

Mitlet Fact Sheet

Eric Boilard, Tom Benson
October 15, 2021

Summary

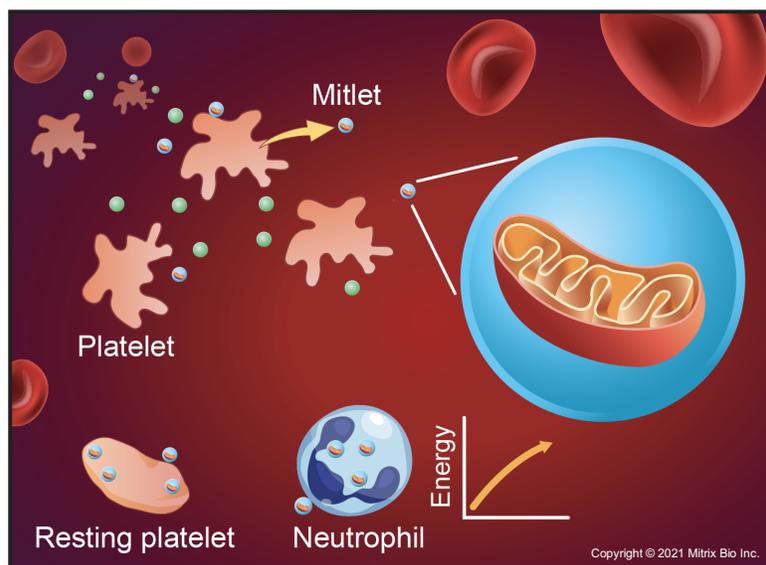
Mitlets are small vesicles containing mitochondria, ejected by platelets and then recycled back into other blood components as a normal part of blood metabolism. Mitlets can be transfused between patients, or perhaps grown in bioreactors, to potentially treat a variety of diseases. Mitlets are still recently discovered and there is much yet to uncover. In this paper we'll describe what is known so far.

Introduction

Human blood contains many different components that can be transfused – red blood cells, white blood cells, plasma, platelets, etc. The most common of these, red blood cells, contain no mitochondria. The second most common, platelets, contain about 5 mitochondria on average, which provide the energy the platelets need to clot and heal damage. When platelets are activated by damage or reach the end of their 10-day lifespan, they eject their contents, including mitochondria, in tiny capsules called vesicles. The mitochondria-containing vesicles – called mitlets – can be absorbed by nearby cells, including other blood cells and nearby damaged cells, where the mitochondria are adopted by the cell and start generating the energy needed to heal tissue. This appears to be a way for the body to recycle and conserve mitochondria, which are a valuable cellular asset.

When were they discovered?

Mitlets (originally called mitochondrial Platelet Extracellular Vesicles, or PEVs) were identified in 2014 by Dr. Eric Boilard and team at Université Laval in Quebec. Mitrix has ongoing research at partner universities that show that mitlets can be extracted safely from the blood and injected in large quantities from donors to recipients.



Mitlets occur naturally in blood

Potential use in medicine

Studies have shown that mitlets can be pooled from multiple donors and injected into a single recipient. This is important because healthy mitochondria are crucial to the healing process. Mitochondrial dysfunction is an underlying factor in multiple diseases including cardiovascular disease, cancer, Alzheimer's, vision loss, frailty, and mitochondrial mutation diseases. The technique of mitochondrial transfusion (transplanting mitochondria from an outside source into the body) has recently been developed by a number of major universities. However, finding a source of mitochondria to transplant is a challenge. Donation of mitochondria via mitlets may provide some help with this problem.

Where do mitlets come from?

Mitlets are extracted from platelets. Platelets are collected routinely by hospitals and blood banks for emergency use, and if not used, must be discarded after a few days. It is possible that blood banks could extract and store the mitlets before discarding unused platelets – thus gaining additional medical value out of a resource that would otherwise be thrown out.

Medical advantages of mitlets

There are several advantages of using this source of mitochondria:

- Mitlets are already designed by nature to be transferred in the blood; they have the proper receptors and chemistry.
- Thus, if properly generated, they should provide an excellent potential therapy for disease.

Logistic advantages of mitlets

Platelet-based mitochondria have several logical and financial advantages:

- The world already has an extensive and very well-developed infrastructure for gathering and storing platelets.
- Because platelets expire after a few days and must be kept for emergency use, there are large quantities of them which are discarded every day by blood banks.
- Thus, blood banks could process the platelets and remove the mitlets prior to the platelets being discarded.
- This may potentially provide another use or revenue stream for blood banks.
- Blood banks already possess the technical skills, clean manufacturing certifications, FDA regulatory permissions, and skilled personnel required.

Limitations of mitlets

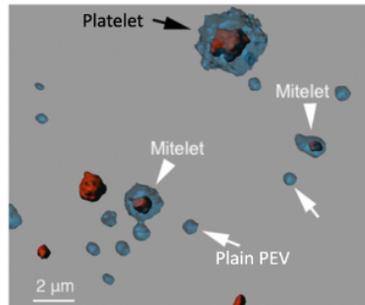
However, mitlets have disadvantages as well:

- It will take large quantities of mitlets to affect any significant cure.
- It may be that mitlets should be treated similar to donor organs such as liver or kidneys, which are managed and tracked to ensure fair distribution.

Is mitlet therapy FDA-approved or available for use?

No. Mitlet therapy is a purely experimental concept with significant risks, not approved for human use, and will likely require many years of research and testing before scientists understand it fully. There are no human trials underway at this time. The purpose of this white paper is information only; some or all of this information may be found to be inaccurate.

Mitlet Data



- Each Platelet has 4-5 mitochondria
- 100 billion platelets/day
- At end of life/when activated, platelets extrude mitochondria PEVs (mitlets)
- Absorbed by local cells
- Triggered by enzymes

Boudreaux, et al. Platelets release mitochondria serving as substrate for bactericidal group IIA-secreted phospholipase A2 to promote inflammation. Blood. 2014 Oct 2;124(14):2173-83.

What's next?

Mitrix Bio is working with research partners to study mitlets for a variety of indications. Mitrix is also testing bioreactor technology to grow mitlets in larger quantities for other diseases.

About Mitrix Bio Inc.

Mitrix Bio (www.mitrix.bio) is a Palo Alto, CA-based startup firm developing mitochondrial transfusion therapeutics. Founded by Tom Benson, former manager at Stanford Linear Accelerator National Lab, with advisors such as Dr. Michael Snyder, chair of the Genetics Department at Stanford University and Dr. Ben Albeni, Chair of the Department of Pharmaceutical Sciences and Co-Director of the B.R.A.I.N. Center at Nova Southeastern University in Florida. Mitrix Bio is funded by R42 Group, Longevity Tech Fund, QuadraScope Health Ventures, Lauder Partners, and others.

Contact

Tom Benson
CEO, Mitrix Bio Inc.
tom@mitrix.bio

Affiliations

Eric Boilard, PhD, Centre de Recherche du Centre Hospitalier Universitaire de Québec, 2705 Laurier Blvd, Room T1-49, Québec G1V 4G2, Canada.
Tom Benson, CEO, Mitrix Bio Inc. 4695 Chabot Dr. #250, Pleasanton, CA 94588
tom@mitrix.bio

References

1. Platelets release mitochondria serving as substrate for bactericidal group IIA-secreted phospholipase A2 to promote inflammation. Boilard et al 2014.
<https://pubmed.ncbi.nlm.nih.gov/25082876/>
2. Mitochondria Are a Subset of Extracellular Vesicles Released by Activated Monocytes and Induce Type I IFN and TNF Responses in Endothelial Cells. Boilard et al 2018.
<https://pubmed.ncbi.nlm.nih.gov/31219742/>
3. Mitochondrial transplantation for therapeutic use. McCully 2018.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4851669/>
4. Prospective Therapeutic Applications of Platelet Extracellular Vesicles. Johnson et al. 2021. [https://www.cell.com/trends/biotechnology/fulltext/S0167-7799\(20\)30268-7](https://www.cell.com/trends/biotechnology/fulltext/S0167-7799(20)30268-7)
5. Endocytosis-mediated mitochondrial transplantation: Transferring normal human astrocytic mitochondria into glioma cells rescues aerobic respiration and enhances radiosensitivity.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6587163/>
6. Intercellular mitochondrial transfer as a means of tissue revitalization. Gao et al. 2021.
<https://www.nature.com/articles/s41392-020-00440-z>
7. Mitochondrial DNA in extracellular vesicles declines with age (and transplantation of young mitochondria increase respiration better than old). Evans et al 2021.
<https://onlinelibrary.wiley.com/doi/full/10.1111/ace.13283>
8. Platelet Extracellular Vesicles: Beyond the Blood. Boilard et al. 2021.
<https://pubmed.ncbi.nlm.nih.gov/33028092/>
9. Platelet-derived extracellular vesicles infiltrate and modify the bone marrow during inflammation. French SL, Butov KR, Allaey I, et al. 2020.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7362363/>

Disclaimer: Mitrix Bio, Inc. makes no representations or warranties as to the accuracy, completeness, or reliability of this information. This paper is presented for informational purposes only and may be found to be inaccurate. Mitlets and related therapies are not approved or tested for human or animal use and should not be used for such purposes without professional medical supervision.

Copyright © 2021 Mitrix Bio Inc. All Rights Reserved.