Medical Hibernation Challenge (SPRIND)

Problem. Humans function constantly 'on,' our metabolism permanently running at full speed. This is a trait known as obligate euthermy. Obligate euthermy of the human organism limits medicine profoundly [1]. Critical organs and tissues remain viable only briefly. Preservation of organs would decouple donation from transplantation in both time and space, and thereby a) improve donor–recipient matching; b) enable elective daytime surgeries; c) lower discard rates by overcoming current logistics.

Additionally, a breakthrough in preservation would increase access to viable human tissue, enabling 'clinical trials at the bench', i.e., studying real human disease in real human tissue alongside animal and cell models. This capability would remove a key bottleneck in the search for prevention and cures for debilitating and deadly diseases such as neurodegeneration and heart failure.

Beyond the hospital, human-applicable hibernation would enhance emergency and military medicine and strengthen health-system resilience in disasters and mass-casualty events. Ultimately, it could increase the options for terminally ill patients and extend the range for human deep-space exploration.

Solution. Hibernating animals like the Arctic ground squirrel and the Canadian wood frog possess a biological "pause button" to slow down metabolism. At cryogenic temperatures, biological time can be paused entirely, via vitrification techniques. Delicate, three-dimensional mammalian tissues can now be cryopreserved via vitrification: instead of freezing, water is arrested as a cryogenic glass, a non-crystalline, solid state close to the liquid state while halting molecular mobility and biochemical reactions.

The rodent kidney has recently been vitrified and successfully transplanted with life-sustaining function [2, 3]. Encouraging results have also been achieved in the rodent liver and brain [4, 5]. Key technical obstacles include translation to the myocardium and scaling to human-sized organs (≈ 100-1000× volume).

Achieving reversible vitrification requires solutions that are simultaneously **minimally toxic** (to maintain viability and function), **minimally viscous** (to be perfused through vascularized tissues), and **highly permeable** (to permeate into interstitial and intracellular regions). Current cryopreservation solutions were discovered heuristically, and their toxicity remains too high at the concentrations needed to preserve human-scale organs. Since their development, huge advancements have been made in molecular thermodynamics [6, 7], nano-engineering [2, 8], multi-omics [9, 10], and AI-powered drug discovery [11, 12], yet these advances have not been applied to the problem of medical hibernation.

Alternative approaches include preconditioning and rescue treatments (e.g., heat-shock protein induction), as well as scalable and uniform cooling and warming techniques (e.g., pressurized persufflation). Teams may contribute to any part of the challenge and employ alternative methods (e.g., ice-active proteins, unorthodox cryoprotectant discovery strategies) to achieve the target objectives.

The timely convergence of technological advances and application of untapped approaches will enable significant and rapid advancements in devising new preservation solutions and protocols.

Challenge. The challenge proceeds in four stages to unlock medical hibernation:

- ***Hackathon: In silico modeling (1 week, 20 teams, 100k€ total).***
  Milestone A: generate predictive physics- & AI-based models of vitrification and multicompartment osmosis. *Metric*: evaluated on goodness-of-fit for experimental data.
  Milestone B: Suggest novel strategies for achieving medical hibernation. *Metric*: judged on originality. The Hackathon functions as a mechanism for forming performer-teams for the subsequent challenge phases but is not a prerequisite for participation.
- ***2D biostasis (1 year, 10 teams, 10M€ total).*** This first stage casts a deliberately wide net: ten performer teams compete to establish low-toxicity vitrification of 2D cell culture monolayers. This reduces regulatory and capability hurdles for participation and enables testing of heterodox and high-throughput approaches like genetic engineering, CRISPR and compound screening.
  Milestones: Cryopreservation of adherent cardiomyocytes and neurons or other sensitive differentiated cell types and predictors of later success in tissue and organ preservation.
  Metrics: After preservation, cells must contract (cardiomyocytes) or play Pong (neurons), with >95% cellular yield and transcriptomes that normalize toward untreated controls.
- ***3D biostasis (1 year, 5 teams, 10M€ total).*** In the second stage, down-selected teams or wild-card entrants compete to demonstrate functional recovery in larger and more complex biomedically relevant systems like organoids and precision-cut tissue slices. This phase explores which strategies can serve the higher demands of preserving intercellular contacts and geometry in larger, multicellular tissues. Relevant samples include organoids and tissue slices from heart, liver, lung, kidney, brain, retina, skin, prostate, breast, and thyroid.
  Milestones: Contracting myocardial slices, retained long-term potentiation in hippocampal circuits or other sensitive differentiated tissues and predictors of later success in organ preservation.
  Metrics: Transcriptomic and proteomic normalization, and intactness of histoarchitecture across cell types after 2 days and 2 weeks.

- ***Human-scale organ biostasis (1 year, 3 teams, 15M€ total).*** In the third stage, down-selected teams or wild-card entrants compete to demonstrate whole-organ cryopreservation. This targets heart, liver, kidney, and limb transplantation, and whole-brain recovery without restoration of consciousness. The lab of Prof. Gerald Brandacher (Med Uni Innsbruck/Johns Hopkins) will provide normothermic perfusion and transplantation capabilities as well as validation and verification for all performers. Prof. Alexey Ponomarenko (Translational Neurometrics) will provide electrophysiology readouts. The final winner will be determined by the score sheet (Table 1) after storage for either >100 days (if > −130°C) or 1 day (if < −130°C). Whole-rodent preservation is defined as a challenge clincher, since it implies progress on all organs at once and is symbolic for transforming emergency, military and space medicine.
  Milestones: Beating heart *ex vivo*, long-term survival of kidney, heart, liver and limb transplant models, *ex vivo* normothermic perfusion.
  Metrics: Respirometry after 4 hours and intactness of histoarchitecture after 4 weeks

Table 1: Challenge Scoring Table

	Heart	**Liver**	**Kidney**	**Limb**	**Brain**
Level 1 Porcine transplant (survival >4 weeks)	15 pts	15 pts	10 pts	10 pts	n.a.
Level 2 Human *ex vivo* (normothermic perfusion >24 hours)	12 pts	12 pts	8 pts	8 pts	n.a.
Level 3 Rodent transplant (survival >4 weeks)	5 pts	4 pts	2 pts	5 pts	n.a.
Level 4 Porcine *ex vivo* (normothermic perfusion >24 hours)	3 pts	2 pts	2 pts	2 pts	10 pts
Level 5 Rodent *ex vivo* (normothermic perfusion >24 hours)	2 pts	1 pt	1 pt	1 pt	5 pts

Together, these capabilities will spawn commercial cell-, tissue-, and organ-banking activities, support European sovereignty in biopreservation and transplantation, and help lay the foundation for human deep space exploration. Since the heart, liver, kidney and brain are highly sensitive

systems, success here provides the platform for translation to virtually every other organ and tissue system in the human body, powering research in and drug discovery for the vast majority of human diseases. Researchers across biotech, pharma, and academia will be able to run plannable experiments on human cells and tissues at scale, including electrophysiology, spatial omics, gene editing, and drug discovery assays, accelerating key aspects of discovery cycles and opening a direct, data-rich path to cures that work in patients.

Table 2: Heilmeier questions

Heilmeier Question	Medical Hibernation Challenge
1.A. What is the proposed work attempting to accomplish or do?	This challenge aims to develop breakthroughs for cryopreservation of functionally viable human cells, tissues and organs. This would decouple transplantation in space and time and enable 'clinical trials at the bench', making differentiated human cells and real human tissues available on-demand and at scale.
1.B. How is the proposed work leading to improved health outcomes?	Every year, thousands of transplant candidates die because usable organs cannot be transplanted quickly enough. Fewer than 60% of transplanted organs survive beyond 10 years primarily due to poor immunological matching. Beyond transplantation, medical hibernation can transform cancer care, emergency and military trauma medicine, and deep-space exploration. Furthermore, expanding access to viable human organs and tissues for research would accelerate the development of therapies and cures for the majority of disease burden.
2. How is it done today; what are the limitations of present approaches?	Today, organ transplantation is a race against time due to the rapid decay of ischemic tissue. Organs are rushed via airplanes and emergency transport to recipients, forcing non-elective surgeries that often occur overnight. This leads to compromises in immunological matching, discard of organs, and logistical costs. Furthermore, medical research currently mainly relies on imperfect animal models because viable human tissues cannot be stored for study.
3. What is new in your approach? Why do you think it will be successful at this time?	Current cryopreservation solutions were discovered heuristically, and their toxicity remains too high at the concentrations needed to preserve human-scale organs. Since their development, huge advancements have been made in molecular thermodynamics [6, 7], nano-engineering [2, 8], multi-omics [9, 10], and AI-powered drug discovery [11, 12], yet they have not been applied to the problem of medical hibernation. The timely convergence of technological advances and application of untapped approaches will enable significant and rapid advancements in devising new preservation solutions and protocols.
4. What are the key technical, programmatic, or translational risks in your approach, and how do you plan to mitigate these?	Technical risks include a) achieving low-toxicity cryopreservation in sensitive cells like cardiomyocytes, and b) in large-scale organs. We mitigate a) and b) via graded metrics and milestones. A too high barrier for entry c) is avoided by starting with 2D systems, proceeding to 3D systems before requiring organ transplantation capabilities in year 3. These year 3 capstone capabilities will be provided by our validation and verification laboratory of Prof. Gerald Brandacher (Med Uni Innsbruck/Johns Hopkins). Programmatic risk includes animal experimentation regulation, which is mitigated by delaying non-terminal animal work to year 3 and providing the validation and verification laboratory in Austria with animal permits in place. Translational risk includes safety of genetic intervention strategies which are anticipated by some performers. These approaches will be encouraged to harness somatic gene editing once developed.
5. Who or what will be affected and what will be the impact if the work is successful?	The immediate beneficiaries are transplant recipients due to better immunological matching, surgery planning and organ utilization, as well as researchers of next-gen therapies, e.g., for heart and brain diseases. Medium and long-term, patients with virtually all diseases could benefit from more accurate models, faster therapeutic translation, and lower development failure rates leading to new cures and treatments, as well as ways to prevent disease in the first place.

6. How long will the program take?	The program spans 3.75 years in total: a one-week *in silico* hackathon in Q2, followed by three consecutive one-year phases starting from Q3, progressing from 2D to 3D to organ preservation.
7. How much will the program cost?	The total projected cost is 35.1 M€. This includes a 0.1 M€ one-week *in silico* hackathon in Q2, followed by three consecutive one-year phases starting from Q3, hackathon to model vitrification and osmosis and form performer teams; a 10 M€ first year for 2D preservation with ten teams; a 10 M€ second year for 3D preservation with five teams; and a 15 M€ third year for organ preservation with three teams.
8. What are the mid-term and final exams to check for success?	In Year 1, successful 2D biostasis is demonstrated by contracting cardiomyocytes and neurons capable of playing Pong, transcriptome normalization and >95% cellular yield. In Year 2, 3D tissue, organoid or organ-on-chip biostasis is demonstrated through, e.g., contracting myocardial slices, retained long-term potentiation, transcriptomic profiles, and histology. Year 3 requires whole-organ biostasis with, e.g., a beating heart after rewarming and demonstrable transplant survival, supported by respirometry and histology.
9. What are specific applications of your project?	This challenge will enable biobanking of delicate human cells, tissues, organoids and organs. This will unlock on-demand organ replacement and living tissue archives, boosting research applications across virtually all diseases.
10. To ensure access, how will cost, accessibility, and user experience be addressed?	By cryopreserving and distributing viable human cells, tissues, and organs on demand, we address access in the following ways: For transplantation, organ banking eliminates the high costs of emergency logistics (e.g., private flights) and transforms the surgical emergency procedure to plannable, elective events. For research, we enable democratized, cost-effective access globally that competes with the cost and relevance of animal models. Workflows compatible with clinical and bench-top routine will be incentivized for commercial scalability.
11. How might this effort be misperceived or misused (and how can you prevent that from happening)?	Misperceptions may include concerns about unauthorized cell, tissue or organ donation/recovery and/or unethical misuse of donor materials. To prevent this, the regulation pertaining to organ transplantation and conventional biobanking efforts applies. Brain organoids and organotypic culture of precision cut brain slices are routine in German government funded biomedical research, with a consensus that no consciousness or high-order perceptive properties could persist at those small tissue scales. The challenge may be misperceived as requiring excessive animal experimentation, which is addressed by delaying invasive animal work to year 3 and adherence to 3R-principles. We provide a shared Ethics & Security Advisory Board (Prof. Vincent C. Müller, Dr. Max Tretter).

Literature

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