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TME Lab
Tissue Microenvironment Lab

Normothermic Perfusion in Organ Preservation and Evaluation. Promising Future in Kidney Transplantation.

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INTRODUCTION

Kidney transplantation remains the best treatment for end-stage renal disease, but the number of people on the waiting list for a deceased donor kidney is stably high or growing, currently standing at ~10.500 patients in UE in 2024 [1]. To meet growing organ demands, using of grafts donated after circulatory death (DCD), or retrieved from extended criteria donors (ECD), is unavoidable. Unfortunately, DCD and ECD grafts are more immunogenic, which leads to difficulties in immune regulation after implantation and a higher risk of acute and chronic rejection. In response to these needs, the Normothermic Machine Perfusion (NMP) emerges as a tool that resolves these problems. Normothermic Machine Perfusion is an emerging preservation modality for kidneys prior to transplantation that maintains the organ at body temperature (35-37°C), in contrast to traditional cold storage methods. NMP circulates a warm perfusion solution through the renal vasculature, delivering oxygen and nutrients to maintain metabolic activity [2]. This restoration of function during preservation represents a significant advancement in transplantation science, as it allows clinicians to assess organ quality before transplantation and provides a platform for delivering pre-transplant therapies to promote recovery [3].

AR Video To Ilustrate Funcionality And Method Of Use

ADVANTAGE OF NMP OVER TRADITIONAL STORAGE

KEY FEATURE	STATIC COLD STORAGE (SCS)	NORMOTHERMIC MACHINE PERFUSION (NMP)	KEY INSIGHTS AND ADVANTAGES
Principle of Preservation	**Reduces metabolic rate** to a minimum by hypothermia, **halting cellular activity.**	Maintains **near-physiological conditions** (normothermia) with **continuous flow** of perfusate.	Similar **in-vivo environment**
Temperature	0-4°C **Hypothermic**	34 - 37 °C **Normothermic**	NMP allows for **active metabolic evaluation**.
Metabolic State of Organ	**Minimal or suppressed**	**Active and functional** (capable of oxygen consumption, ATP production, and waste removal).	Facilitates **ex vivo organ reconditioning**.
Assessment of Organ Viability	**Limited**	**Dynamic & Real-Time** (e.g., O2 consumption). Offers objective viability markers.	Offers **objective viability markers** and prognosis.
Duration of Preservation	**Limited,** typically 18-24 hours for kidneys; **longer durations increase risk of injury.**	**Potentially longer preservation times** (6 - 48 + hours). **Allows for more thorough evaluation.**	**Reduces ischemia-reperfusion injury**.
Therapeutic Interventions	**Not possible** during preservation.	**Allows during preservation**: • **Drugs administration** • **Cell therapy (MSC, MAPC)** • **Gene therapy (siRNA)** • **Biological therapy (αCD47ab)** • **Nanotechnologies**	Enables **organ optimization before transplantation**.
Organ Quality/Utilization	May exacerbate injury in marginal organs; **limits use of DCD** or expanded criteria donor **(ECD) kidneys**.	Can **potentially recondition and improve marginal organs**; **expands** the **pool of transplantable organs**, especially **DCD** and **ECD**.	Increases the **number of organs available for transplant**.
Complexity/Cost	**Low**	**High** (specialized equipment and personnel)	**Initial investment** often offset by **improved clinical outcomes**.

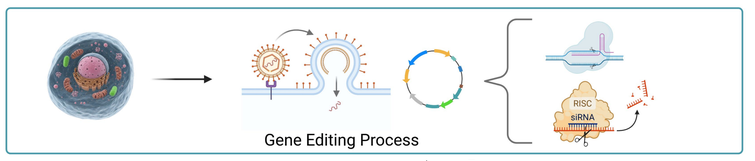
THERAPEUTICS INTERVENTIONS ON NMP AND RESULTS

TARGET MECHANISM/PATHWAY	ORGAN MODEL	MAIN FINDINGS
Mesenchymal Stromal Cell (**MSC**) **[4]**	Porcine kidneys	LDH NGAL **Regenerative Effect In Ischemia Reperfusion Injury**
Anti-CD31 Nanoparticles (**NP**) **[5]**	Non-transplantable human kidneys	**Anti-human CD31** (endothelium) Abs **NPs loaded** had **enhanced retention**
FpGalNAc deacetylase and **FpGalactosaminidase** through ***Flavonifractor plautii*** to enzymatically convert **donor blood antigen group A to Group O. [6]**	Non-transplantable human kidneys	**A antigen loss of aprox. 80% ~ 2h in NMP** (A → O)

OUR FUTURE APPROACH

Our approach, based on the background above context, will be to use the organ *ex vivo* maintenance machine in normothermia **ARK KIDNEY® of EBERS Medical Technology SL**. to perform **genetic modifications in kidneys**.

With the help of this machine will be able to **use gene editing tools such as RNAi or CRISPR-Cas9** using lentiviral vectors, depending on the desired intensity of modification, to try to **downregulate** the expression of the **Major Histocompatibility Complex** (MHC) and **increase compatibility** in kidneys that were **not previously compatible**.



CONCLUSIONS

- ❑ **Normothermic machine perfusion is a transformative technology that allows donor kidneys to function and be evaluated outside the body, improving graft viability prior to transplantation.**
- ❑ **This unique capability not only reduces complications such as delayed graft function (DGF), but also makes it possible to use kidneys previously considered marginal or unsuitable.**
- ❑ **NMP offers an innovative platform for research and development of new therapies, allowing for testing the efficacy of treatments or organ repair outside the body prior to transplantation.**
- ❑ **By providing a platform for real-time assessment and therapeutic interventions, NMP promises to expand the donor pool and optimize long-term outcomes for kidney transplant patients.**

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