Rejet de greffe d'organes solide et Photo-chimiothérapie ExtraCorporelle
Aspect physiopathologique: quoi de neuf ?

Société Française d'Hémaphérèse
29/01/2026

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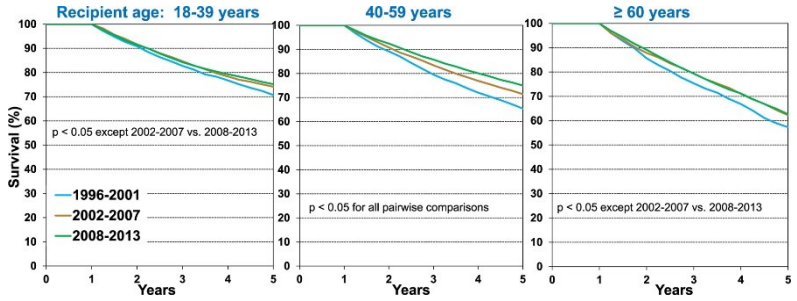
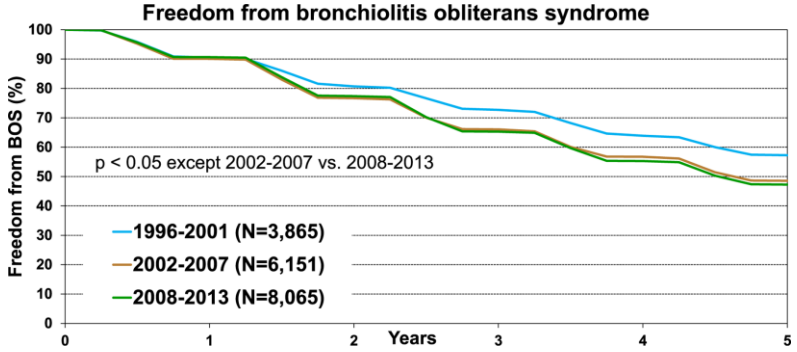
Conflits d’intérêts

- Société Therakos: Invitation au « *5° workshop on solid organ transplantation and photopheresis: clinical evidence and best practice ».* Monte Carlo-septembre 2022

CLAD/
BOS

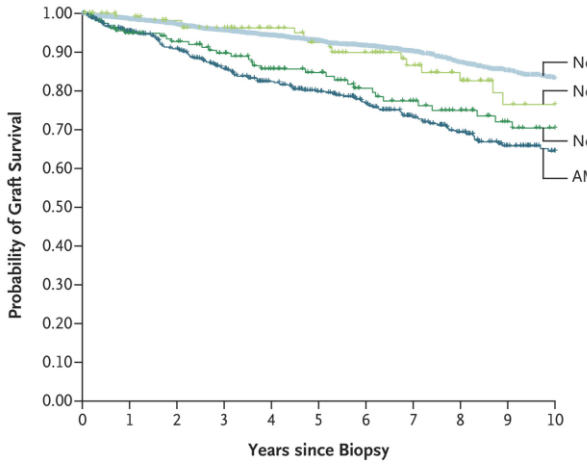




Chambers et al. J Heart Lung Transplant. 2021

Sablick et al. NEJM 2024

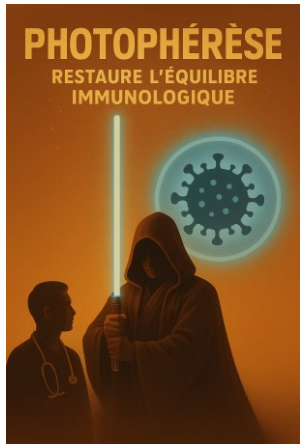
AMR/
MVI

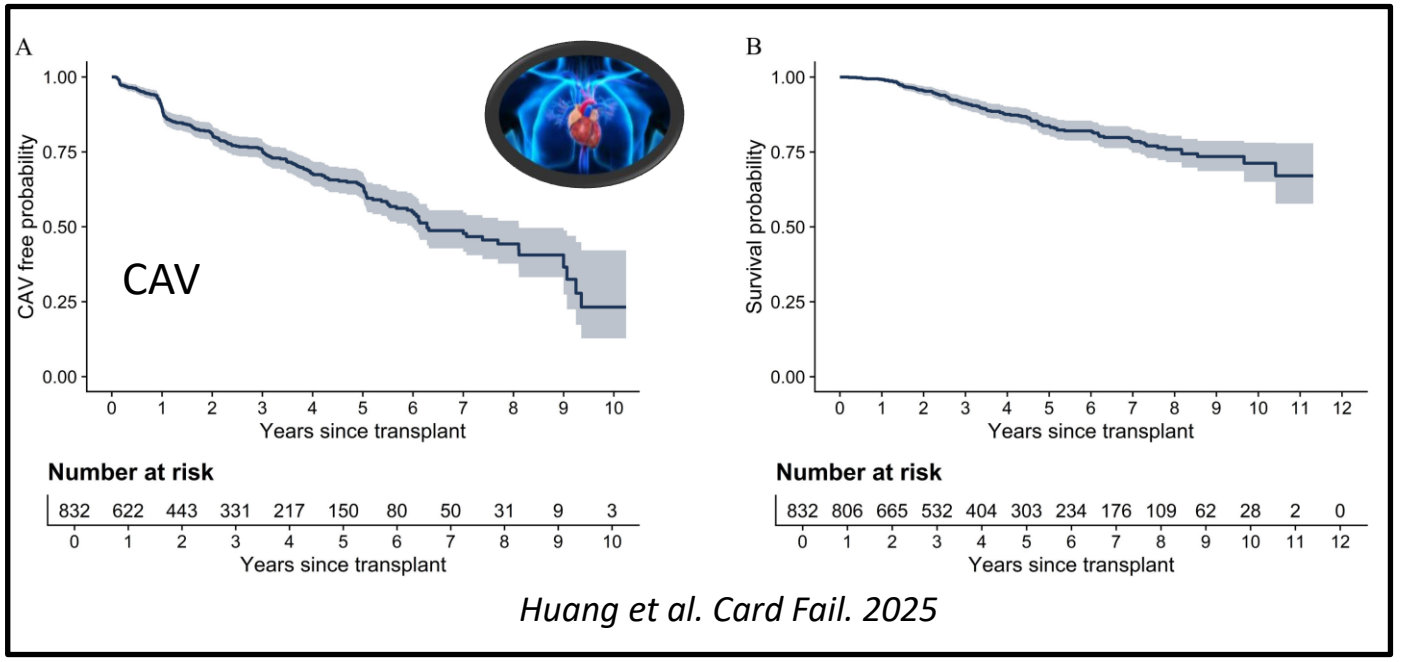


No. at Risk

Nonrejection; nonrejection	3604	3167	2893	2537	2145	1762	1466	1243	999	829	676
Nonrejection; probable AMR	122	110	101	93	80	72	63	50	39	25	23
Nonrejection; MVI DSA–C4d–	159	139	128	116	99	88	74	66	57	45	38
AMR; AMR	489	423	380	331	292	256	222	185	150	116	94

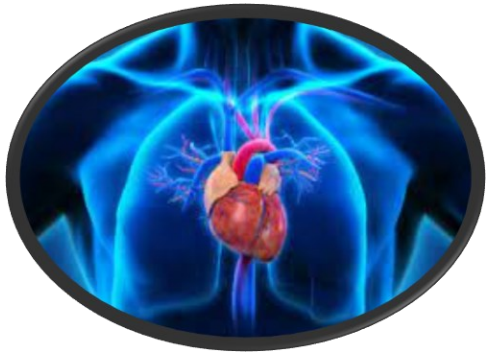
Nécessité d'améliorer le contrôle de l'allo-réactivité





Huang et al. Card Fail. 2025

Photophérèse: Pour qui / Pour quoi ?



Benazzo et al. Transplant Int 2023
Greer et al. J Herat Lung Transplant 2023

Barten et al. J Heart Lung Transplant 2023

Données cliniques / place dans la stratégie et recommandations des sociétés savantes:
CLAD/BOS/CAV
Stabilisation / Prolonge survie greffons/patient

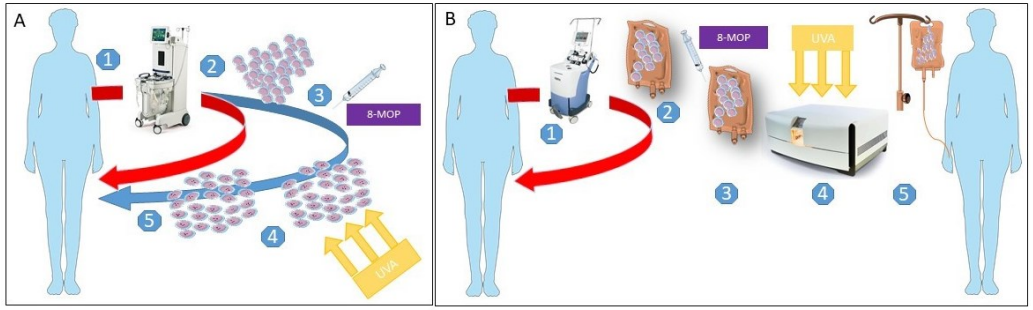
ISHLT 2010-2023

Retour d'expériences / pas d'études randomisées / Pas de recommandations des sociétés savantes

Barten et al. AJT 2024

Contrôle de l'allo-réactivité: prévention et traitement de rejet
Quels modes d'action ? Différences selon l'organe ?

Quelles techniques ?



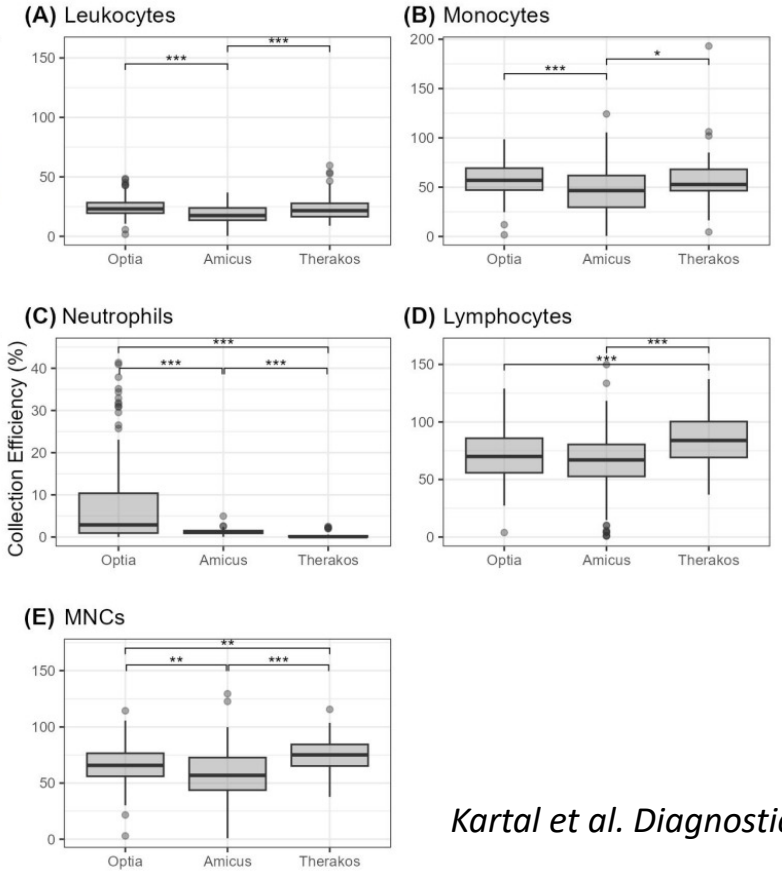
Crépin et al. Nephrol Therap 2023

A) Technique fermée « on line »

- Simple à réaliser
- Séances plus courtes

B) Technique ouverte « off line »

- Nécessite une réglementation spécifique
- Séances plus longues



Kartal et al. Diagnostics 2024

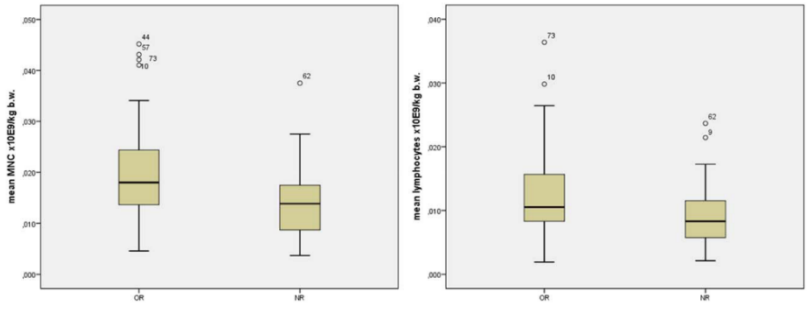
	Amicus	CELLEX	*p**	Median difference
Procedures (*n*)	40	40		
MCP volume (mL)	200 (200–200)	151 (137–159)	<.0001	−49
MCP cell blood counts				
WBCs (×10^9/L)	11.1 (8.2–15.4)	12.9 (8.1–19.2)	.13	0.89
Hct (%)	3 (2.3–4.3)	3 (2.6–3.8)	.60	0.20
Platelets (×10^9/L)	182 (84–308)	497 (294–804)	<.0001	282
Neutrophils (%)	7.2 (3.3–12.2)	16.1 (8.3–36.9)	<.0001	8.75
Lymphocytes (%)	55.2 (40.0–68.1)	48.1 (22.1–60.5)	<.0001	−8.3
Monocytes (%)	24.0 (17.4–29.4)	20.2 (16.5–25.1)	.38	−0.2
MNCs (%)	92.9 (87.8–96.7)	84.0 (63.1–91.7)	<.0001	−8.75
Absolute cell counts				
TNCs (×10^9)	2.25 (1.65–3.05)	1.90 (1.10–2.9)	.022	−0.35
MNCs (×10^9)	2.0 (1.20–2.95)	1.65 (0.87–2.4)	.002	−0.55
Neutrophils (×10^9)	0.16 (0.06–0.33)	0.33 (0.15–0.63)	.007	0.105
Platelets (×10^{11})	0.36 (0.17–0.62)	0.84 (0.40–1.21)	<.0001	0.28
Collection efficiency				
TNCs CE2%	25.9 (15.9–40.8)	28.5 (21.4–33.6)	.93	−0.69
MNCs CE2%	72.13 (50.9–92)	60.0 (52.7–71.8)	.067	−7.9
Neutrophils CE2%	2.5 (1.2–6.4)	7.6 (4.1–13.5)	<.0001	3.54
Platelets CE2%	12.5 (7.5–23.3)	35.1 (26.4–47.1)	<.0001	18.5
Absolute cell counts normalized according to processed blood volume				
TNCs (×10^6/L processed blood volume)	1.1 (0.81–1.51)	1.19 (0.69–1.85)	.44	0.12
MNCs (×10^6/L processed blood volume)	0.99 (0.59–1.46)	1.06 (0.55–1.55)	.23	−0.11
Neutrophils (×10^6/L processed blood volume)	0.078 (0.03–0.16)	0.21 (0.10–0.40)	<.0001	0.08
Platelets (×10^9/L processed blood volume)	18 (8–31)	53 (26–77)	<.0001	0.23

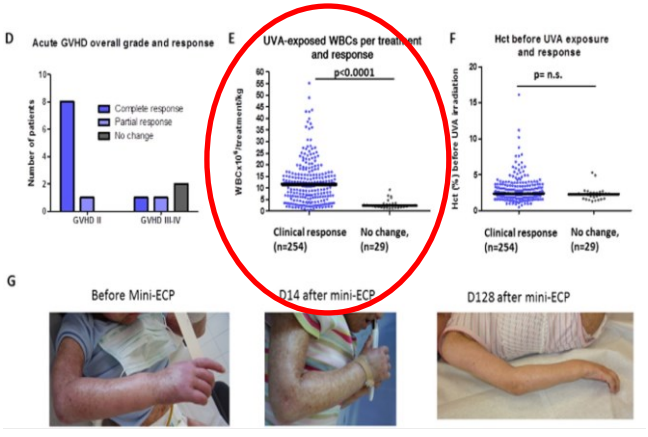
Piccirillo et al. Transfusion 2025

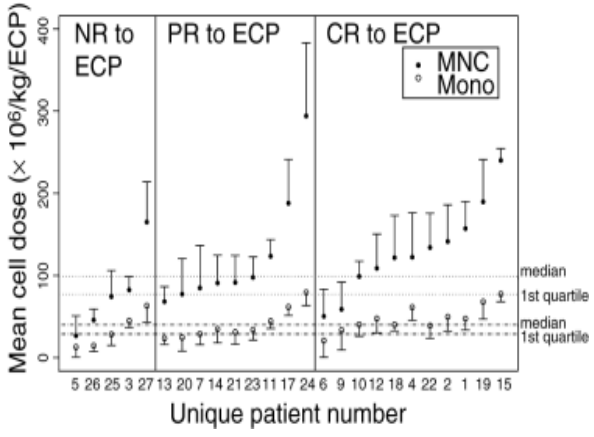
Des produits de cellulaires différents mais une efficacité équivalente ?

Objectif unique:
Réinjection de leucocytes apoptotiques autologues

Quelle dose de cellules ?







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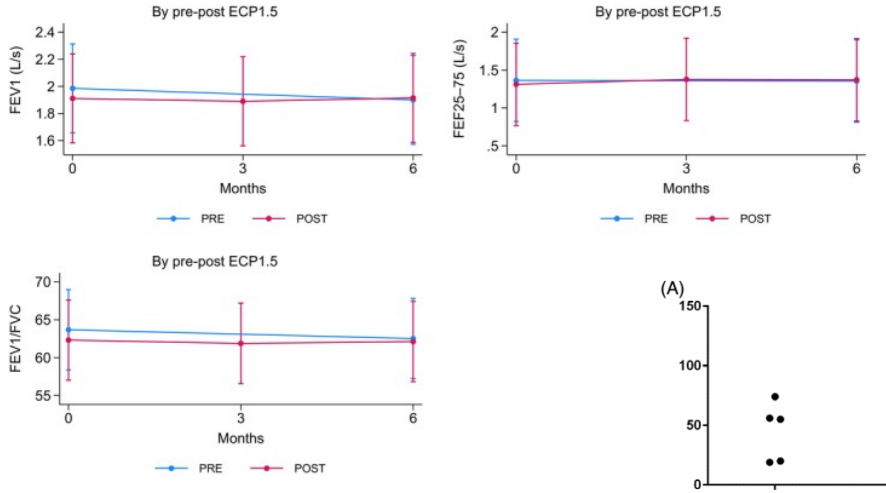
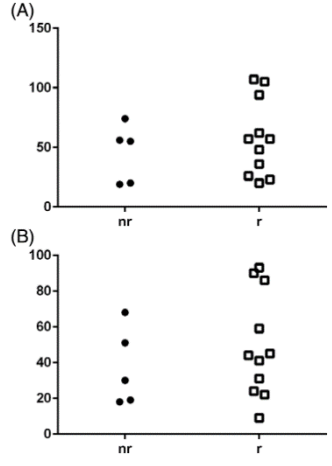




Effet dose :

Perseghin et al. Ther Apher Dial. 2007
Worel et al. Transfusion. 2018
Hackstein et al. Transfusion. 2014

VS.

Pas d'effet dose:

Perotti et al.Transfusion 2010
Berger M. et al.Transfusion 2015
Piccirillo n. et al. J Clin Apher 2021
Del Fante et al. Transfusion 2025

Rôle d'un effet dose des leucocytes irradiés ré-injectés ?

Quelle fréquence/dose de traitement ?

TABLE 5. Studies treating patients with one ECP procedure

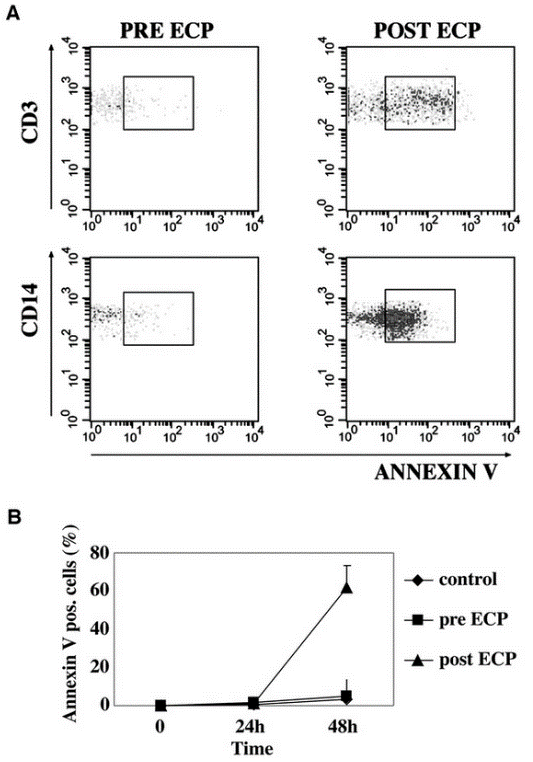
Year	First author	Patients	ECP procedure	ECP schedule
2005	Garban[24]	Acute and chronic GVHD	Offline	6 treatments during the first 3 weeks; 1 per week until CR.
2006	Bisaccia[25]	Chronic GVHD	Inline	3 treatments per week; 2 per week; 1 per week; 1 every 2 weeks (decrease depending upon patient response).
2006	Couriel[26]	Chronic GVHD	Inline	2-4 treatments per week; 1 per week when PR; 2 every 2 weeks as maintenance.
2012	Tsirigotis[27]	Chronic GVHD	Inline	2 treatments per week for 4 weeks; 1 per 1-2 weeks afterwards (according to clinical response).
2016	Kitko[28]	GVHD prophylaxis	Inline	1 treatment per week for 7 weeks; 1 every 2 weeks; 1 every month (in total 11-12 treatments).
2018	Iniesta[29]	Acute and chronic GVHD	Offline	Acute GVHD: 1 treatment per week (2 per week for Grades III-IV acute GVHD) for 6 weeks; chronic GVHD—1 every 2 weeks for 6 weeks; 1 per month until maximal response.
2018	Michallet[30]	GVHD prophylaxis	Inline	2 treatments per week for 2 weeks; 1 per week for 4 weeks.S
2018	Richet[31]	Chronic GVHD	Inline	1 treatment per week (3 patients for logistic reasons).
2018	Sakellari[32]	Acute and chronic GVHD	Inline	Acute GVHD—2 treatments per week for 1 month; 1 every 2 weeks for 3 months; 1 per month for 6 months. Chronic GVHD—1 treatment per week for 1 month; 1 every 2 weeks for 3 months; 1 per month for 6 months.

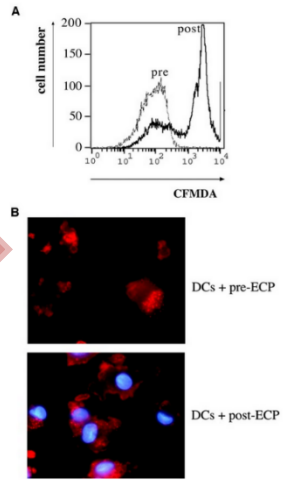
Cid J. et al. Transfusion. 2019

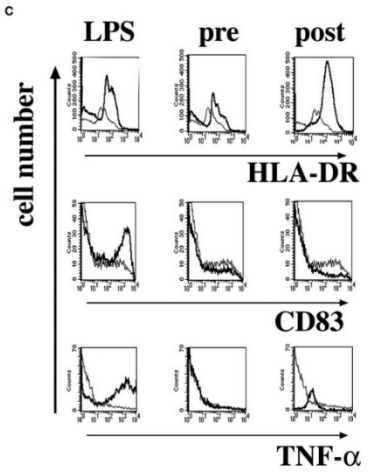
Manque d'études sur comment utiliser/prescrire au mieux la technique :
Impact sur le mode d'action ?

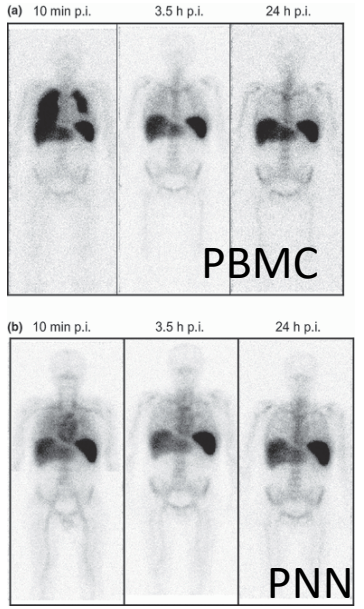
Rythme : effet centre / empirisme
Consensus : phase d'attaque puis phase d'entretien puis sevrage ?

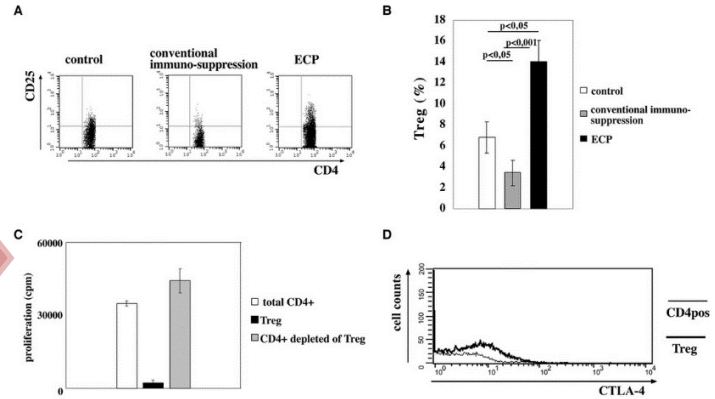
Quel mode d'action *in vitro-in vivo* ?











Lamioni A. et al. Transplantation 2005

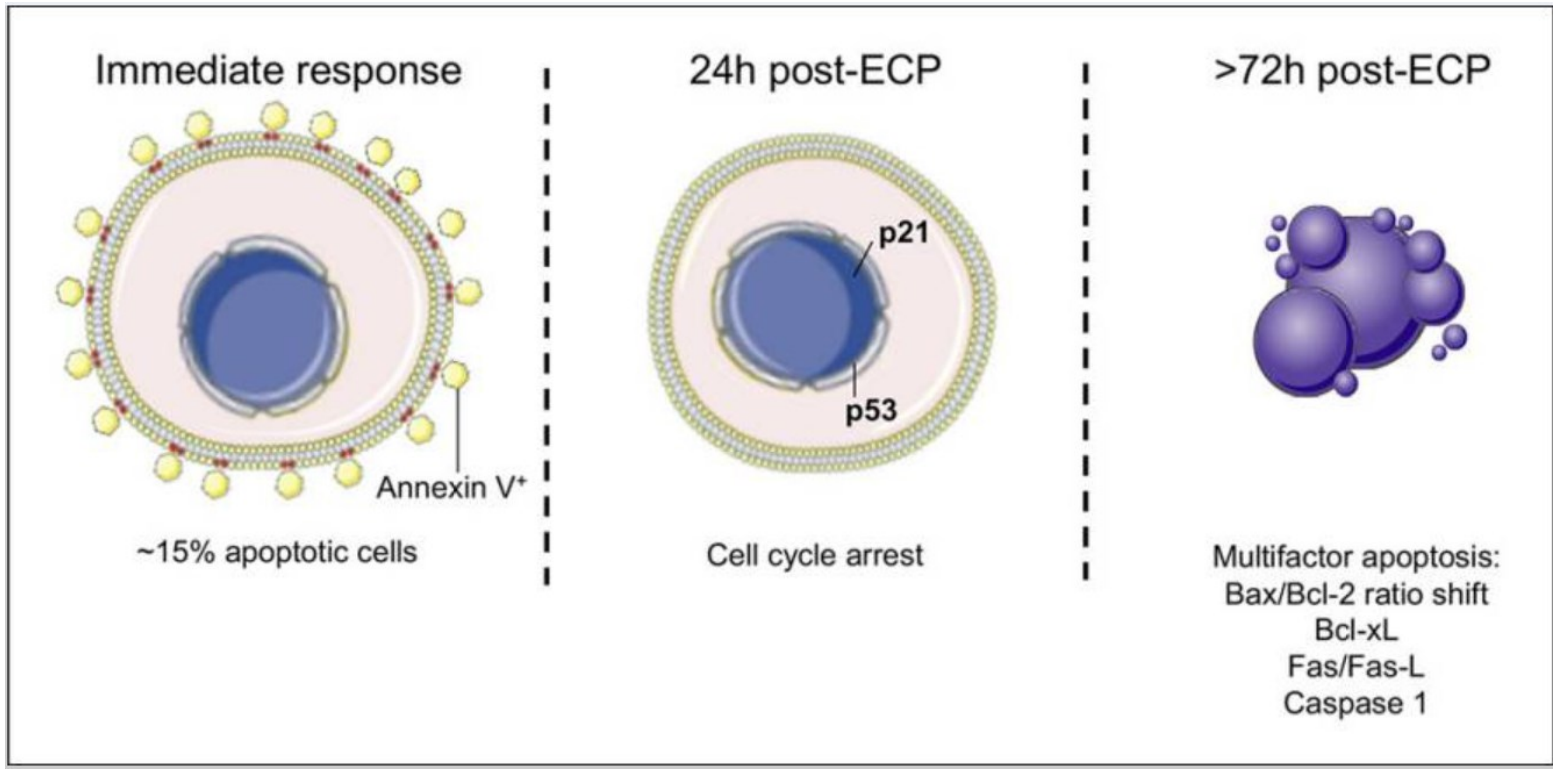
Just U. et al. Exp dermatol 2012

1 Apoptose à 48h

2 Phagocytose des cellules apoptotiques par DC tolérogènes foie/rate/poumon

3 Expansion de Treg *in vivo*

Quel mode d'action *in vitro* ?



Lymphocytes activés
LT CD4/CD8

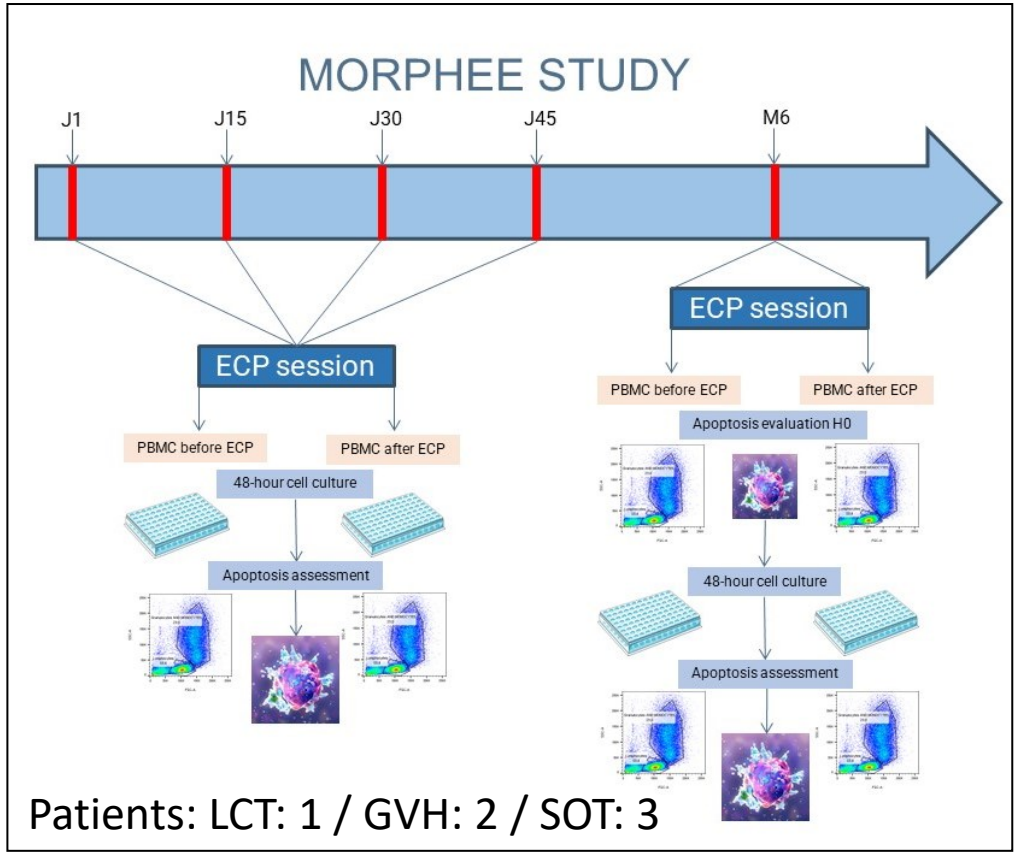
LT CD4/CD8
LB
NK

Treg
Monocyte
NK

Budde H et al. Cent Euro J Immunol 2017
Vieyra-Garcia P-A et al. Transf Med Hemoth 2020

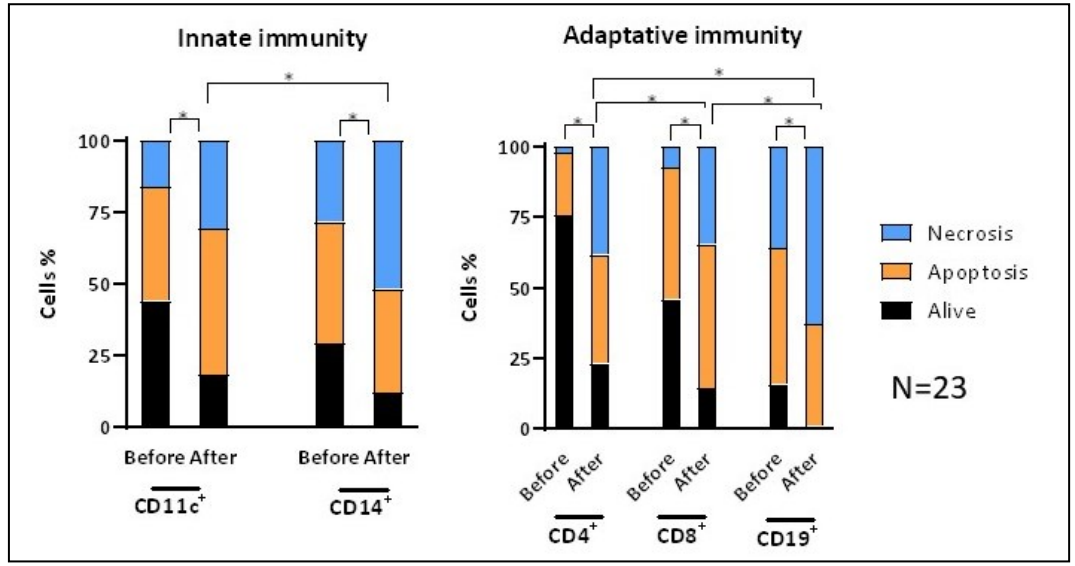
Apoptose *in vitro :* variable dans le temps et selon le type cellulaire

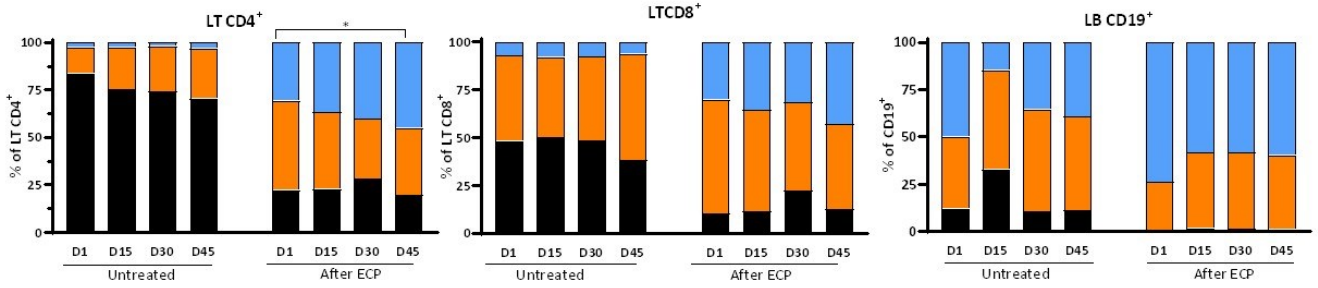
Quel mode d'action *in vitro-in vivo* ?

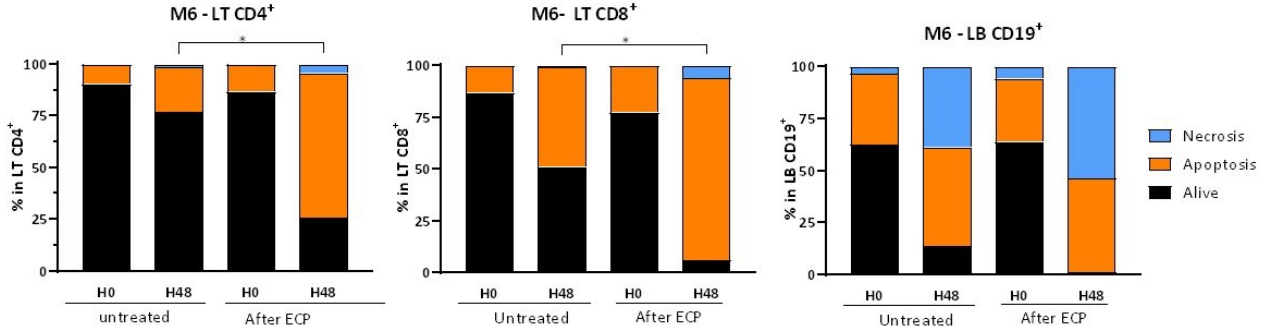


Patients: LCT: 1 / GVH: 2 / SOT: 3

Autres marqueurs cellulaire (NK) ?
Autre techniques ?
Patient plus homogènes



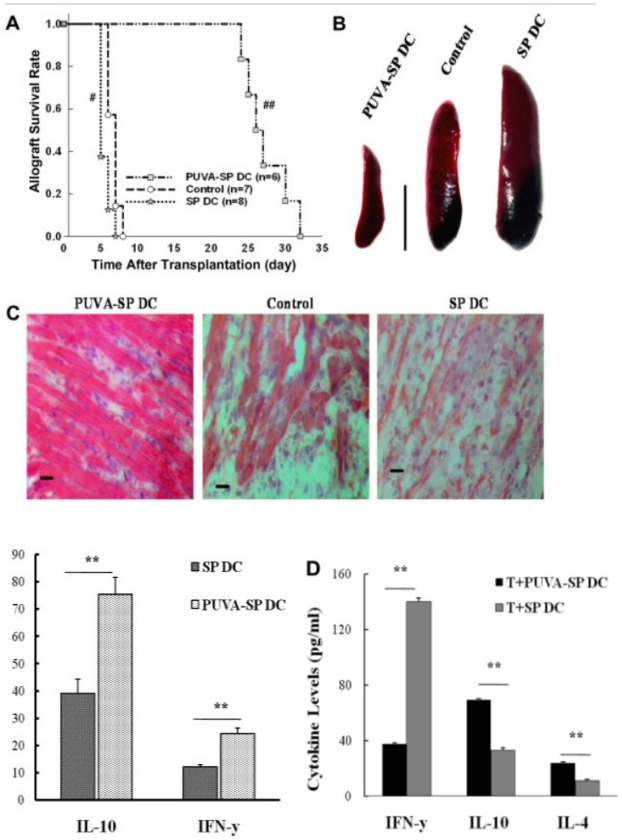


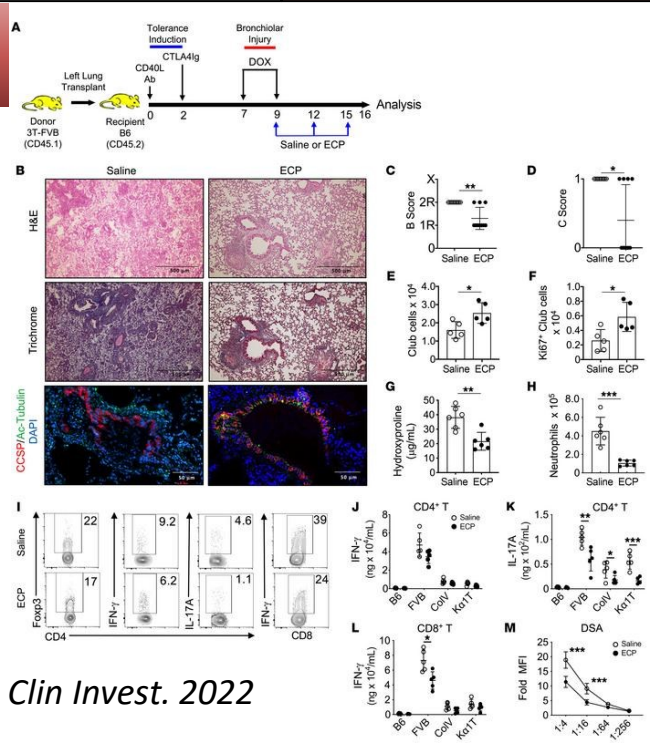


(Unpublished data)

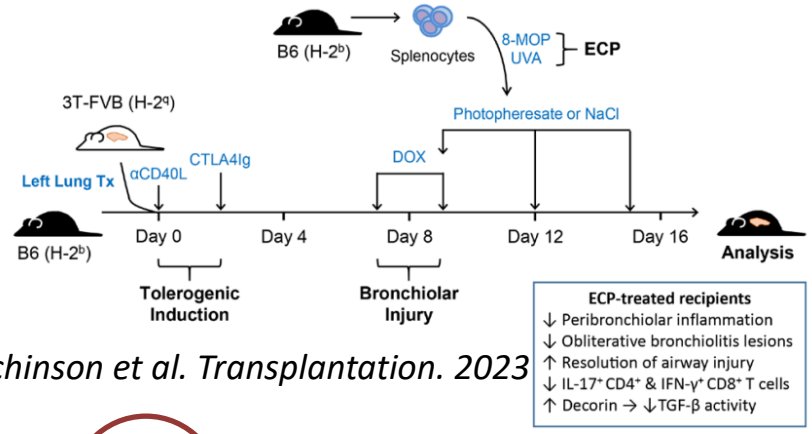
Quel apport des modèles animaux ?

Zheng et al. Biochem Biophys Res Commun. 2010



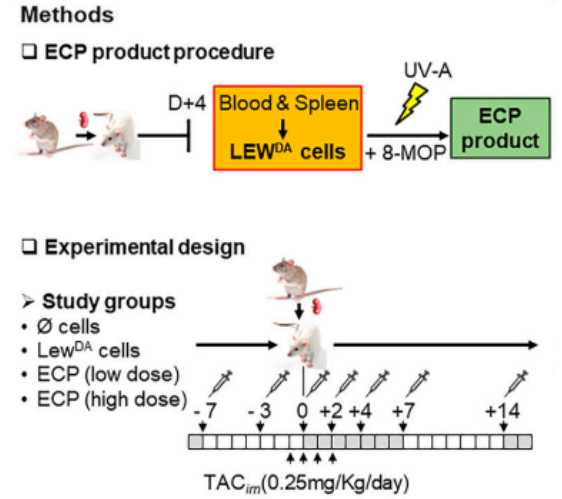


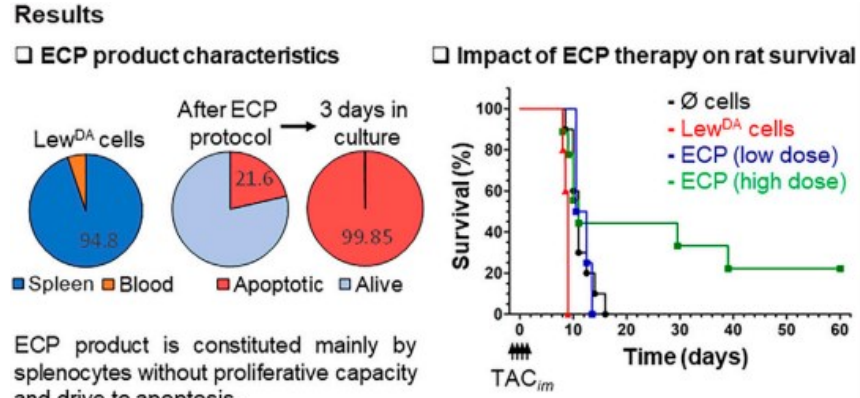
Liu et al. J Clin Invest. 2022



ECP-treated recipients
- ↓ Peribronchiolar inflammation
- ↓ Obliterative bronchiolitis lesions
- ↑ Resolution of airway injury
- ↓ IL-17⁺CD4⁺ & IFN-γ⁺CD8⁺ T cells
- ↑ Decorin → ↓TGF-β activity

Hutchinson et al. Transplantation. 2023





Pineiro et al. Transplant Int. 2023

1 Coeur

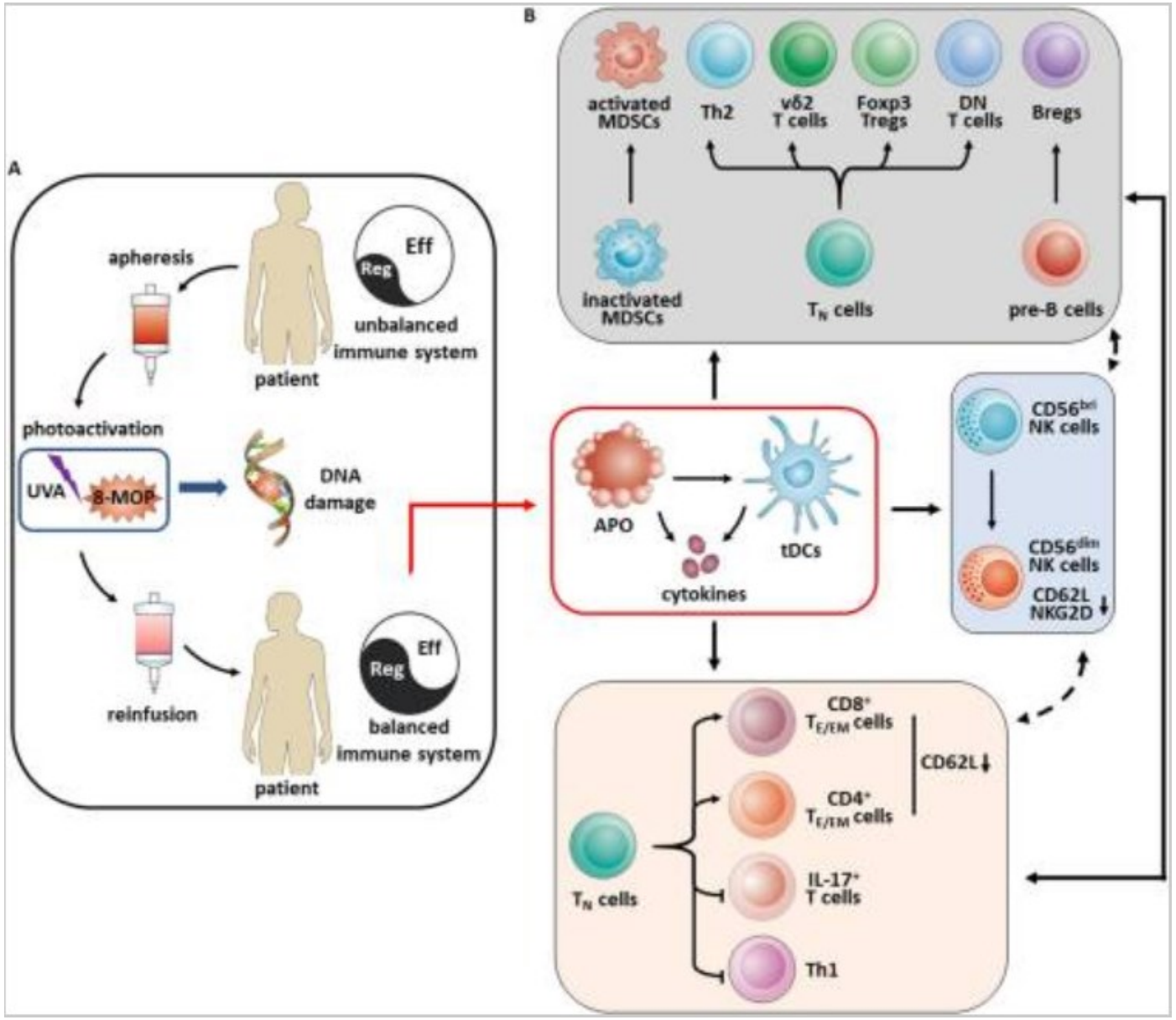
2 Poumon

3 Rein

Action multi-cellulaires ?

++ Données en GVH ++

Quid en transplantation d'organes solides ?



Wang L. et al. Front Immunol. 2018

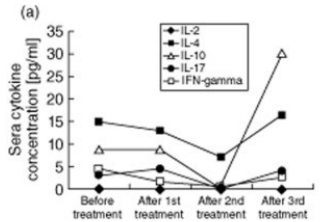
Action multi-cellulaire ?

1 Cœur

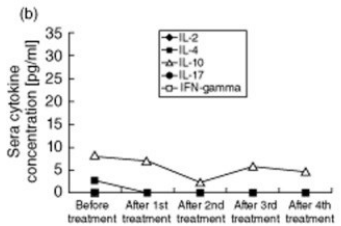
Dieterlen et al. Clin Exp Immunol 2014

- Observationnelle n=9/9
- Prévention/traitement du rejet

- ↗ des Treg
- Modulation DC selon l'indication
- DC tolerogène (PDL-1 $^{+}$)



	Cumulative value Th1	Cumulative value Th2	Th17 value
Before treatment	4·53	23·89	3·01
After 1st treatment	1·67	21·71	4·75
After 2nd treatment	0·49	7·00	0·00
After 3rd treatment	2·70	46·55	4·15

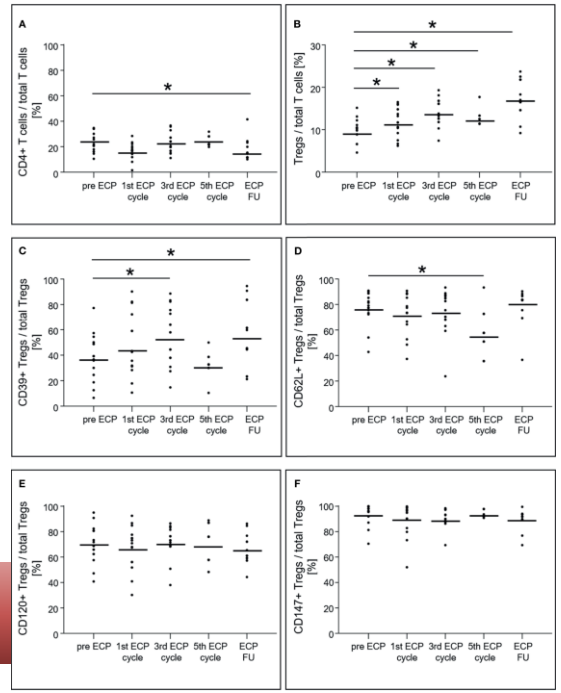


	Cumulative value Th1	Cumulative value Th2	Th17 value
Before treatment	0·00	10·86	0·00
After 1st treatment	0·00	6·98	0·00
After 2nd treatment	0·00	2·13	0·00
After 3rd treatment	0·00	5·87	0·00
After 4th treatment	0·00	4·62	0·00

Dieterlen et al. Font immunol 2021

- Observationnelle n=17
- Prévention du rejet

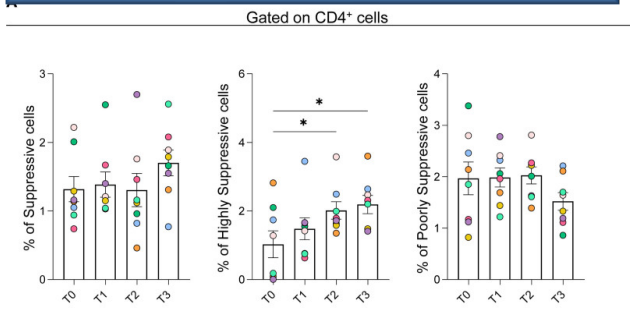
- ↗ des Treg effecteur et résistant à l'apoptose
- Augmentation transitoire des pDC

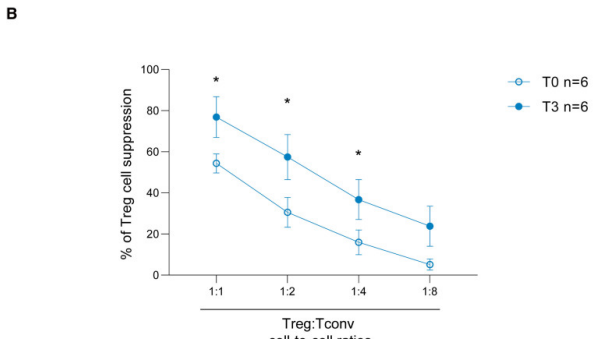


Mottola et al. Transplantation 2025

- Observationnelle n=8
- Prévention du rejet

- ↗ des Treg dont analyse fonctionnelle

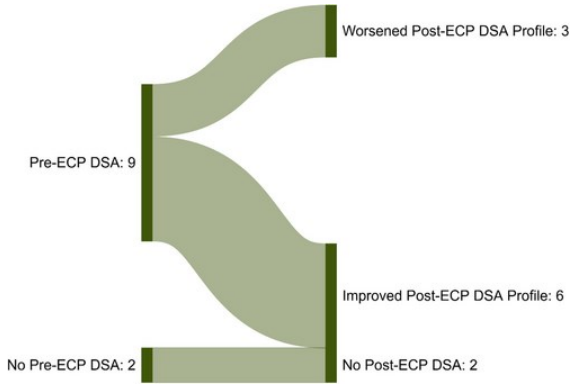




Rubinstein et al. Clin Transplant 2025

- Observationnelle n=12
- Traitement du rejet
- 93% de réponse

- ↘ DSA 66%
- ↘ dd-cdDNA



Action multi-cellulaire ?

Baskaran et al. J Heart Lung Transplant 2015

- Observationnelle n= 88
- Traitement du rejet
- VEMS amélioration

- ↘ DSA
- ↗IL 4 et IL 10
- ↘ Cytokines inflammatoires
- Effet sur LB ? Coopération T-B ?

Benazzo et al. transfu Med Hemother 2020

- Observationnelle n= 41
- Traitement du rejet
- Autre thérapie

- ↘ DSA
- Effet sur LB ? Coopération T-B ?

Righi et al. Front Immunol 2025

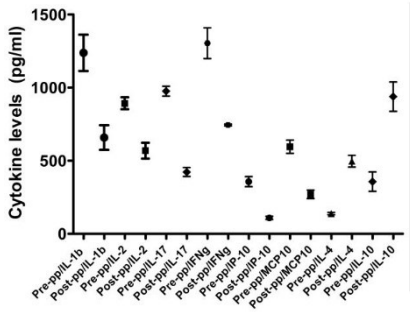
- Randomisée n= 9/12
- Prévention du rejet
- Corrélation immuno/VEMS

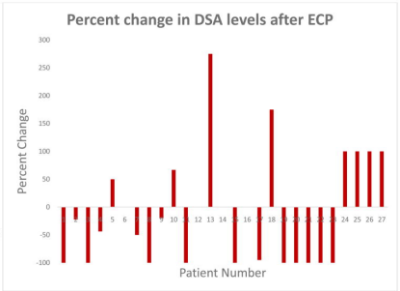
- ↗ des Treg et ↗ PD-1/PD-L1
- ↘ Polarisation Th1-Th17
- ↘ LT CD8 CTL
- ↗ L NK reg (IL10+)

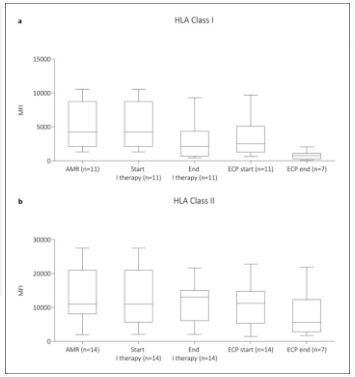
Benazzo et al. Eur Respir J 2025

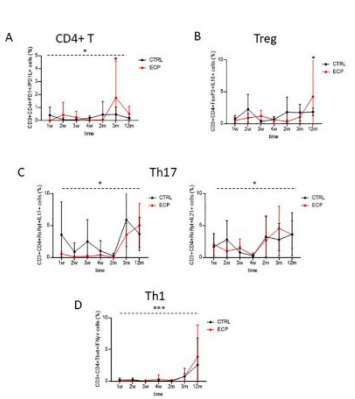
- Randomisée 31/31
- Prévention du rejet
- Moins de rejet
- Moins d'infection
- Meilleure survie

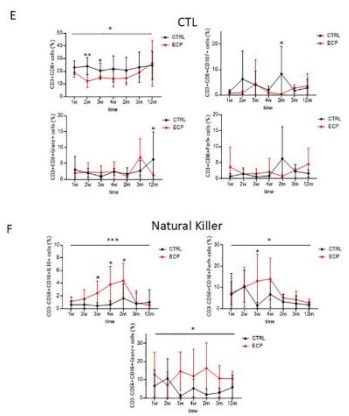
- Pas d'effet sur sous population lymphocytaire

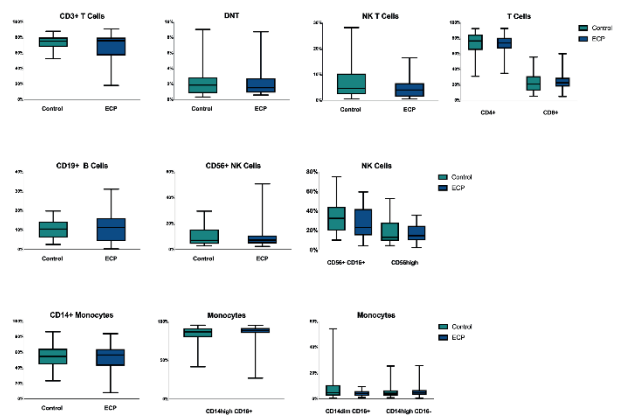












1 Cœur

2 Poumon

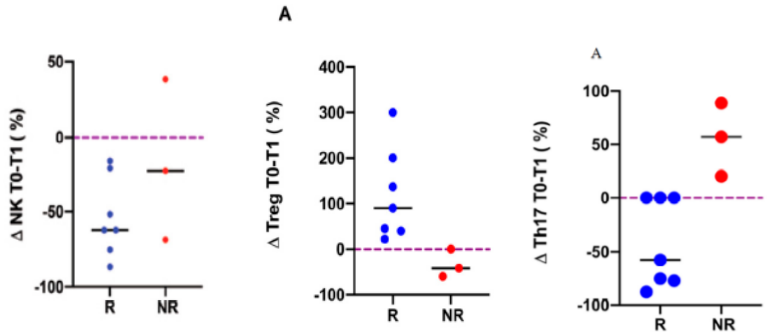
Action multi-cellulaire ?

Gregorini M. et al. Biology 2021

- Observationnelle n= 11
- Traitement ABMR
- 72% de répondeurs

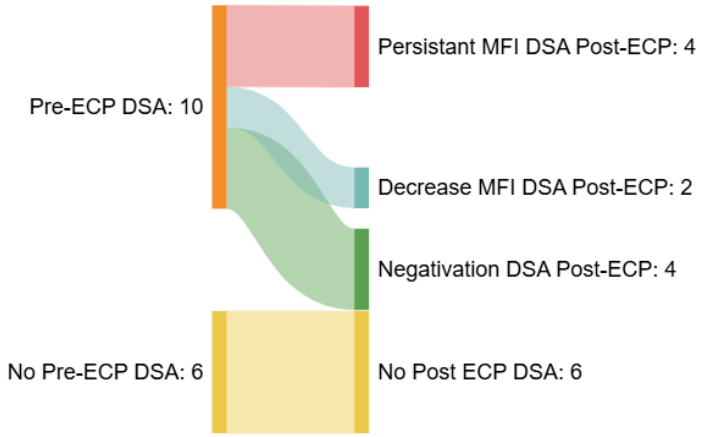
- ↗ des Treg
- ↘ Polarisation Th17
- ↘ L NK
- ↘ IL-6
- ↘ MFI DSA
- Négativation DSA >60%

ID Patient	DSA	Anti-HLA-Ab	DSA (MFI) Baseline	DSA (MFI) 1Y	DSA (MFI) 2Y	DSA (MFI) 3Y
# 1	DQ7		36,780	31,500	18,330	26,000
	DQA1		21,811	18,800	13,750	18,000
# 2	DQ4		12,000	4890	Neg	Neg
	DQ4		6800	3800	Neg	Neg
	DQ6		3900	1700	Neg	Neg
# 3		CW7	3000	Neg	Neg	Neg
# 4	B47		2197	Neg	Neg	
# 5	DQ5		5474	5000	Neg	
	DQA		3045	Neg	Neg	
# 6	DQ61		15,800	Neg	Neg	
	DQ62		4000	Neg	Neg	
	DQ53		19,120	Neg	Neg	
	DQ64		3785	Neg	Neg	
	DQ69		14,000	Neg	Neg	
# 7	DQ7		47,000	27,000		
# 8	DR11		4000	Neg	Neg	Neg
	DR15		1500	Neg	Neg	Neg



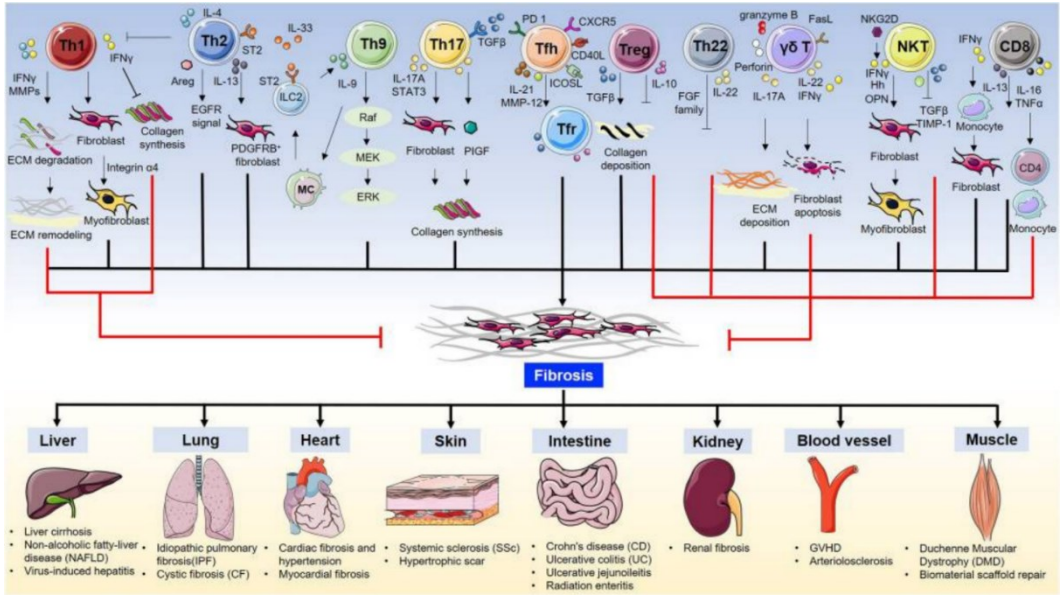
Unpublished personal data

- Observationnelle n= 16
- Traitement ABMR/MVI
- ↘ MFI DSA



(Unpublished data)

Action anti-fibrotique ?



Zhang et al. Front Immunol 2020

Extracorporeal photopheresis reduces fibrotic and inflammatory transcriptomic biological marker of chronic antibody-mediated kidney rejection

8 kidney transplants recipients with biopsy-proven cABMR

treated by extracorporeal Photopherisis (ECP)

With a control biopsie after 3 months of treatment

Study of the mRNAs of graft biospies using nanostring technology (B-HOT panel)

Comparaison before-after treatment

Volcano plot before-after treatment

CD19
IL21
PAX5
SFTPA2

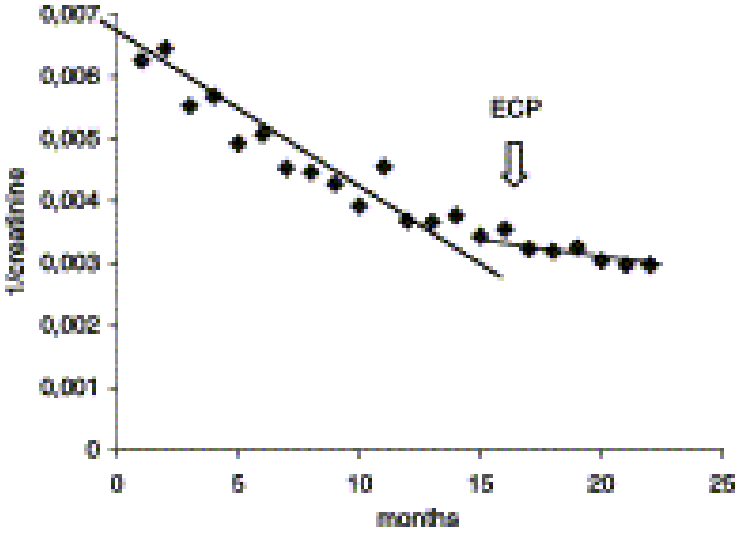
Cav1

Conclusion : Omic analysis of biopsies shows a reduction in fibrotic and inflammatory transcriptomic biomarkers after photopheresis treatment.

Author et al. *Transplantation Direct*. Month Year
@TXPDirect

Transplantation DIRECT

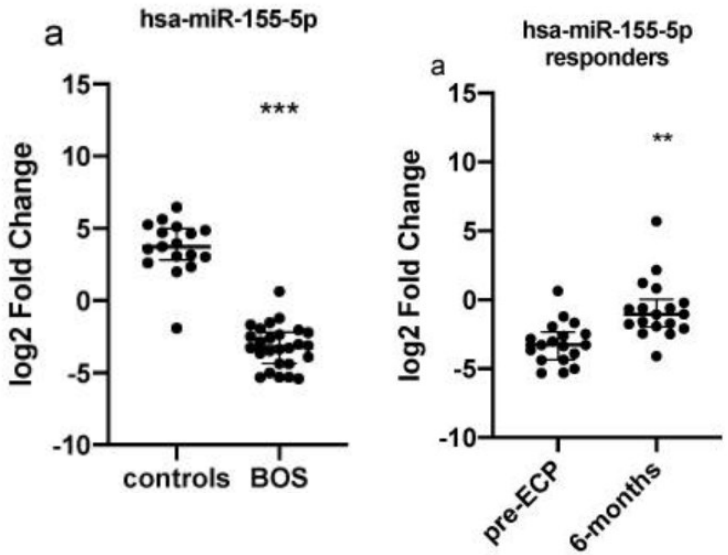
Lionet A. et al. Transplant Direct. 2024



Dall' Amico R. et al. JASN. 1998

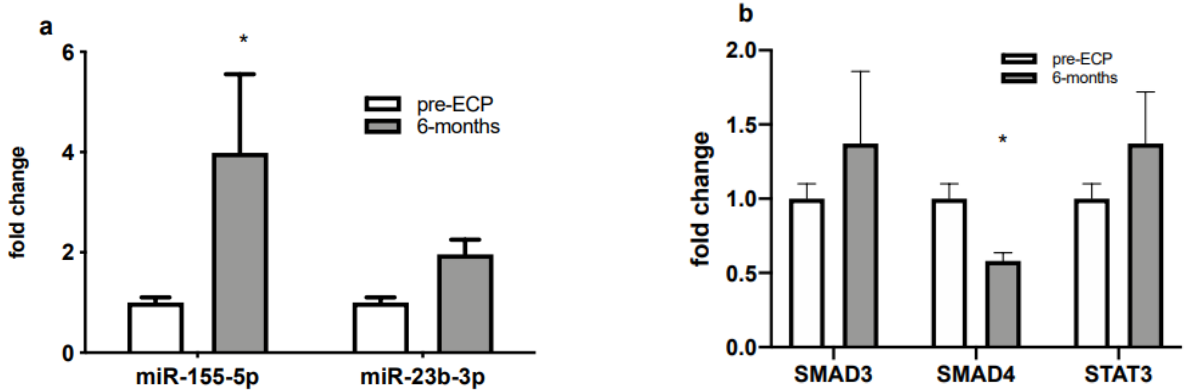
- ↘ de la pente de dégradation de la fonction rénale
- 6 PBR de contrôle :
  - ↘ infiltration lymphocytaire
  - ↘ HLA-DR,
  - ↘ TGFβ1
  - ↘ marqueur de fibrose

Action anti-fibrotique des microARN?



26 transplantés pulmonaires avec BOS
70% de répondeurs
Diminution des microARN avec le rejet

Bozzini S. et al. Cells 2022

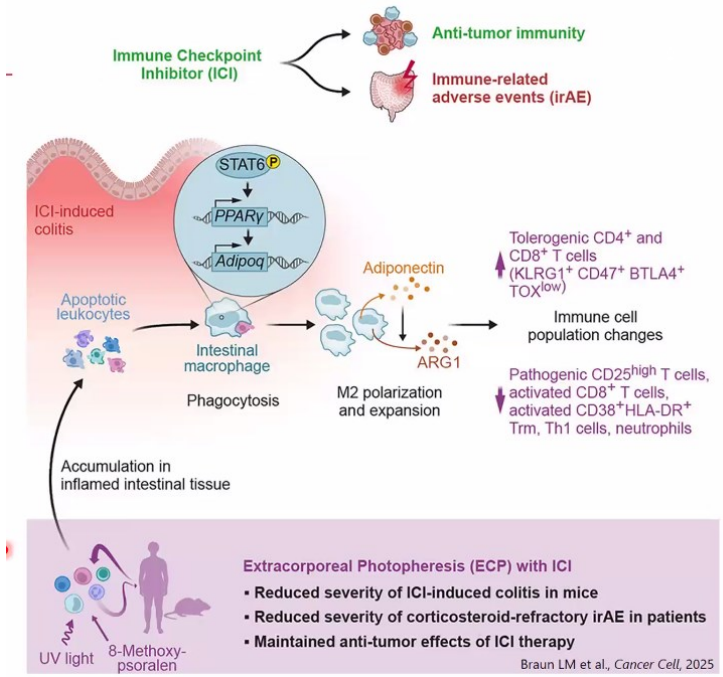


Augmentation de microARN après la PEC
Correlation avec voie smad4 (anti-fibrosante)

Rôle des microARN dans la PEC: immunité-fibrose?
Modulation des microARN circulant / tissulaire ?
Modulation des microARN pro/anti fibrosant ?

Action anti-fibrotique: Piste de l'adiponectine ?

↗ Adiponectine par la PEC ?



Braun et al. Cancer cell. 2025

↗ Adiponectine

contrôle du rejet

Am J Respir Crit Care Med. 2011 Nov 1;184(9):1055–1061. doi: 10.1164/rccm.201104-0728OC

Obesity and Primary Graft Dysfunction after Lung Transplantation

The Lung Transplant Outcomes Group Obesity Study

David J Lederer [1,✉], Steven M Kawut [2,3,4], Nancy Wickersham [5], Christopher Winterbottom [1], Sangeeta Bhorade [6], Scott M Palmer [7], James Lee [2], Joshua M Diamond [2], Keith M Wille [8], Ann Weinacker [9], Vibha N Lama [10], Maria Crespo [11], Jonathan B Orens [12], Joshua R Sonett [13], Selim M Arcasoy [1], Lorraine B Ware [5], Jason D Christie [2,4], for the Lung Transplant Outcomes Group

Front Med (Lausanne). 2023 Feb 17:10:1117819. doi: 10.3389/fmed.2023.1117819. eCollection 2023.

Adiponectin/leptin ratio as a predictor of acute rejection in early post-transplant period in patients after kidney transplantation

Karol Graňák [1,2], Matej Vnučák [1,2], Monika Beliančinová [1,2], Patrícia Kleinová [1,2], Margaréta Pytliaková [3], Marián Mokáň [2], Ivana Dedinská [1,2]

Transplantation. 2009 Oct 15;88(7):879-83. doi: 10.1097/TP.0b013e3181b6efbf.

Adiponectin inhibits allograft rejection in murine cardiac transplantation

Yoshihisa Okamoto [1], Thomas Christen, Koichi Shimizu, Kenichi Asano, Shinji Kihara, Richard N Mitchell, Peter Libby

moins de fibrose

PLoS One. 2015 May 6;10(5):e0125169. doi: 10.1371/journal.pone.0125169. eCollection 2015.

Adiponectin attenuates lung fibroblasts activation and pulmonary fibrosis induced by paraquat

Rong Yao [1], Yu Cao [1], Ya-rong He [1], Wayne Bond Lau [2], Zhi Zeng [1], Zong-an Liang [3]

Affiliations + expand

PMID: 25945502 PMCID: PMC4422712 DOI: 10.1371/journal.pone.0125169

Adiponectin protects against angiotensin II-induced cardiac **fibrosis** through activation of PPAR-alpha.

Fujita K, Maeda N, Sonoda M, Ohashi K, Hibuse T, Nishizawa H, Nishida M, Hiuge A, Kurata A, Kihara S, Shimomura I, Funahashi T.

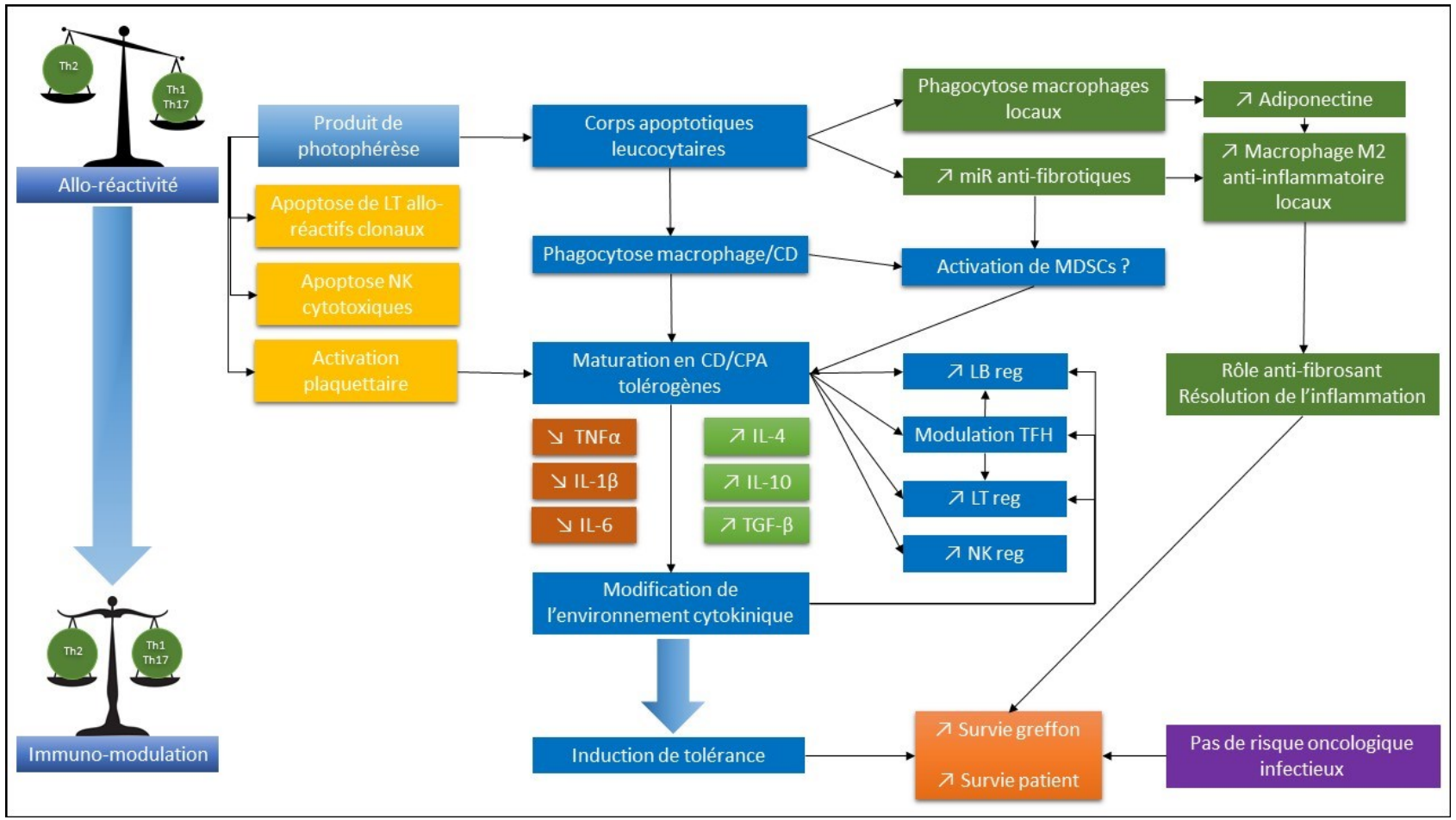
Arterioscler Thromb Vasc Biol. 2008 May;28(5):863-70. doi: 10.1161/ATVBAHA.107.156687. Epub 2008 Feb 28.

PMID: 18309113

Review Nephrology (Carlton). 2021 Feb;26(2):197-203. doi: 10.1111/nep.13808. Epub 2020 Oct 28.

Advances in understanding the role of adiponectin in renal fibrosis

Dan Zhao [1], Xiaoyu Zhu [1], Lili Jiang [1], Xiu Huang [1], Yangyang Zhang [1], Xuejiao Wei [1], Xiaoxia Zhao [1], Yujun Du [1]



Revisited , Crépin T. et al. Nephrol Therap 2023

Hypothèses des mécanismes d'action en transplantation d'organe solide 2026

Plus de questions que de réponses

Nécessité d'avancer

De la preuve de concept,… à la preuve scientifique!

⇒Etudes mécanistique en transplantations d'organes solides

⇒Marqueurs prédictifs de réponse clinique

=> Etudes cliniques randomisées

Merci de votre attention

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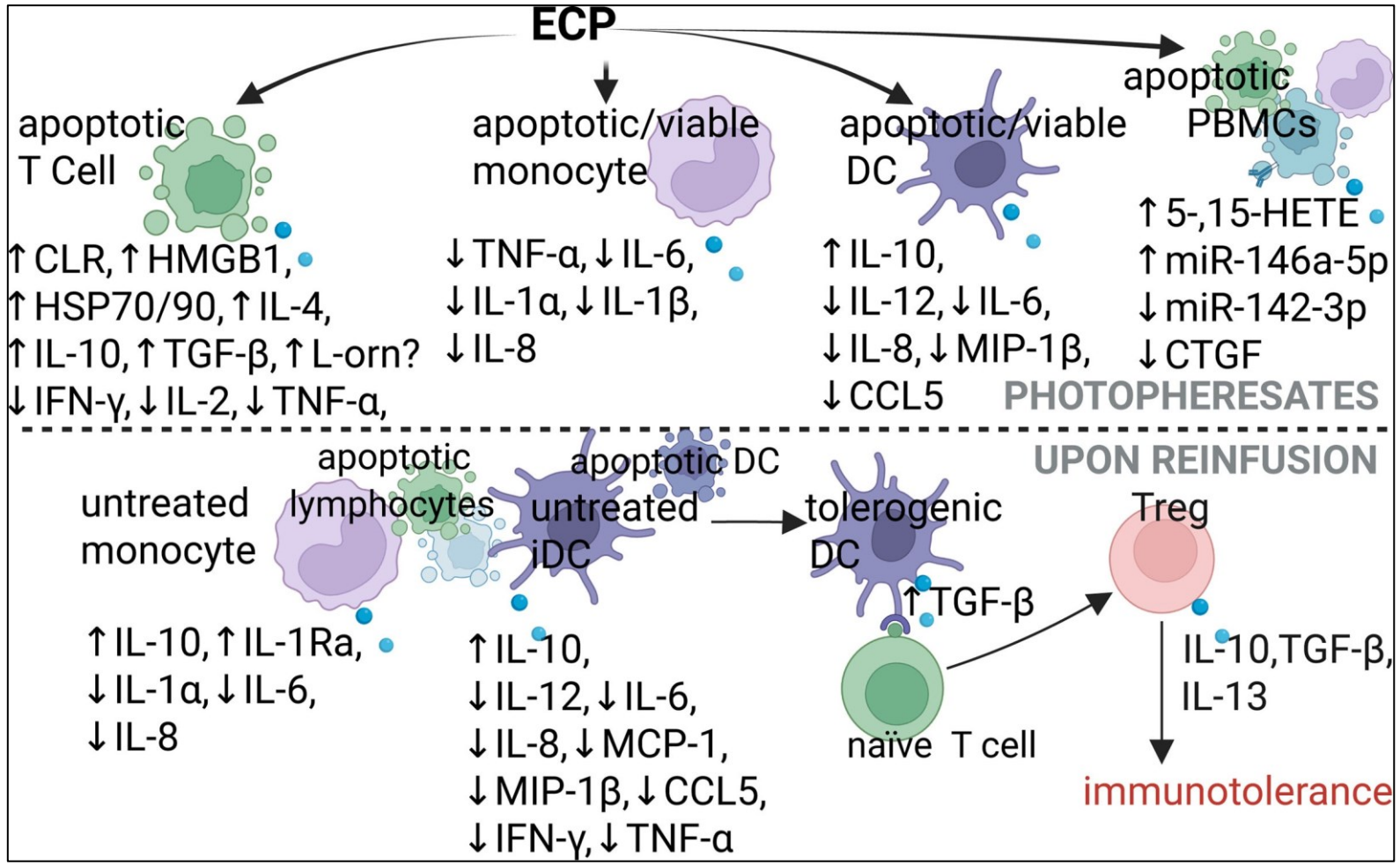

Garcia-Almeida et al. Transplant direct 2025