 6-10, including kidneys and pancreatic islets. We will also work with organ-derived tissues such as liver and kidney slices, which have many of the same benefits as MPS. Depending on our advances and advice from our Scientific and Industrial Advisory Boards (SAB and IAB), we may also work with human tissues such as skin, cartilage, and blood vessels.
- **Whole Organisms.** In this testbed, we will primarily use Danio rerio, the common zebrafish. Zebrafish are key model systems for cryopreserving other fish species for aquaculture and biodiversity efforts. They are also particularly suited for biomedical research since their genome—which has 70% homology with the human genome—is sequenced and annotated, and thousands of key mutant lines have been generated. Moreover, major organs are formed within 24 hours, embryonic tissues are translucent for live imaging studies, and stocks are easy to breed and can be raised in multi-well plates, facilitating the application of high-throughput screens.

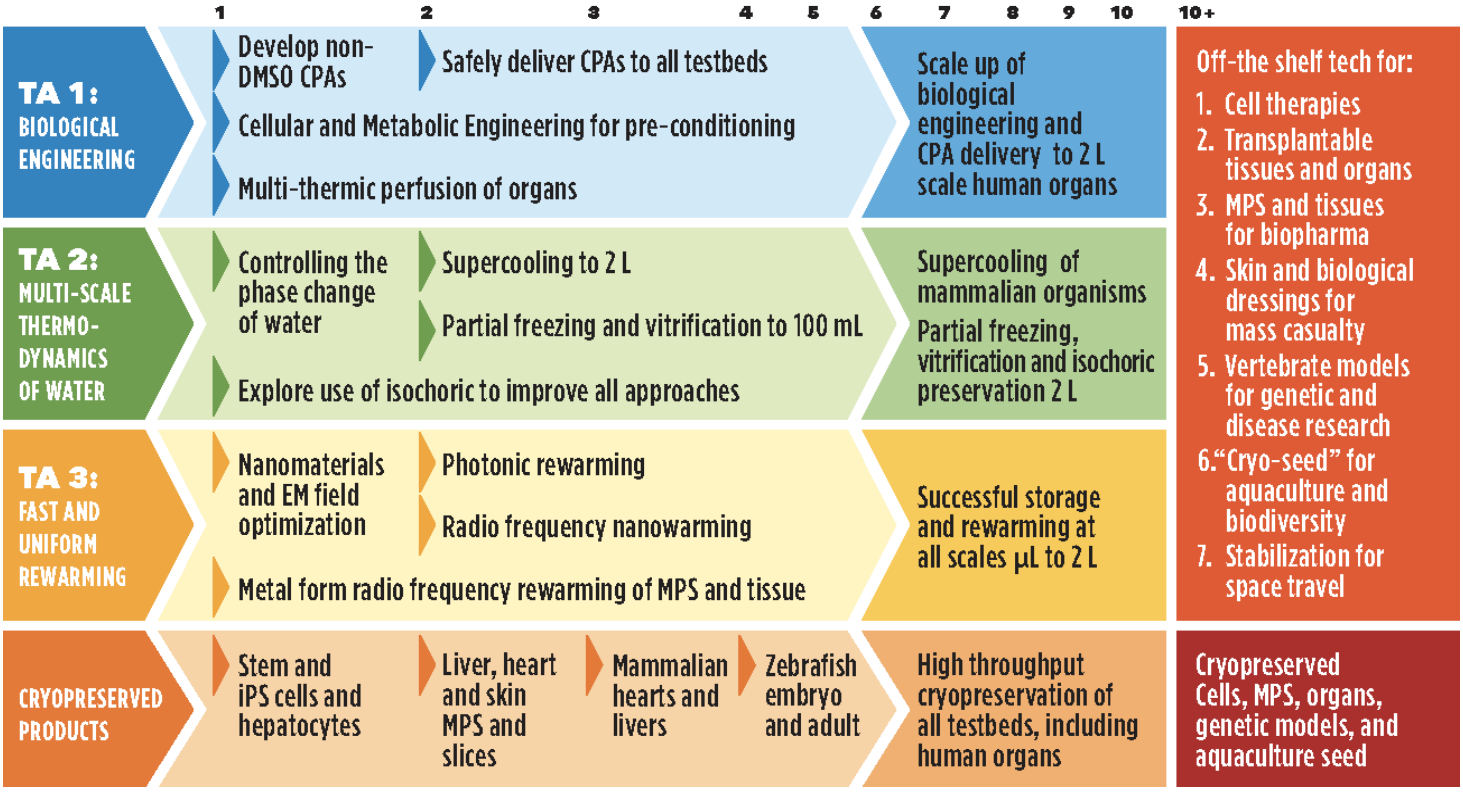

Fig.3. ATP-Bio Research Milestones

A high-level summary of our research deliverables is shown in Figure 3.

EDUCATION

Regenerative medicine, aquaculture, and other industries related to ATP-Bio are valued between $300B–$600B (US – World) and are predicted to grow substantially by 2025, making workforce development a critically important part of the Center. As NSF and others have demonstrated, building a sustainable STEM workforce pipeline demands including women, African-Americans, Hispanic/Latinx-Americans, Native Americans, and other under-represented groups in STEM education at universities and in industry. Thus, we aim to promote a STEM workforce that is a demographic reflection of our current and future nation while also recognizing that diversity of perspective will only strengthen STEM fields. Below, we summarize our programs for each level of student or trainee:

- **Grades 6-10.** We work with our partner middle schools and high schools to design in-school engagement that fits their curricular goals and emphasizes STEM integration for real-world problem-solving. Students in grades 9-10 also have opportunities to participate in summer STEM camps hosted by each core institution.
- **Grades 11-12.** Students from our partner schools entering their junior and senior years have the opportunity to complete a summer research experience in an ATP-Bio lab. They fully participate in setting up and carrying out experiments, recording and analyzing data, and preparing data for presentation and publication.
- **Undergraduates.** We host an REU program for undergraduates at all the core ATP-Bio institutions. We also partner with existing programs on each campus to offer summer "bridge" internships to STEM students transferring from community colleges. In conjunction with our Innovation Ecosystem pillar, we also plan to develop summer internship opportunities with our many industry partners.
- **Graduate students and postdocs.** We aim for all ATP-Bio graduate students and postdocs to participate in at least one industry-related research project while part of the Center. We also train them to be mentors to younger students in their labs and offer several leadership opportunities within the Center.

DIVERSITY AND CULTURE OF INCLUSION

Each core institution will partner with their Equity and Diversity office (or its equivalent) to provide ongoing training, beginning with events at the Annual Conference, for researchers, staff, and students to create a culture of inclusion within our research

groups and programs. We will use existing resources to train graduate student and postdoc mentors for undergraduates to help them navigate the potentially unfamiliar and "unspoken" culture of academic laboratories and industry-focused research. The ATP-Bio Harassment Policy will also be strictly enforced.

We also aim to characterize the effects of engaging in evidence-based STEM educational practices and programs as well as to identify the mechanisms by which such practices increase retention in STEM degree programs. We will collect metrics for under-represented student engagement in ATP-Bio and other university programs. We will track student engagement and STEM identity development using existing validated surveys. In addition, interviews with select students will be used to develop a deeper understanding of barriers and benefits to STEM identity development. This data will also provide critical feedback to the design and improvement of programs to support under-represented undergraduate STEM students.

INNOVATION ECOSYSTEM

We aim to build an innovation ecosystem that integrates the best of academia (driven "to know how things work") and industry (driven "to make things work") and converges research and development across traditional academic and academic-industry boundaries. Moreover, we aim for this ecosystem to be a key feature of our workforce development efforts for undergraduates, graduate students, and postdocs. ATP-Bio's innovation ecosystem will consist of the following components:

- **Innovation Teams** are a key instrument for merging academic and industry research. We will use the project-specific NSF I-Corps Teams model (which is already in place at three of the ERC's core institutions) and a similar model in place at Massachusetts General Hospital (CRAASH). Briefly, when a particular technology has reached a critical stage on the path to commercialization, we will recruit researchers who will (1) work in tight collaboration across multiple projects and labs, (2) apply an industry-focused mentality of "making things work" (i.e., developing commercializable technologies rather than publishing papers), (3) be able to flexibly redeploy their efforts when promising leads emerge, and (4) be motivated by incentives similar to those of industry, including an interest in industry career paths—especially start-ups developed around ATP-Bio technologies. We strive to include as many ATP-Bio graduate students and postdocs (and some undergraduates) as possible in these Innovation Teams as part of our aim to have all Center students gain industry-oriented research experience. These teams aresupported by the many existing resources at the core institutions as well as the Biopreservation Venture Accelerator described below.
- **ATP-BioPartners** are the industry organization of the Center. Many of the companies committed to membership in ATP-BioPartners are current research partners and provide crucial expertise and equipment in several research projects of the Center. There are currently 50+ organizations committed to ATP-BioPartners.
- **Commercialization assessment and skill-building.** We take full advantage of the commercialization resources at each university to help Innovation Teams and others within ATP-Bio evaluate technologies for commercialization potential and learn the skills necessary to navigate the paths to commercialization. Each Innovation Team applies the I-Corps or CRAASH methodology to develop a Value Proposition Design Canvas that connects the team to stakeholders outside the lab and informs their research design. Likewise, medically focused innovation teams access Harvard's Catalyst and UMN's Clinical Translational Science Institute regarding clinical trial design, regulatory pathway planning, and reimbursement strategies.
- **Biopreservation Venture Accelerator**. We have accelerator partners who help guide teams through the funding stages of commercialization. These partners further develop networks of mentors, venture capital sources, and professional services tailored for biopreservation.

ETHICS AND PUBLIC POLICY

- We will guide ethical development and deployment of ATP-Bio technologies by conducting embedded ethics analyses with research teams, developing plausible use cases and anticipatory governance approaches to ATP-Bio technologies, and publishing guiding ethics and policy analyses.

- We will advance ethics in ATP-Bio research by augmenting standard review (i.e., IRB and IACUC), identifying and analyzing ethical issues across the institutions involved in our research, and providing a forum for ATP-Bio participants to raise ethical questions related to research.
- We will collaborate on training ATP-Bio participants in ethics through use of a web portal for resources, featured ethics and policy events and discussions, development of trainings and courses, and opportunities for trainees to participate with Ethics and Policy leaders in analysis of the challenges, appropriate societal adoption, and anticipated impact of ATP-Bio technologies.

FACILITIES

ATP-Bio has substantial institutional administration and state-of-the-art laboratory facilities, including the following:

- **University of Minnesota:** Space for ERC Administration, Zebrafish Core, Visible Heart Laboratory, Characterization Facility, Minnesota Nano Center, Imaging Core, NMR Center, Center for Magnetic Resonance Research, Minnesota Supercomputing Institute, Experimental Surgical Services, Research Animal Resources
- **Massachusetts General Hospital**: Center for Engineering in Medicine, BioMEMS Resource Center, Cleanroom Facility, Transplantation Center, Shriners Facilities for Clinical Studies, Cell, Tissue and Organ Resource Core, MIT Microsystems Technology Laboratories, Mitochondrial Assessment Facilities, MGH Research Cores, Harvard Catalyst Program, Center for Integration of Medicine and Innovative Technology, Clinical Research Program
- **University of California Riverside**: UCR Center for Nanoscale Science and Engineering Nanofabrication Cleanroom Facility, UCR Central Facility for Advanced Microscopy and Microanalysis, Analytical Chemistry Instrumentation Facility, Chemistry Department Equipment, High Performance Computer Laboratory
- **University of California Berkeley**: CIRM/QB3 Shared Stem Cell Facility, Biomolecular Nanoechnology Center, Marvell Nanofabrication Lab, Berkeley Sensor and Actuator Center, Mass Spectrometry Facility, Central California 900 MHz NMR Facility, High-Throughput Screening Facility, Functional Genomics Laboratory, Berkeley Preclinical Imaging Center, Cancer Research Laboratory, QB3 Macrolab, Machine and Electrical Shops

CENTER CONFIGURATION, LEADERSHIP, TEAM STRUCTURE

ATP-Bio's ambitious goals are led by a collaborating team from the University of Minnesota and Mass General Hospital, in close partnership with the University of California-Berkeley and the University of California-Riverside. The team includes experts in education, diversity and inclusion, evaluation, innovation, and ethics. The primary governing body of ATP-Bio is the Executive Committee, which is an accomplished group of researchers with extensive experience managing and participating in multi-disciplinary, multi-investigator projects and centers. The ATP-Bio team represents a range of expertise and experience to enable ATP-Bio to achieve its stated mission and vision. The Executive Committee is supported by an institutional Council of Deans, and external stakeholders, the Scientific Advisory Board (SAB), and representatives from ATP-BioPartners, who comprise the Industry Advisory Board (IAB). These entities serve a critical role in helping to guide and advise all ATP-Bio strategic priorities.

CENTER HEADQUARTERS

ATP-Bio
University of Minnesota

420 Delaware St SE
Mayo Memorial Building
Minneapolis, MN 55455-0341

atp-bio@umn.edu

www.atp-bio.org
www.atp-bio-education.org

Director: John Bischof (UMN)
bischof@umn.edu

Deputy Director: Mehmet Toner (MGH)
mehmet_toner@hms.harvard.edu

Administrative Director: Alyssa Burger (UMN)
(612) 964-3996 • atp-bio-ad@umn.edu