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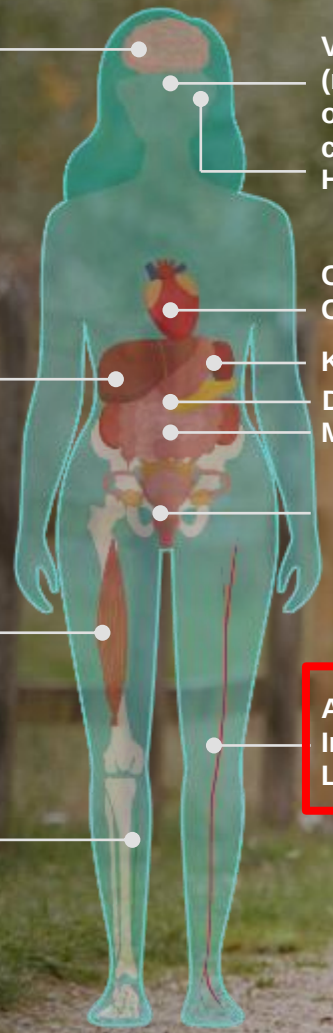
Minovia Therapeutics

Pioneering Mitochondrial Therapies

The Multi-Systemic Impact of Mitochondrial Dysfunction

Genetic or age-related mitochondrial damage cause profound effects on the function of multiple organ systems:



Neurodegeneration
Stroke
Demyelination
Epilepsy
Ataxia
Parkinsonism
Migraines
Cognitive decline
Psychiatric symptoms

Visual impairment (retinitis pigmentosa, optic neuropathy and cataracts)
Hearing deficit

Cardiomyopathy
Conduction defects

Liver disease

Kidney insufficiency
Diabetes
Malabsorption

Infertility
Premature menopause

Muscle weakness
Cramps
Exercise fatigue

Anaemia
Immunological defects
Lactacidaemia

Sensory or motor neuropathies

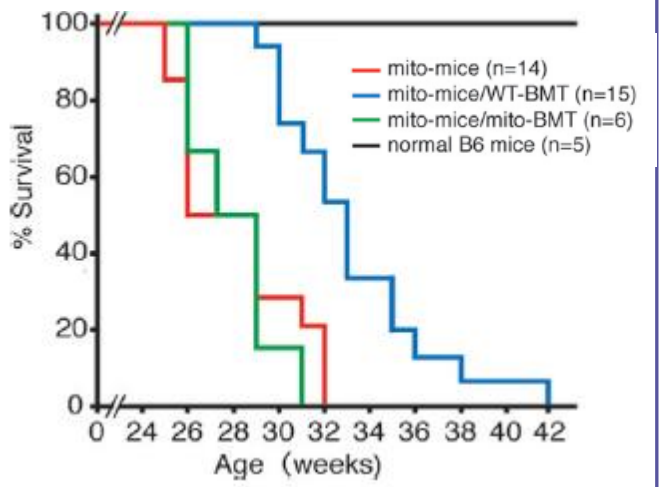
Suomalainen 2017, *Nature Reviews MCB*

Mitochondrial dysfunction can affect anyone from birth to late adulthood. Mitochondrial dysfunction not only occurs in primary mitochondrial diseases, but also accumulates with age, implicating it as a cause of many common age-related diseases

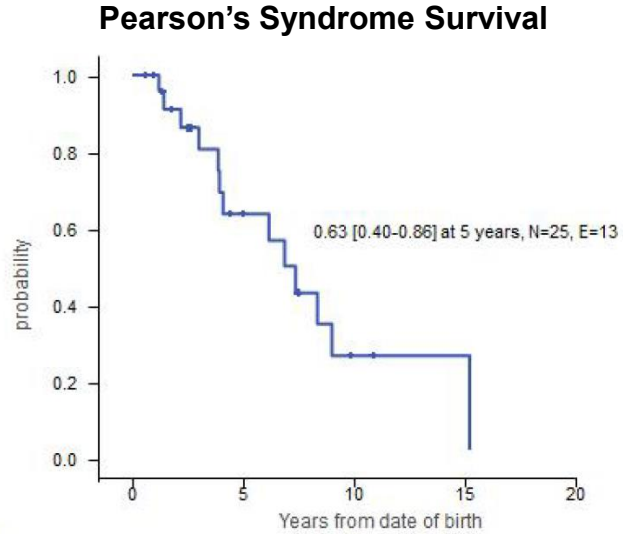
Criticality of Mitochondrial Function of Hematopoietic Stem Cells and the Hematopoietic System

Literature demonstrates that mitochondrial function of hematopoietic cells is crucial for lifespan and wellbeing.

HSPCs improves survival in mtDNA deletion mouse model



mtDNA deletion in primary mitochondrial diseases is fatal



Optimal mitochondrial functionality of the hematopoietic system is critical for lifespan and healthspan

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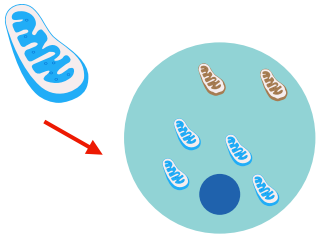
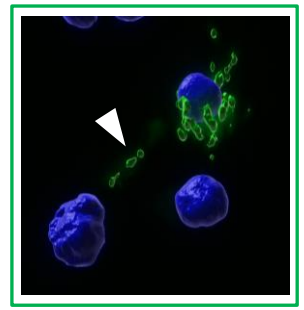
Sources: (1) Yoshimi Blood 2019 (2) Desdin-Mico Science 2020 (3) Lopez-Otin Cell 2023

MAT Enabled by Breakthroughs in Mitochondrial Science

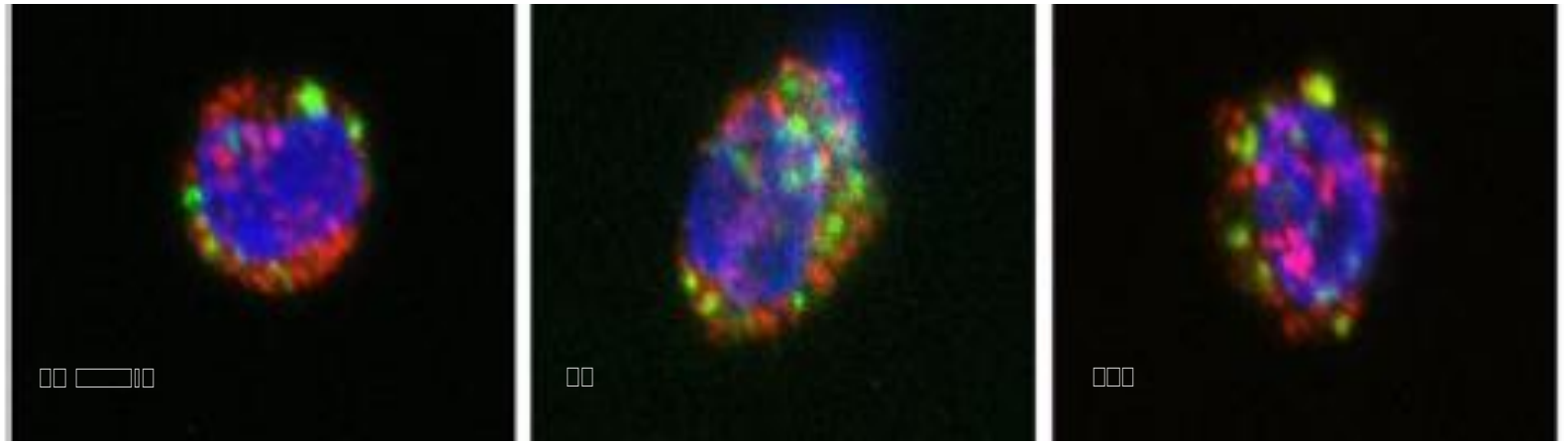
Scientific breakthroughs in understanding the ability for exogenous mitochondria to transfer into human cells form the foundation for mitochondrial augmentation technology (MAT).





Mitochondria can enter cells[1], rebuild normal mtDNA content in recipient cells[2], restore functionality and transfer between cells [3,4,5]

Minovia Invented a Process of Mitochondrial Transfer into Human HSPCs:



GFP-Mitochondria: HeLa Cells, Recipient Cell: Human CD34+
Jacoby *Nat Regen Med* 2021

What if we could rescue mitochondrial function in autologous HSPCs and avoid the risk of allogeneic transplant?

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Sources: (1) Clark and Shay, Nature 1982. (2) King and Attardi, Cell 1988 (3) Spees, PNAS 2006, (4) Islam, Nat Med 2012, (5) Rocca, Science 2017

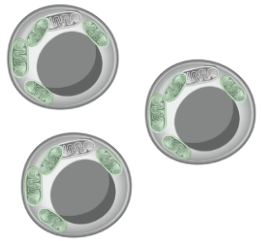
Technology Overview

Minovia developed a proprietary allogenic platform to augment the number of healthy mitochondria in patients with mitochondrial dysfunction.

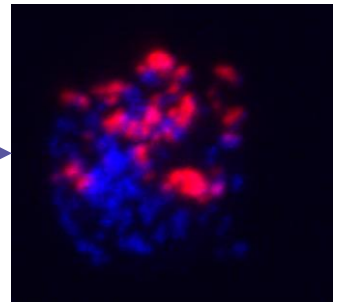
Restore mitochondrial performance

- **Potent Allogeneic Mitochondria Products (AMP)**

- **Mitochondrial Augmentation Technologies (MAT)**



Mitochondrially Augmented HSPC

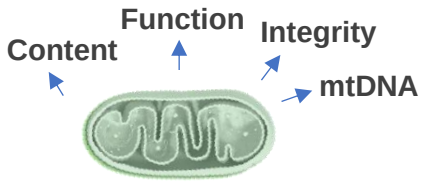


Exogenous
Endogenous

+

Measure mitochondrial function

- **Analytical methods to measure mitochondrial function (Mitochondrial Health Index)**



>70

Total Patent Assets protecting:

Mitochondrial compositions

Augmented cells and analytical methods

Therapeutic areas

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Pearson's Syndrome offers Dual Proof of Concept

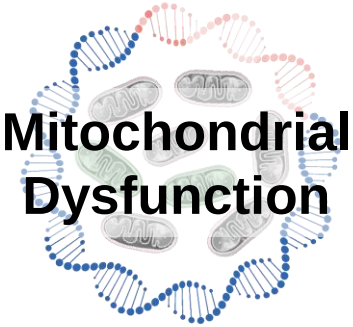
Pearson's Syndrome offers clinical proof of concept in diseases where mitochondrial dysfunction is the underlying driver of disease phenotype.

Primary Mitochondrial Myopathy

Heterogeneous group of severe progressive disorders driven by **mutations or deletions in mtDNA** that prevent the body from making energy

Age-related low risk MDS

Mitochondrial dysfunction in HSPCs inhibits ability for blasts to differentiate in **bone marrow** causing MDS, and ring sideroblastic phenotype consistent with PS



Mitochondrial Dysfunction

Mitochondrial Genetic Diseases

Bone Marrow Diseases

Pearson's Syndrome
Initial PoC, Accelerated approval pathway (PRV eligible)

Ultrarare, lethal pediatric disease caused by **deletions of mtDNA**, causing **bone marrow failure as well as multiple organ systems**

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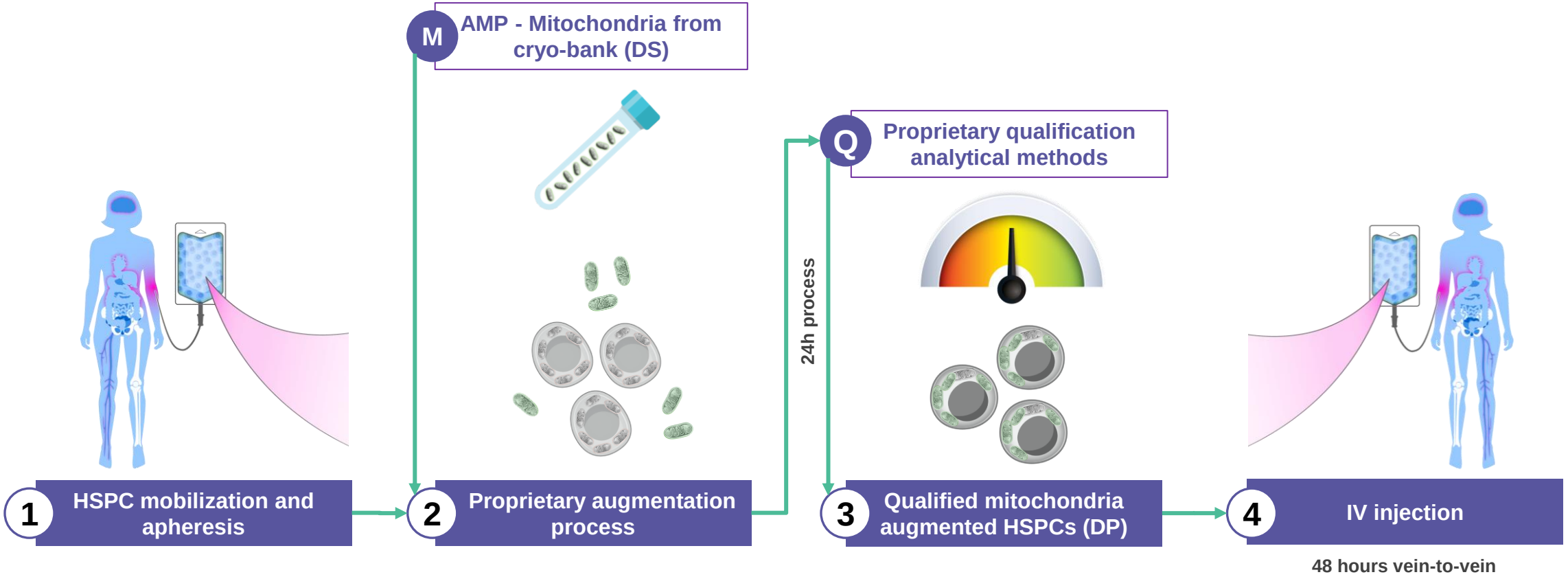
Abbreviations: PoC: Proof of Concept; HSPC: Hematopoietic Stem Cell; MDS: Myelodysplastic Syndrome

Mitochondrial Augmentation Technology (MAT)

Minovia's MNV-201 delivers AMP to HSPCs to improve disease outcomes.



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Abbreviations: HSPCs: Hematopoietic Stem and Progenitor Cells, DS: Drug Substance, DP: Drug Product

MAT Clinical Efficacy in PMD with First-Gen Product

First generation syngeneic/maternal derived product (MNV-101) demonstrated efficacy in primary genetic mitochondrial diseases, providing proof of concept for MAT.

MNV-101 Clinical Data[1]:

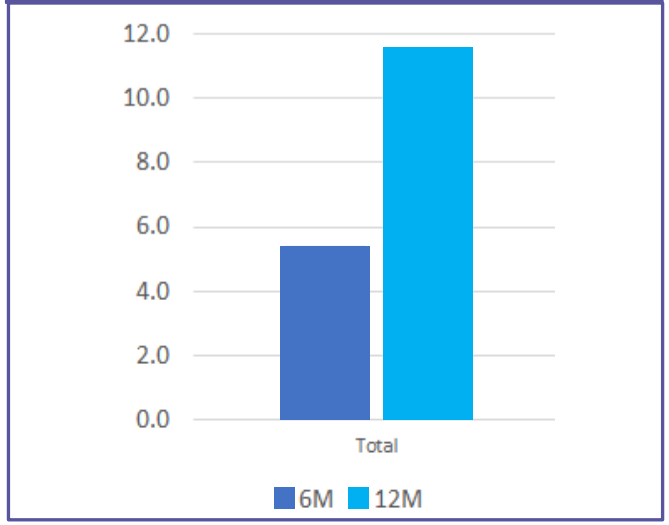
Compassionate use open-label treatment

- **7 patients**: 4 Pearson's Syndrome, 2 Kearns-Sayre Syndrome, 1 Leigh Syndrome
- 3 to >6 years follow-up post treatment

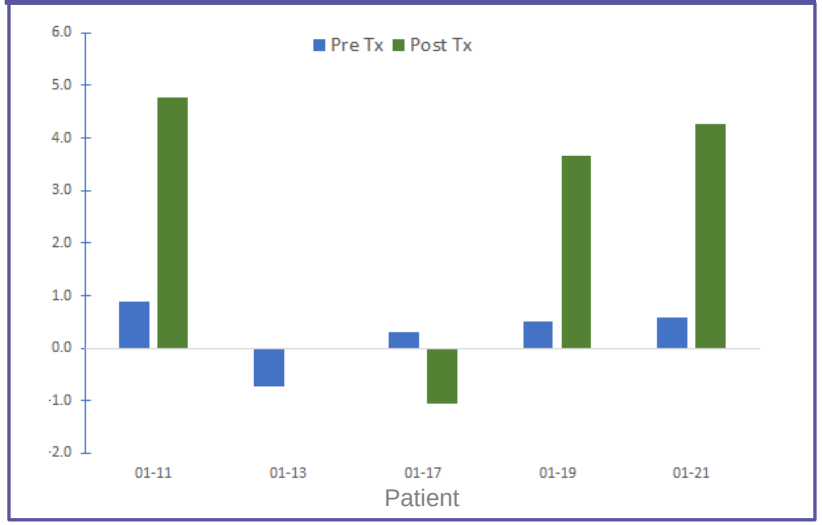
Phase 2 Clinical Study in Pearson's Syndrome

- **5 Pearson's Syndrome patients**
- **Primary endpoint:** International Pediatric Mitochondrial Disease Scale (IPMDS)
- **Secondary endpoint:** body weight gain one year before treatment vs one year after

IPMDS: Total Score (Mean Improvement from Baseline)



Body Weight Gain (kg/yr) One year before treatment vs one year after



Additional areas of improvement across patients:

- Neurocognitive function
- Muscle function
- Coordination
- Mobility
- Growth (weight gain)

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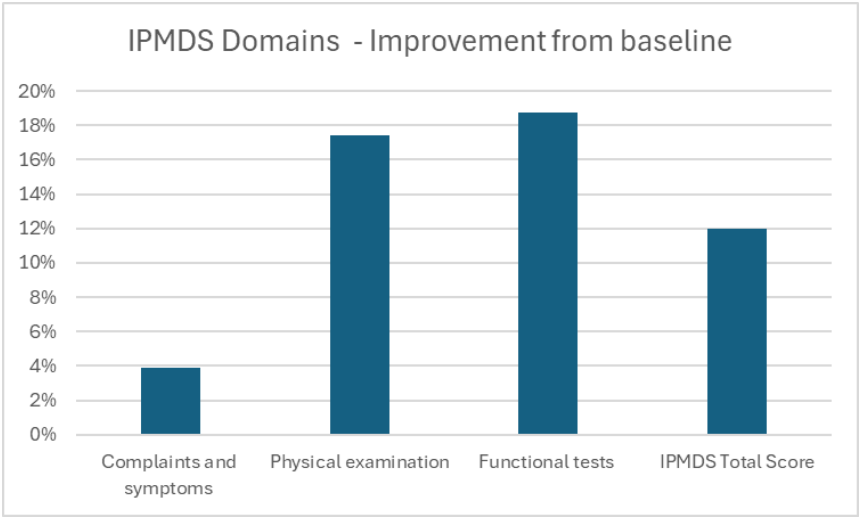
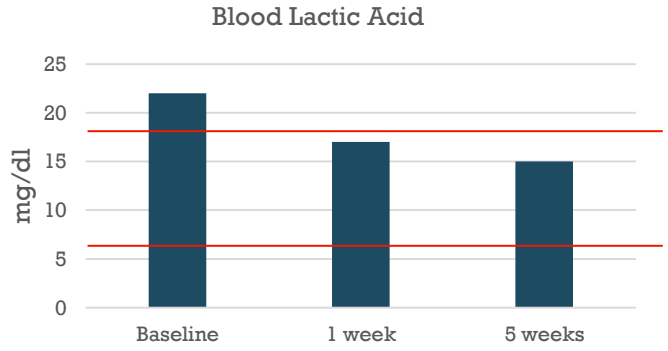
Sources: (1) Jacoby, Toren and Minovia STM 2022. https://www.science.org/doi/10.1126/scitranslmed.abo3724; **Abbreviations:** PMD: Primary Mitochondrial Diseases

Clinical Update: First in Human MNV-201

KSS Compassionate Use (CU)

- 14 years old patient, 22 kg body weight. Diagnosed a year ago with KSS.
- Single large mtDNA deletion (8kb); 60% heteroplasmy in peripheral blood
- Short stature, hypoparathyroidism, ptosis, vision and hearing loss. Significant intension tremor.
- Received G-CSF and Plerixafor (Mozobil), single apheresis.
- Patient's mitochondrial haplogroup was H41a; placental mitochondria selected from bank: H14a2 (total of 11 SNVs different).
- So far (8 weeks post treatment), **no adverse events** associated with the DP reported.
- Safety and efficacy measures (compared to baseline) at 1w, 1m, 3m, 6m and 12m: IPMDS, functional score, neurological evaluation, heteroplasmy level, exogenous mtDNA and blood mitochondrial biomarkers. If exogenous mtDNA is detected in the blood, we will also evaluate a muscle biopsy.





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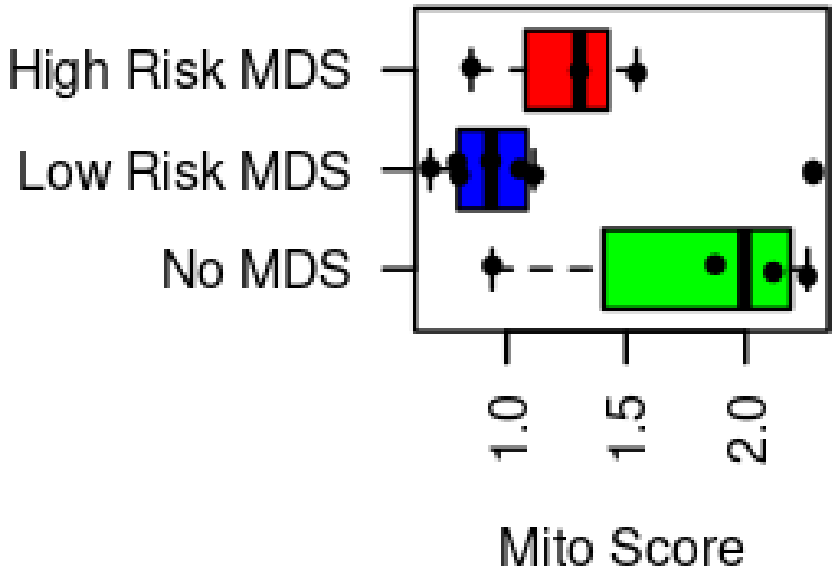
Mitochondrial Biomarkers can Stratify Diseased Patients

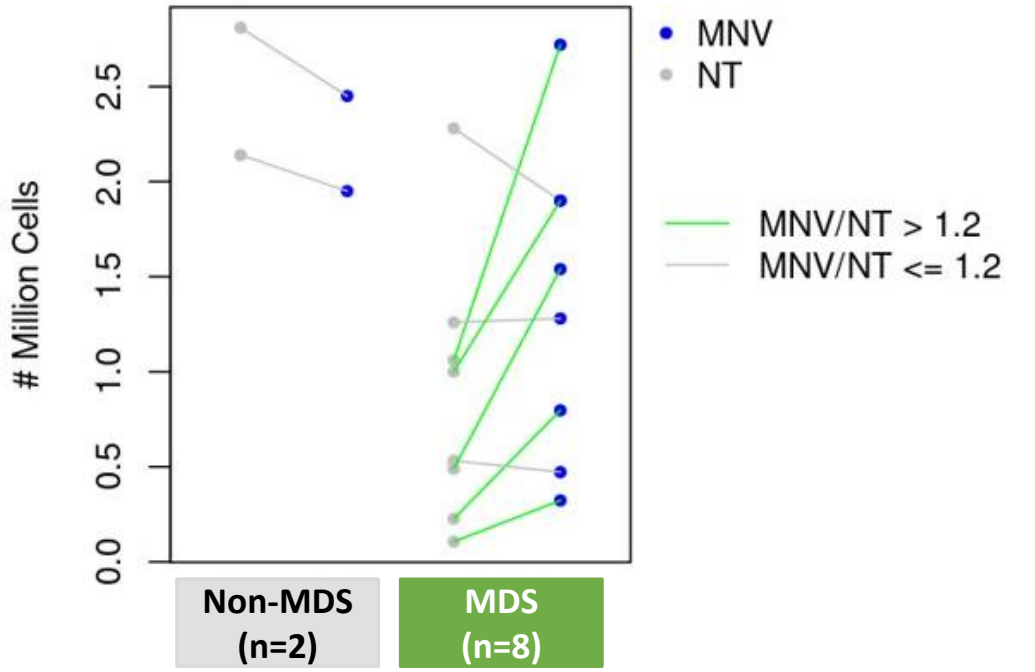
MDS patients demonstrate alterations in mitochondrial content and function in peripheral blood

MitoScore is a combined score of all 3 biomarkers (ATP, Succinate Utilization and mtDNA copy number) that represents specific mitochondrial activity



MAT improves differentiation in MDS cells

In vitro mitochondrial augmentation of MDS patient-derived cells demonstrated higher levels of differentiation to erythroid lineage



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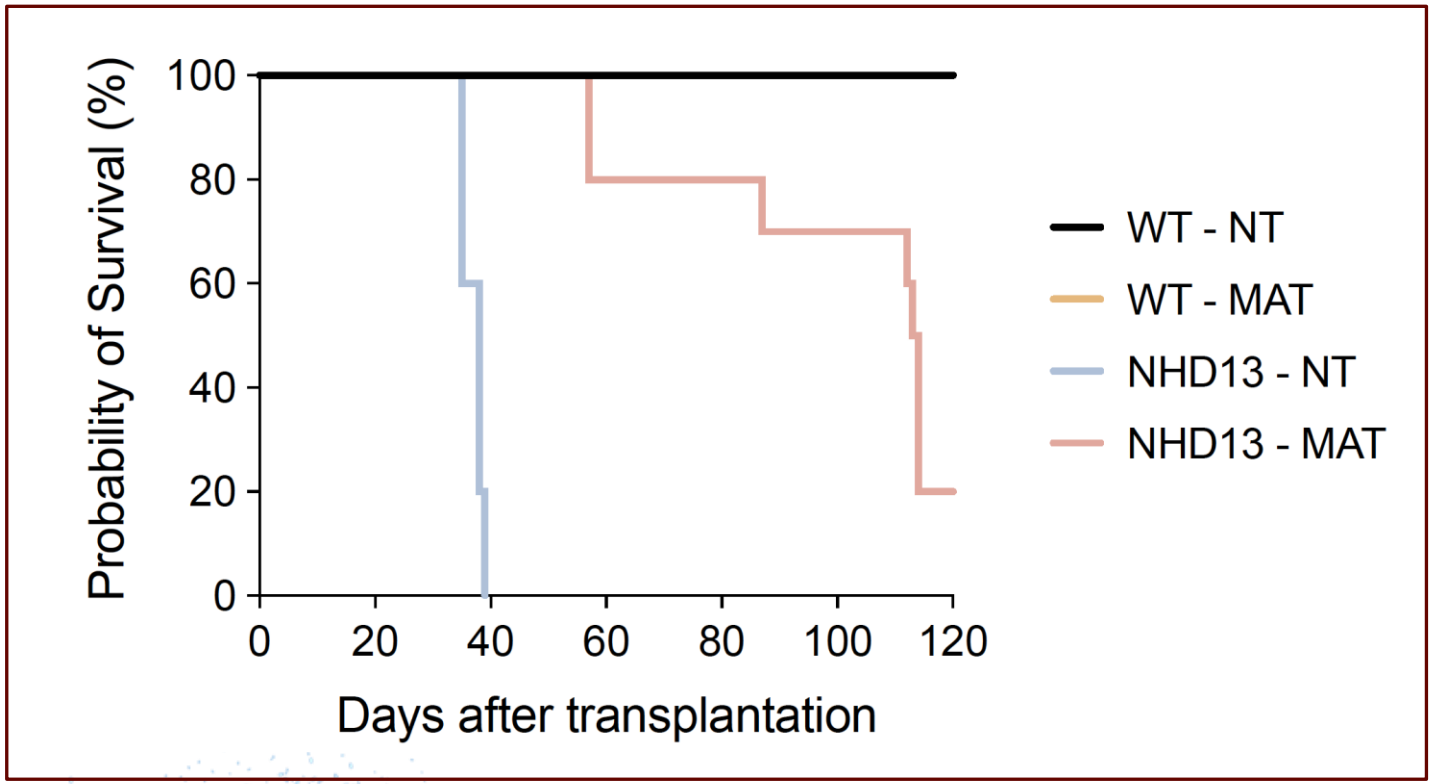
Clinical trial to collect BM samples in collaboration with Dr. Yishai Ofran, Shaarei Tzedek, Jerusalem

MAT improves survival in NHD13 mouse model

Preliminary data suggest MAT improve survival and delays progression to MDS in mouse model



MSK Collaboration/Dr. Omar Abdel Wahab

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Minovia's Current Pipeline

Minovia's lead candidate MNV-201 is initiating Phase 1b trials in Pearson's Syndrome, with preclinical data in MDS available this fall.

Product	Indication	Discovery	Preclinical	Phase I/II	Phase III	Key Upcoming Milestones
MNV-201	Pearson's Syndrome (100-400 p)			*3 pts.*	*Pivotal trial, 5 pts.*	1st in Human H1 2024
MNV-201	Myelodysplastic Syndrome (Low Risk ~70K)			*5 pts.*		Preclinical Data in Q1 2024; Ph1 in H2 2024
MNV-201	PMD/PMM (~40K)					Compassionate Use Program in H1 2024

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Executive Summary

Allogeneic Mitochondrial Product (MNV-201) Ready for Mitochondrial Diseases and Myelodysplastic Syndromes

Technology Highlights

- First and only company to **transduce allogeneic mitochondria into stem cells**
- Peer-reviewed **scientific publications demonstrating biological affect of our transduced stem cells in humans**
- Demonstrated In-vivo and in-vitro **restoration of "stemness"** using our transduced stem cell
- Proprietary analytics to **measure and rescue** mitochondrial dysfunction

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Clinical Platform Highlights

- **Human clinical proof of concept** demonstrated in multiple primary mitochondrial diseases;
- **Safely dosed first patient (ever) with allogeneic mitochondria** transduced stem cells
- **Potential for a rapid path to registration in Pearson's Syndrome**; priority review voucher eligible
- **INDs approved in Israel for Pearson's Syndrome and lower-risk MDS**
- **Efficacy biomarkers expected from Phase I trials by mid 2025**

CMC Highlights

- Scalable and Cost-Effective **cGMP manufacturing process** established
- World's First **allogeneic mitochondrial cryo-bank inventory** created

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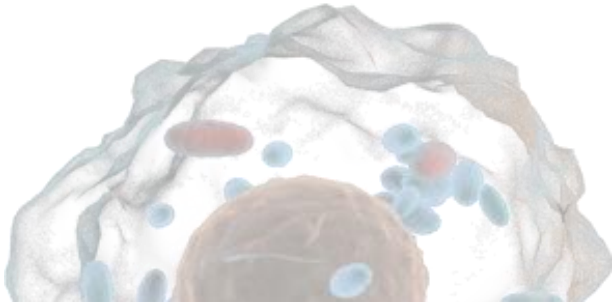

Thank You

Information contained herein does not purport to be complete and is subject to change. Actual performance may differ from the assumptions used in preparing these materials. Changes in assumptions may have a material impact on the information set forth in these materials.