

---


# OSSIUM

## THE PROMISE OF BONE MARROW BANKING

---



# Ossium Health came out of our search for a better way to preserve organs for transplant



Contents lists available at ScienceDirect

Cryobiology

journal homepage: [www.elsevier.com/locate/ycryo](http://www.elsevier.com/locate/ycryo)

## The Grand Challenges of Organ Banking: Proceedings from the first global summit on complex tissue cryopreservation

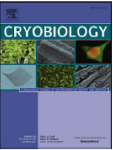
Jedediah K. Lewis<sup>a, b</sup>, John C. Bischof<sup>c</sup>, Ido Braslavsky<sup>d</sup>, Kelvin G.M. Brockbank<sup>e, f</sup>, Gregory M. Fahy<sup>g</sup>, Barry J. Fuller<sup>h</sup>, Yoed Rabin<sup>i</sup>, Alessandro Tocchio<sup>a, b</sup>, Erik J. Woods<sup>j, k</sup>, Brian G. Wowk<sup>g</sup>, Jason P. Acker<sup>j, l, m</sup>, Sebastian Giwa<sup>a, n, \*</sup>





Beta Roadmap Report

**SOLVING ORGAN SHORTAGE THROUGH ORGAN BANKING AND BIOENGINEERING**



nature  
biotechnology

Vitreous cryopreservation maintains the function of vascular grafts

Ying C. Song, Bijan S. Khirabadi, Fred Lightfoot, Kelvin G.M. Brockbank, and Michael J. Taylor\*

Organ Recovery Systems, Inc., 751 East Bay Street, Charleston, SC 29403 USA. \*Corresponding author (mailto:info@organ-recovery.com).



Capitol Hill Roundtable:  
*Emerging Technologies in Organ Preservation*



Second global Organ Banking Summit at Harvard Med School



ARMY SBIR TOPIC

TOPIC #: A15-059

TITLE: Cryopreservation for Regenerative Medical Applications

KEY TECHNOLOGY AREA(S): Transplant Medicine / Regenerative Medicine

OBJECTIVE: A capability is sought to develop cryopreservation methods that can place organs and vascularized composite tissues into storage for long-term storage and subsequent use.

DESCRIPTION: The preservation of organs and vascularized composite tissues after donor harvest is a central problem in transplant and reconstructive medicine. The feasibility of many transplant procedures is limited not by the availability of donor tissue but by the transportation time required to deliver donor tissue to the recipient. The development of methods to extend the viability of tissues beyond several hours post-harvest would transform the practice of transplantation and reconstructive medicine by making donor tissue available to many more recipients than is currently possible. It is envisioned that cryopreservation methods may also be used to salvage damaged extremities following trauma by permitting their preservation until advanced surgical procedures are available to repair the limb. One aspect of cryopreservation that remains a challenge regardless of the approach is the rewarming phase. This topic focuses on the optimization of solutions and methods for rewarming of cryopreserved tissues.

Cryopreservation through vitrification holds great promise as demonstrated in cells and described in theory for tissues in the mid 1980s [1][2]. Vitrification involves freezing to a "glassy" rather than crystalline phase, thereby avoiding damaging rates and extracellular ice crystals that are known to damage cells and tissues in the frozen state. In practice vitrification relies on loading a high enough concentration of a cryoprotectant (CPA) (up to 50% w/v) and cooling rapidly enough such as to reach below the glass transition temperatures (T<sub>g</sub>) while minimizing or avoiding nucleation of ice. The full realization of this technology could potentially make heart, liver, lung, kidney and every leading part of medical practice. It would also enable storage of 3D engineered tissues for regenerative medicine. However, practical applications to tissues has been difficult to realize due to diffusive heat and mass transfer and phase-change limitations that cause the procedure to fail. For instance, insufficient diffusion of the cryoprotective solution, insufficient cooling or warming rates, and thermal gradients that can impose thermal stress can all lead to vitrification failures. These are compounded as ice growth due to devitrification and stress driven fractures and cracking during thawing. More recently some groups have shown promising approaches to address these different limitations in this tissue, by working with thin veins, blood vessels [1][4] organs [3][6][7] and limbs [8]. This has continued to highlight the promise of vitrification, but also underlines the need to find a way to broaden the ability to work with thicker bulk tissue systems to fully realize the potential of the technology [9].

Assessing sufficiently uniform cryoprotective loading can be achieved as previously reported [11][10], the most important issues to address relate to uniformity and speed of cooling and thawing rates such that failures such as cracks and devitrification can be avoided. While cooling and thawing can already occur within suitable tissue systems, these problems only grow as tissues scale up in volume. Thermal-mechanical fractures are caused by differential contractions in the tissues, and they may be caused by differences in coefficients of expansion in different tissue types, by thermal gradients, and perhaps by other causes. Viable tissue layers that are 4 mm or less in thickness, during large scale scale fractures [11]. But, since most research and all commercial applications of cryopreservation has focused on cryopreservation of cells or very small tissue little attention has gone to avoid cracking and cracking. (In fact little attention has gone to reversing methods of large tissue systems at all, since

ARMY SBIR TOPIC

TOPIC #: A15-059

TITLE: Cryopreservation for Regenerative Medical Applications

KEY TECHNOLOGY AREA(S): Transplant Medicine / Regenerative Medicine

OBJECTIVE: A capability is sought to develop cryopreservation methods that can place organs and vascularized composite tissues into storage for long-term storage and subsequent use.

DESCRIPTION: The preservation of organs and vascularized composite tissues after donor harvest is a central problem in transplant and reconstructive medicine. The feasibility of many transplant procedures is limited not by the availability of donor tissue but by the transportation time required to deliver donor tissue to the recipient. The development of methods to extend the viability of tissues beyond several hours post-harvest would transform the practice of transplantation and reconstructive medicine by making donor tissue available to many more recipients than is currently possible. It is envisioned that cryopreservation methods may also be used to salvage damaged extremities following trauma by permitting their preservation until advanced surgical procedures are available to repair the limb. One aspect of cryopreservation that remains a challenge regardless of the approach is the rewarming phase. This topic focuses on the optimization of solutions and methods for rewarming of cryopreserved tissues.

Cryopreservation through vitrification holds great promise as demonstrated in cells and described in theory for tissues in the mid 1980s [1][2]. Vitrification involves freezing to a "glassy" rather than crystalline phase, thereby avoiding damaging rates and extracellular ice crystals that are known to damage cells and tissues in the frozen state. In practice vitrification relies on loading a high enough concentration of a cryoprotectant (CPA) (up to 50% w/v) and cooling rapidly enough such as to reach below the glass transition temperatures (T<sub>g</sub>) while minimizing or avoiding nucleation of ice. The full realization of this technology could potentially make heart, liver, lung, kidney and every leading part of medical practice. It would also enable storage of 3D engineered tissues for regenerative medicine. However, practical applications to tissues has been difficult to realize due to diffusive heat and mass transfer and phase-change limitations that cause the procedure to fail. For instance, insufficient diffusion of the cryoprotective solution, insufficient cooling or warming rates, and thermal gradients that can impose thermal stress can all lead to vitrification failures. These are compounded as ice growth due to devitrification and stress driven fractures and cracking during thawing. More recently some groups have shown promising approaches to address these different limitations in this tissue, by working with thin veins, blood vessels [1][4] organs [3][6][7] and limbs [8]. This has continued to highlight the promise of vitrification, but also underlines the need to find a way to broaden the ability to work with thicker bulk tissue systems to fully realize the potential of the technology [9].

Assessing sufficiently uniform cryoprotective loading can be achieved as previously reported [11][10], the most important issues to address relate to uniformity and speed of cooling and thawing rates such that failures such as cracks and devitrification can be avoided. While cooling and thawing can already occur within suitable tissue systems, these problems only grow as tissues scale up in volume. Thermal-mechanical fractures are caused by differential contractions in the tissues, and they may be caused by differences in coefficients of expansion in different tissue types, by thermal gradients, and perhaps by other causes. Viable tissue layers that are 4 mm or less in thickness, during large scale scale fractures [11]. But, since most research and all commercial applications of cryopreservation has focused on cryopreservation of cells or very small tissue little attention has gone to avoid cracking and cracking. (In fact little attention has gone to reversing methods of large tissue systems at all, since

To Your Health

The Washington Post

White House, private sector act to reduce organ transplant waiting list

AST AMERICAN SOCIETY OF TRANSPLANTATION

Organ and Tissue Preservation



**We studied cryopreservation techniques used in tissues where long-term preservation was commonplace**

NHS CORD BLOOD BANK  
HPC, CORD BLOOD  
START PRODUCT  
RETRIEVAL SITE UCH  
TIME 12 20  
DATE 08/03/12  
WEIGHT (g) 1.6  
VOLUME (ml) 0.4  
STORE AT: 2°C

**Umbilical cord blood and autologous bone marrow are cryopreserved thousands of times per year**



**125,000 patients per year  
could be treated by bone  
marrow transplant**



**Fewer than 10,000 allogeneic  
bone marrow transplants are  
performed each year**





**20,000 blood cancer patients per year search for a donor**





**No Conventional  
Match for 45%**



**5-year survival falls by 1% with  
every 3 days of wait**

**Can we find another source  
of bone marrow?**

**~ 30,000**

**deceased organ and tissue donors  
in the US each year**





**But could deceased donor bone marrow be safely used in patients?**

# Extensive research from world class institutions provided proof of concept for deceased donor bone marrow use

[Regen Med.](#) 2011 Nov;6(6):701-6. doi: 10.2217/rme.11.89.

## Clinical implementation of a procedure to prepare bone marrow cells from cadaveric vertebral bodies.

[Donnenberg AD](#)<sup>1</sup>, [Gorantla VS](#), [Schneeberger S](#), [Moore LR](#), [Brandacher G](#), [Stanczak HM](#), [Koch EK](#), [Lee WA](#).

### Bone Marrow Transplantation

Case Report | Published: 08 April 1998

## Bone marrow transplantation from a cadaveric donor

[J Kapelushnik](#), [MAker](#), [T Pugatsch](#), [S Samuel](#) &

*Bone Marrow Transplantation* **21**, 857–858 (1998)



ELSEVIER

Immunosuppression

## Donor bone marrow infusion in cadaveric renal transplantation

[G Ciancio](#) <sup>a</sup>

### Transplantation Proceedings

Volume 35, Issue 2, March 2003, Pages 871–872



## Alternative donor sources in HLA-mismatched marrow transplantation: T cell depletion of surgically resected cadaveric marrow.

[Lucas PJ](#)<sup>1</sup>, [Quinones RR](#), [Moses RD](#), [Nakamura H](#), [Gress RE](#).

### CYTOTHERAPY

The Journal of Cell Therapy

## Development and validation of a procedure to isolate viable bone marrow cells from the vertebrae of cadaveric organ donors for composite organ grafting

[Vijay S. Gorantla](#)<sup>\*</sup>, [Stefan Schneeberger](#)<sup>\*</sup>, [Linda R. Moore](#), [Vera S. Donnenberg](#), [Ludovic Zimmerlin](#), [W. P. Andrew Lee](#), [Albert D. Donnenberg](#)



ELSEVIER

### Transplantation Proceedings

Volume 29, Issues 1–2, February–March 1997,

Pages 714–715

## Immune markers and hematopoiesis of cadaveric bone marrow for transplantation

[G. Söderdahl](#) , [C. Tammik](#), [M. Remberger](#), [J. Sandberg](#), [G. Tufveson](#), [J. Tollemar](#), [O. Ringdén](#)



## Donor Bone Marrow Infusion in Deceased and Living Donor Renal Transplantation

[Gaetano Ciancio](#) , [George W. Burke](#), [Jang Moon](#), [Rolando Garcia Morales](#), [Anne Rosen](#), [Violet Esquenazi](#), [James Mathew](#), [Yide Jin](#) and [Joshua Miller](#)

### Advances in Hematology

[Adv Hematol.](#) 2016; 2016: 6471901.

Published online 2016 Apr 30. doi: [10.1155/2016/6471901](#)

PMCID: PMC4867066

PMID: [27239198](#)

## Combined Bone Marrow and Kidney Transplantation for the Induction of Specific Tolerance

[Yi-Bin Chen](#), <sup>1</sup> [Tatsuo Kawai](#), <sup>2</sup> and [Thomas R. Spitzer](#) <sup>1</sup>, <sup>\*</sup>



**5+ clinical doses per deceased donor**

**X**

**30,000 donors each year**

**=**

**150,000+ doses of BM per year**

**That's a lot of bone marrow, virtually all of  
which was going unused**

**What could we do with it all?**





**35,000 U.S. organ recipients per year**

**Organ rejection is  
common**



**Immunosuppressants  
lead to infection**





# Ending organ rejection without immunosuppressants

## Immune tolerance induction:

- Obviates need for immunosuppressants
- Builds off 6 decades of bone marrow transplant experience

# Two Problems



## **Treating Blood Cancers**

- ✓ More matches
- ✓ Faster transplants



## **Improving Organ Transplants**

- ✓ Permanent transplants
- ✓ Fewer complications

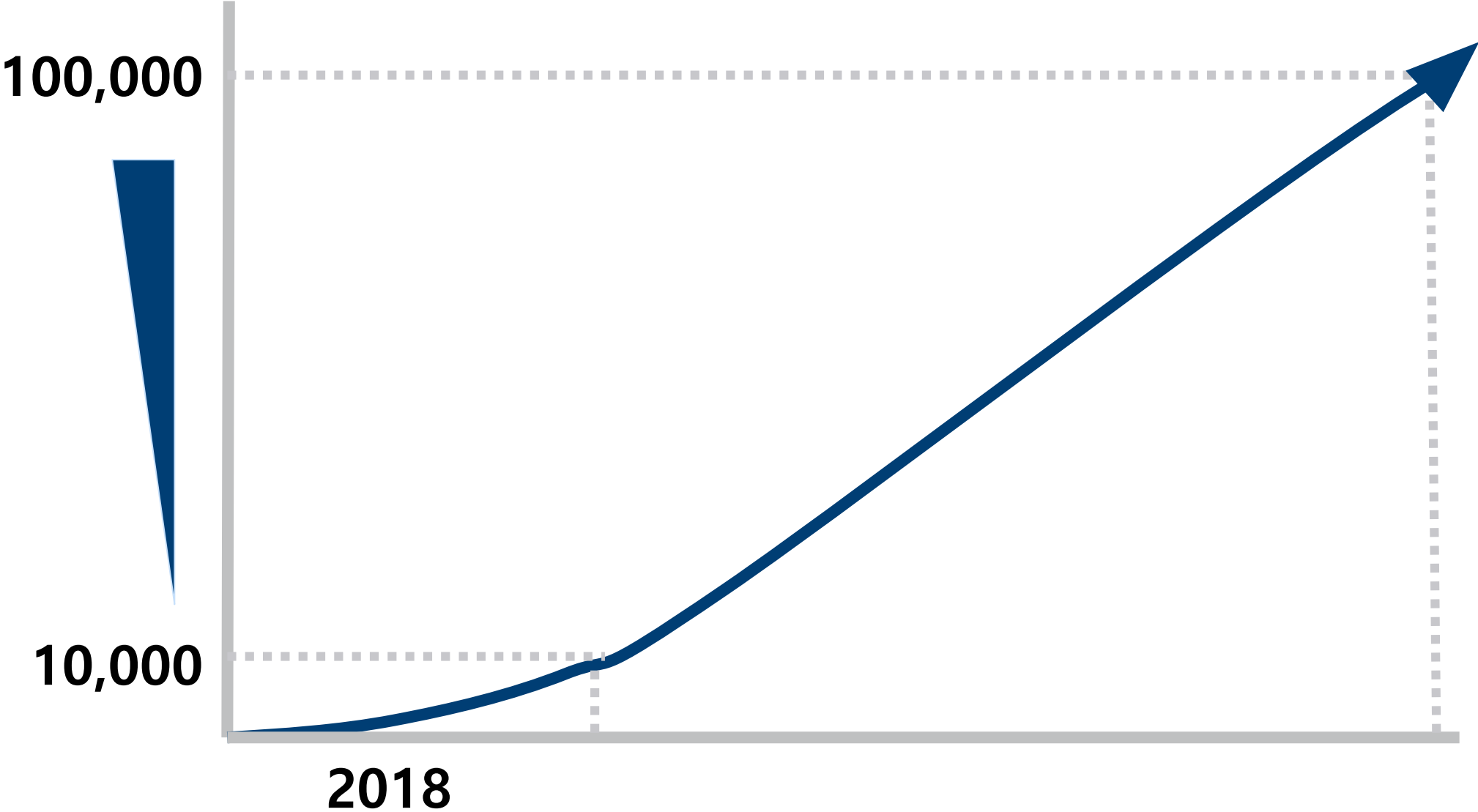


# **Two Problems : One Solution**



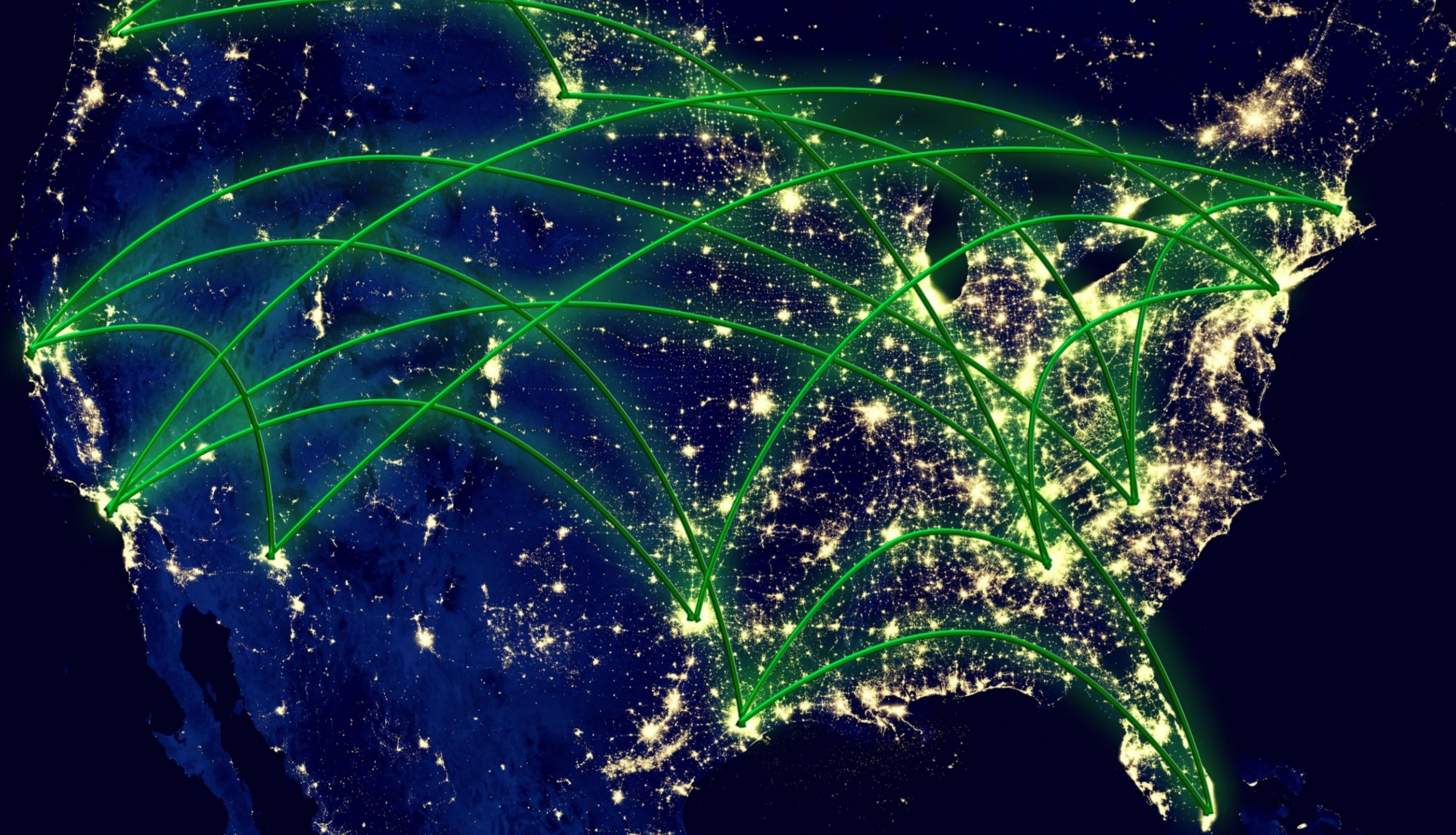
**Banking bone marrow from organ donors**

# Ossium's bank aims to scale to more than 100k donors over the next several years



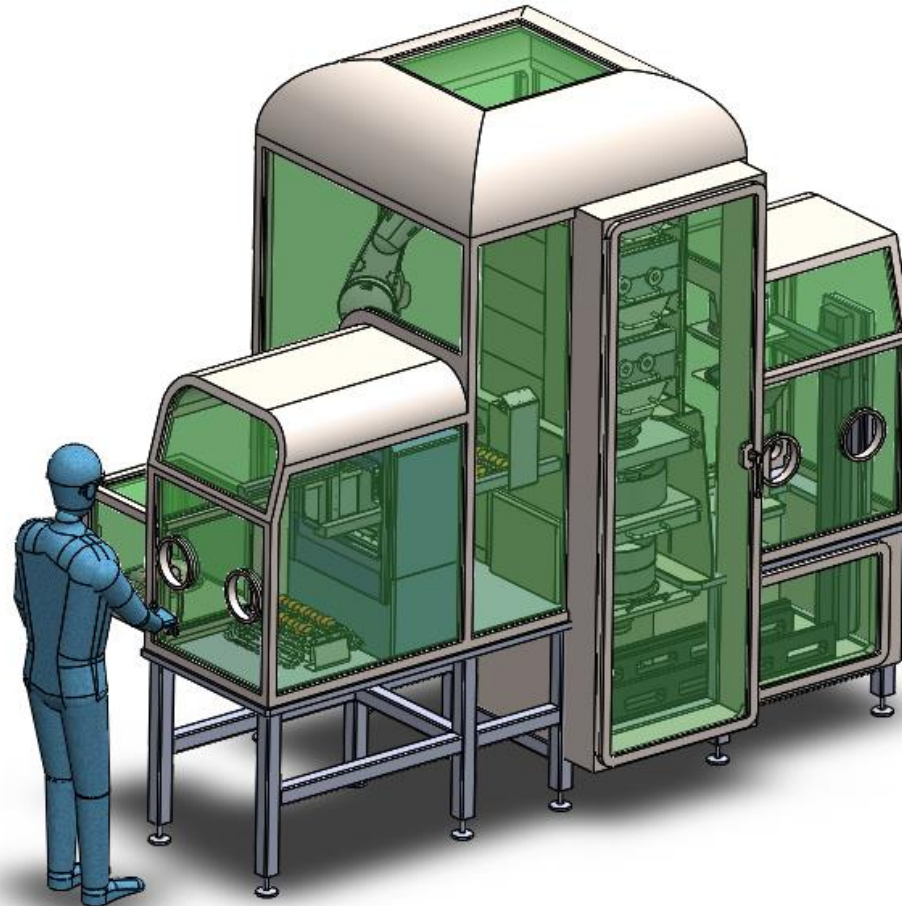
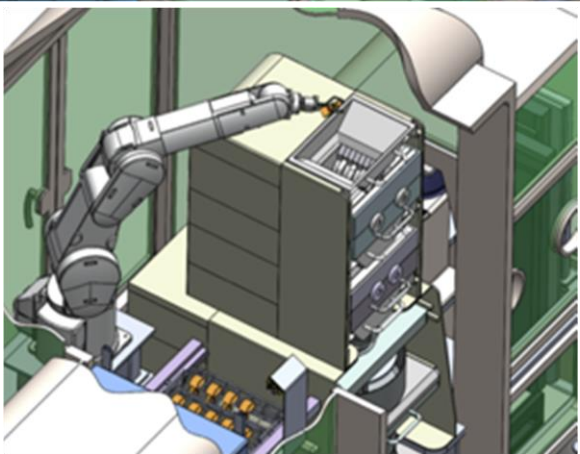
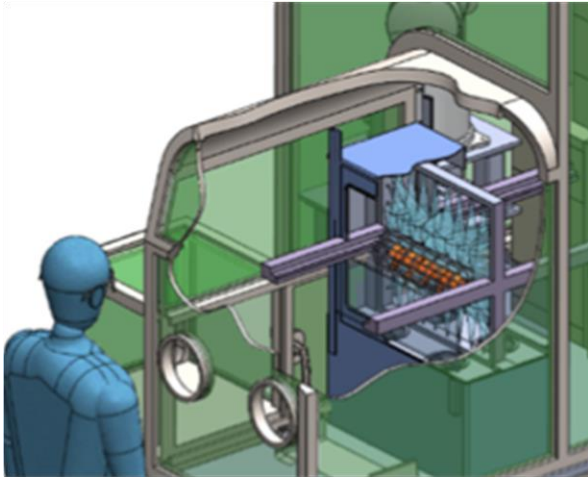
**How do we scale?**







# In time, Ossium will manufacture Maxwell for 3-hr automated processing without cleanroom requirement



- Can deployed almost anywhere
- Minimal footprint and training required
- “Plug and play” technology
- One operator runs multiple processes simultaneously

## Current Clinical Practice

- Lymphoma
- Multiple Myeloma
- Sickle cell
- SCID
- Leukemia
- Aplastic anemia

35,000 US  
patients / year



## Future therapies

- Treating autoimmune disease
- Using gene therapy to introduce cure hematologic diseases
  - CCR5  $\Delta 32$  mutation for HIV resistance

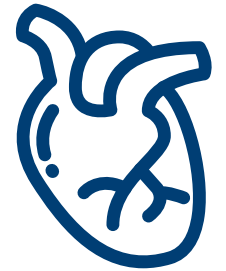


How many patients' lives can Ossium save or improve?

**33,000** per year

**2,700** per month

**90** per day



A person wearing a red jacket and dark pants stands on a dark, rocky outcrop, looking out over a night landscape. In the background, a city with lights is visible, and the sky is filled with stars and streaks of light, suggesting a long-exposure photograph. The overall scene is dark and atmospheric, with a focus on the vastness of the night sky.

Reimagining immunity...

A wet, organic, information processing system

The human immune system can be repaired,  
rebooted, and reengineered