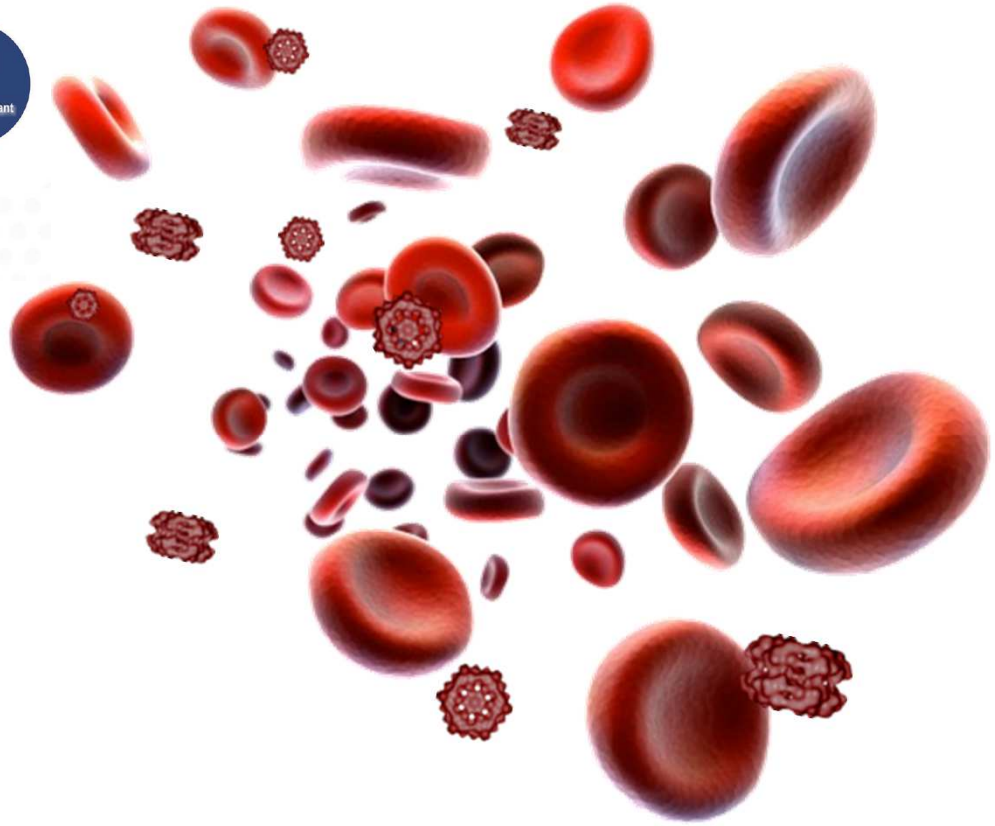
30ÈME CONGRÈS
OUEST TRANSPLANT



$HEMO_2life$® : une rupture technologique pour la préservation des greffons

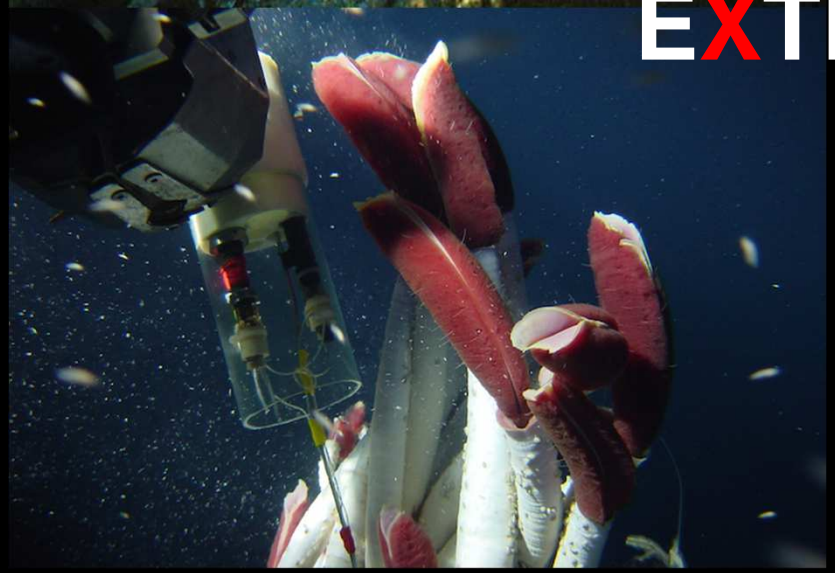
HEMARINA
Committed to saving lives

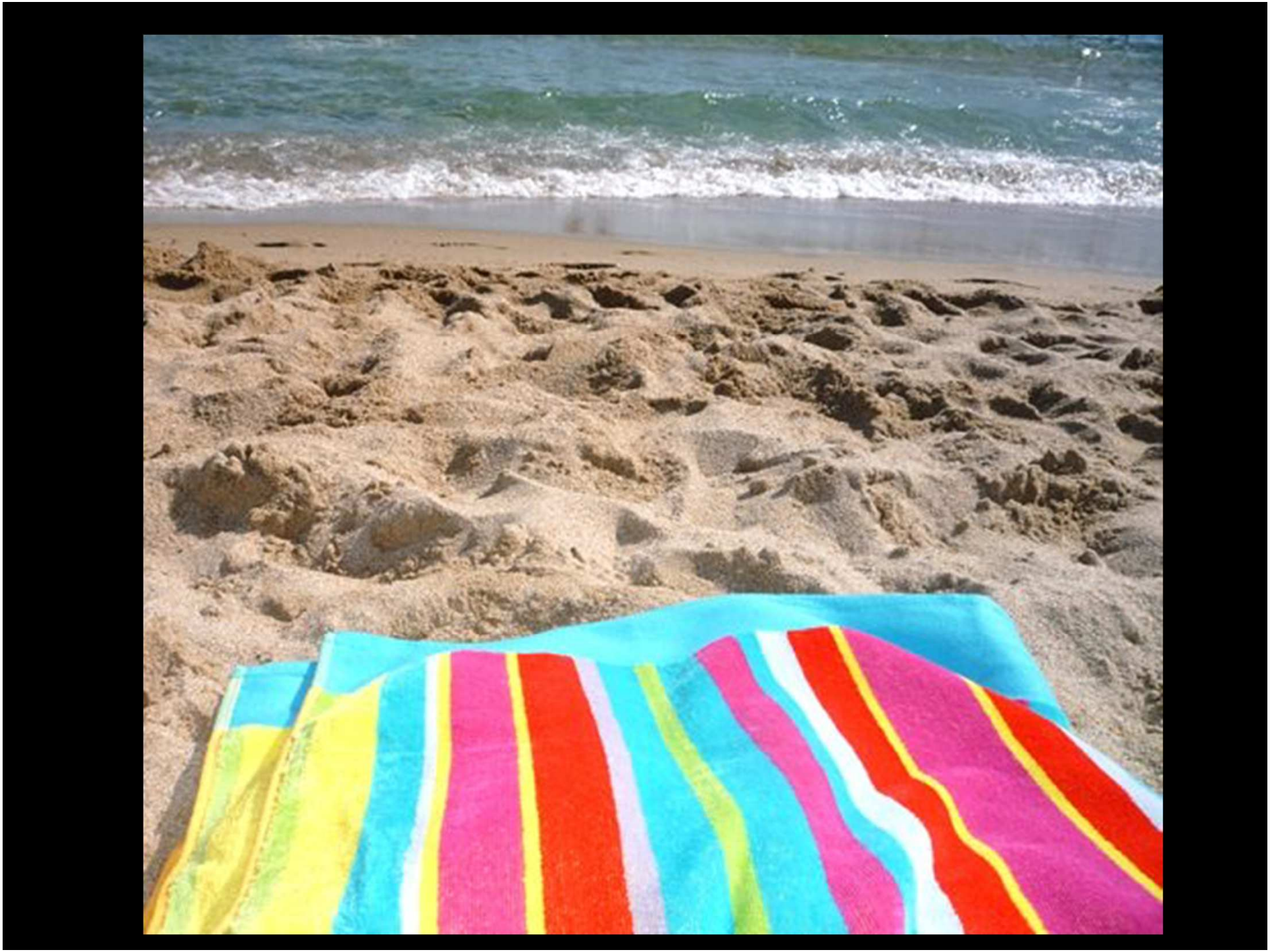
Dr. Franck ZAL
CEO HEMARINA

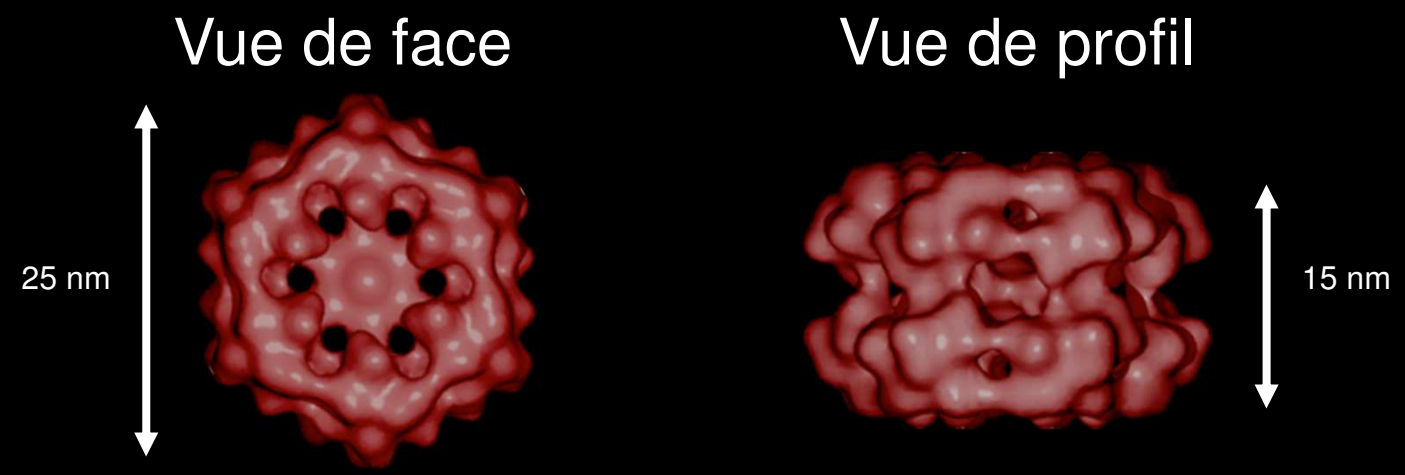

Une prodigieuse révélation...
LE MONDE DU SILENCE
UN GRAND FILM EN EASTMANCOLOR
DE J.Y. COUSTEAU ET LOUIS MALLE
AVEC FREDERIC DUMAS, ALBERT FALCO, LES PLONGEURS ET L'EQUIPAGE DE LA CALYPSO

Centre National de la Recherche Scientifique

MILIEUX MARINS EXTRÊMES





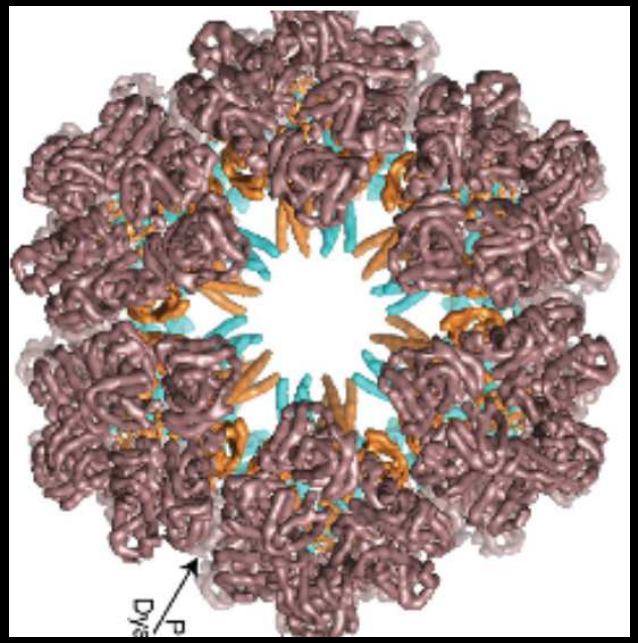


Principales caractéristiques

- 40 fois plus oxygénante que l'hémoglobine humaine
- 250 plus petite qu'un globule rouge
- Activité anti-oxydante
- Charge et décharge son oxygène dans un simple gradient
- Fonctionne à différentes températures

Arénicole

156 oxygènes



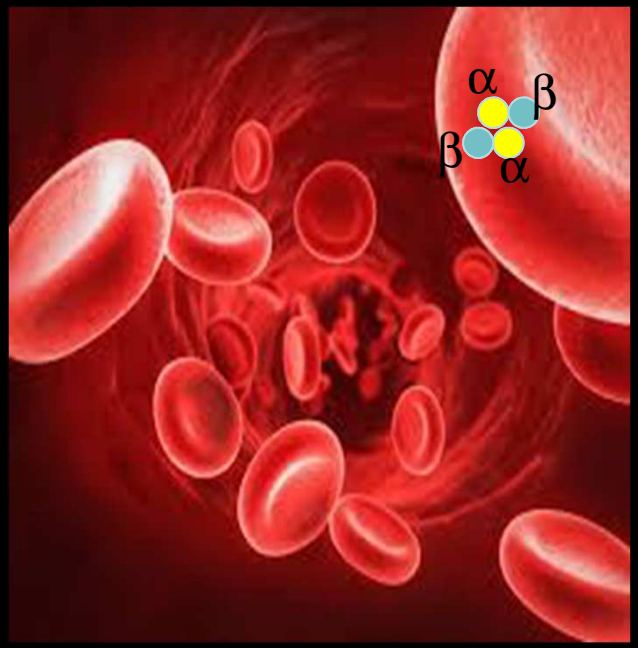
nm

Hémoglobine extracellulaire

450 MA

Homme

4 oxygènes



µm

Hémoglobine intracellulaire

3 MA

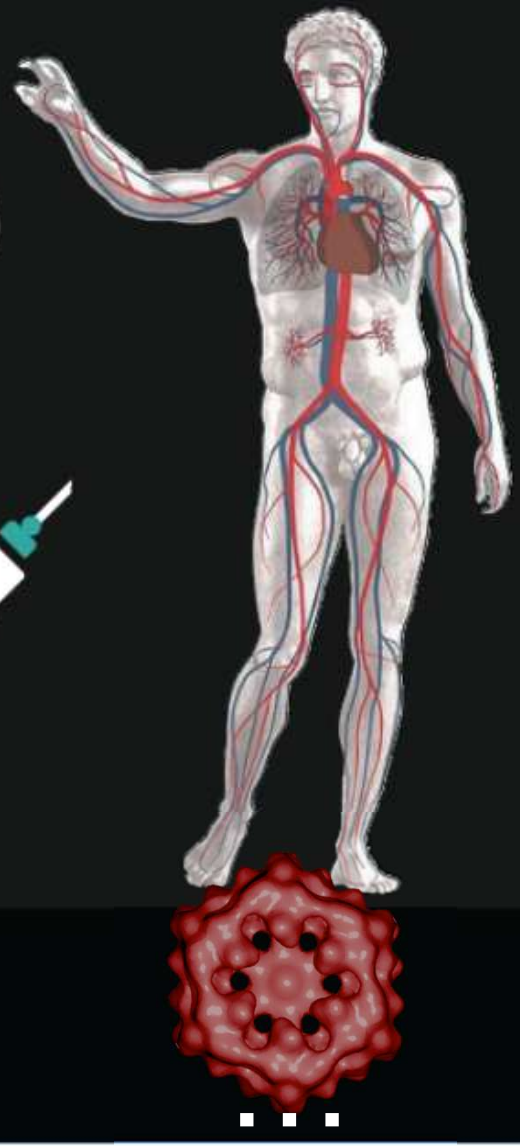
EVOLUTION

Conservation des structures et de la fonction


HEMARINA
Committed to saving lives

From the bench to bedside : a breakthrough innovation

Plateforme technologique



Cellule
HEMOXCell®

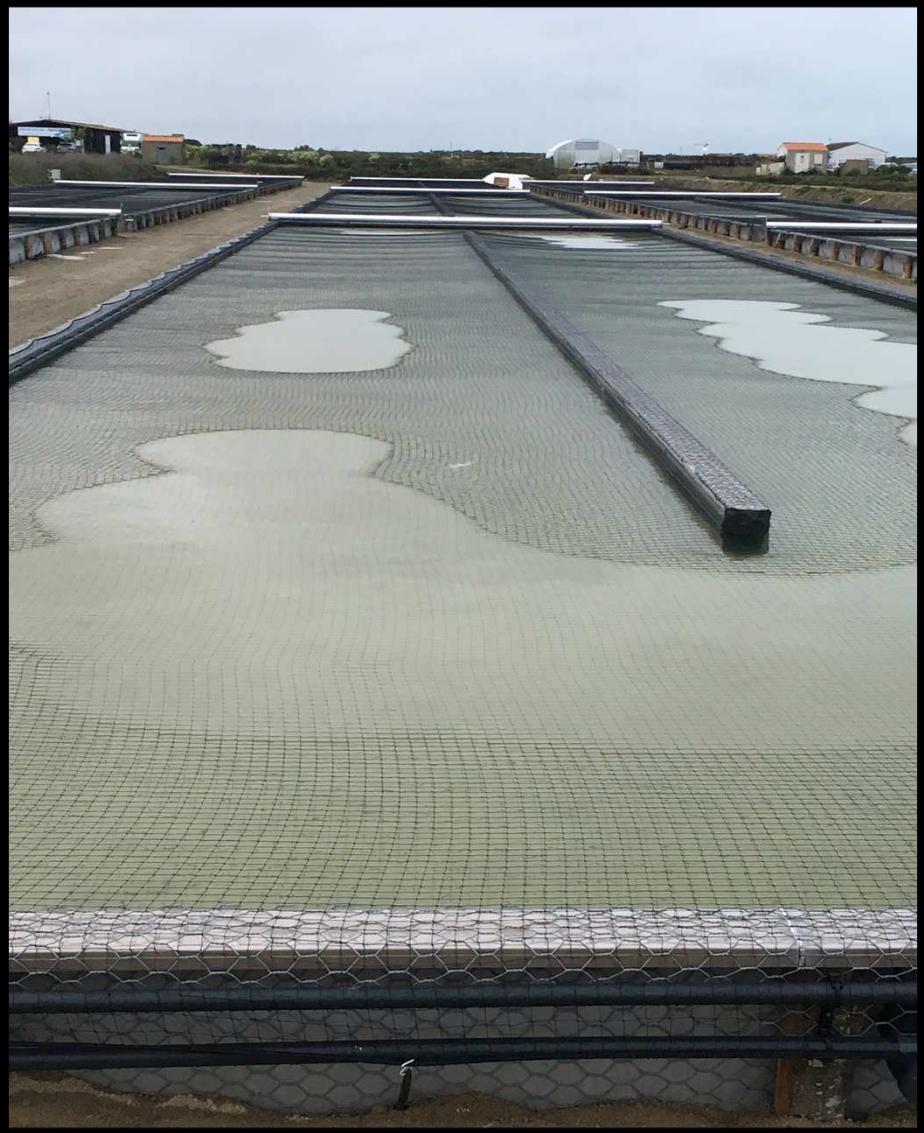
Organisme
HEMOXYCarrier®

Organe
HEMO2life®

Tissu
HEMHealing®

...

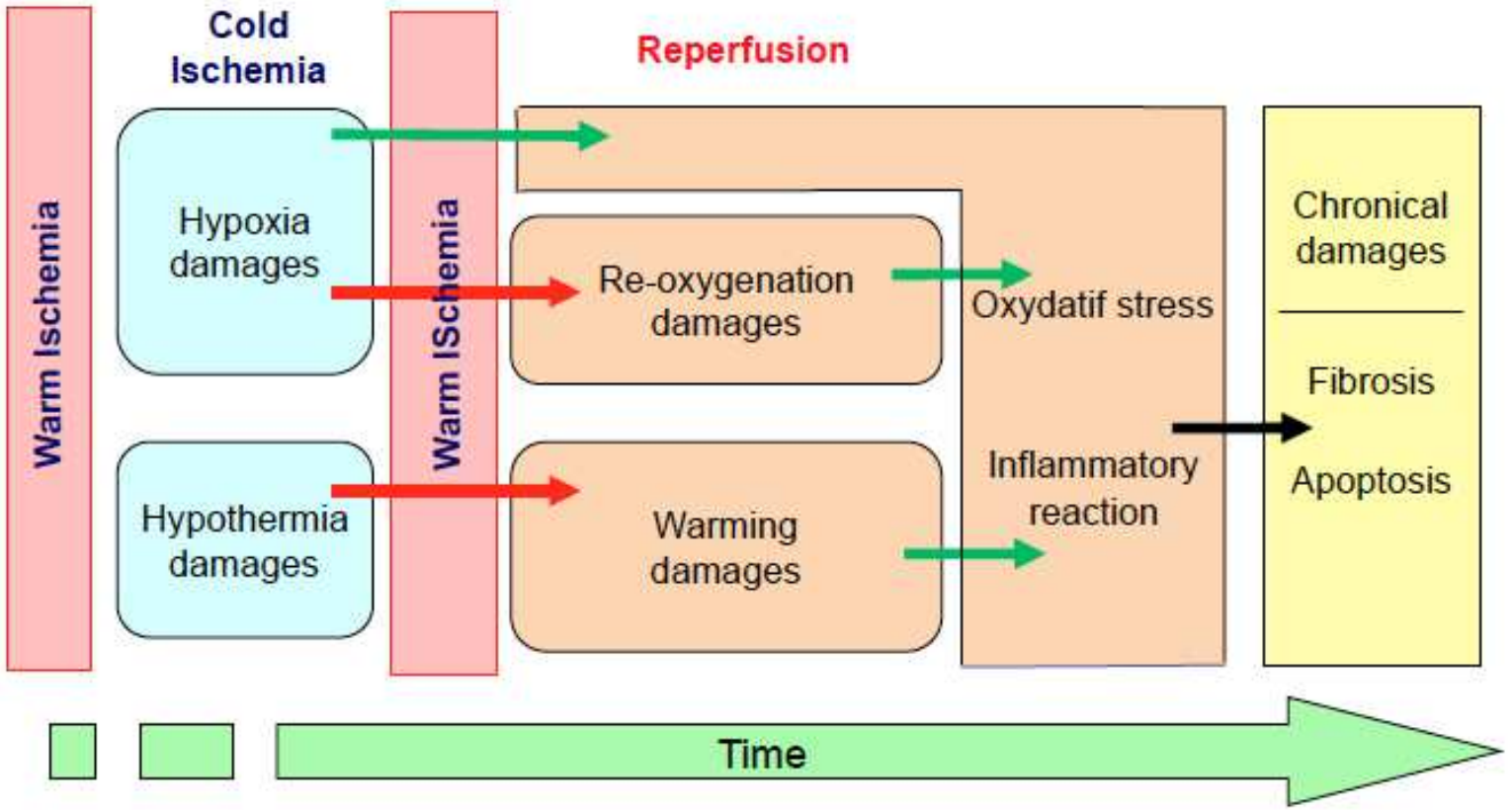
Production : les molécules




HEMO2life®
Additive to hypothermic graft preservation solutions
1g
Additif aux solutions de préservation hypothermique de greffons
Dispositif médical stérile d'origine animale
HEMARINA
Additive to hypothermic graft preservation solutions
Sterile medical device of animal origin
HEMO2life®
Additif aux solutions de
hypothermique des
Dispositif médical stérile
A conserver au maximum
NE PAS RECONGE
NE PAS CHAUF
2014-12

La transplantation d’organes

Ischemia – reperfusion: main issue in organ transplant



DGF Low

Preservation solution = Bassement
Strong bassement/ graft will survive a longer time in the receiver

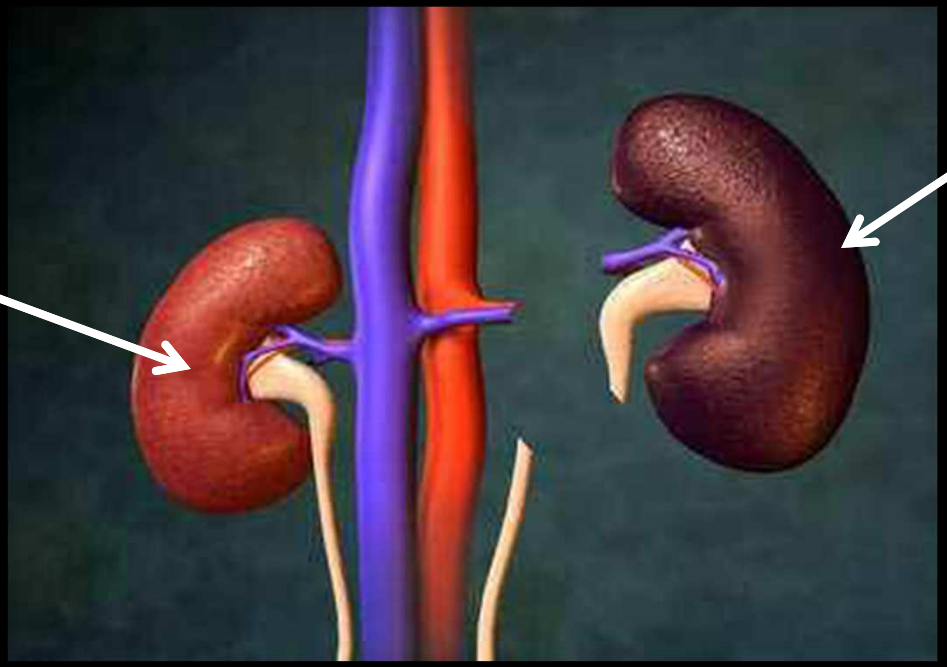
The DGF is an indicator of the bassement quality

DGF High

Preservation solution = Bassement
Fragil bassement/ graft will survive a shorter time in the receiver

The DGF is an indicator of the bassement quality

BIOMIMÉTISME ou BIO-INSPIRATION



O_2

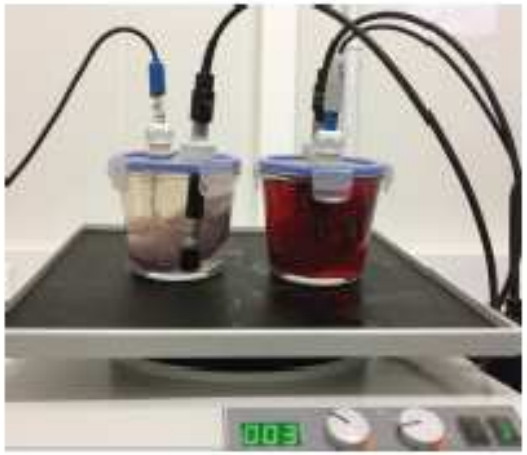
O_2

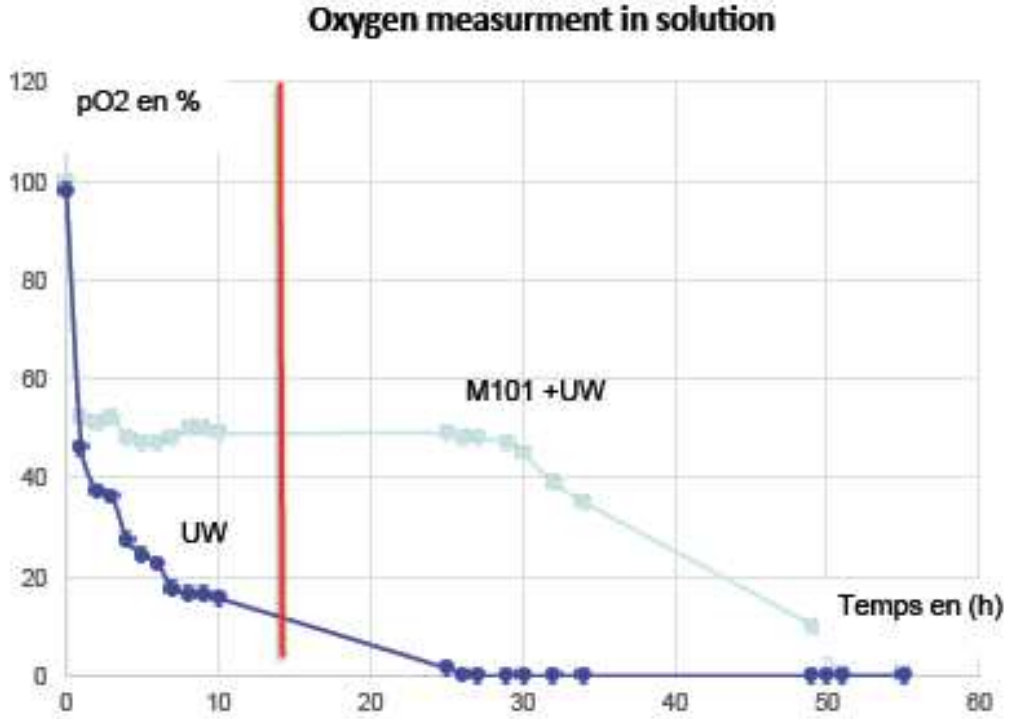
MARÉE HAUTE

MARÉE BASSE

HEMO$_2$life® - Preclinical

Kidney coming from the same pig placed in a **close recipient** with a small amount of air at 4°C.





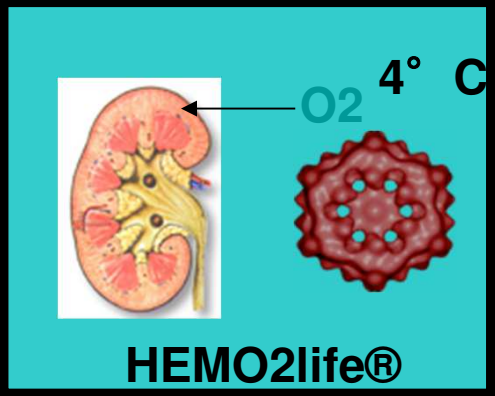
- **Without HEMO2life®** : rapid decreasing of oxygen content in solution after 6 hours less only 21% remaining ar. 64,7 µMol = 2 mg/l = 1.47 ml/l
- **With HEMO2life®** : when the PO2 is below the P50 of M101 there is a slow release of oxygen stable during 30h at 6 h over 55% remaining ar. 169 µMol = 5.4mg/l = 3.85 ml/l

Nobel Prize in Medicine 2019

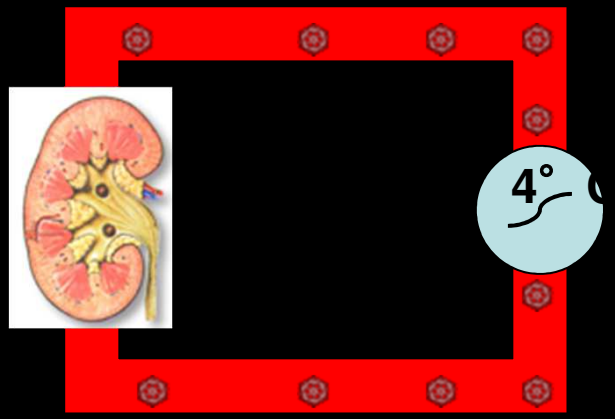
Scientists William G Kaelin, Jr, Peter J Ratcliffe and Gregg L Semenza

Adaptation of Cells to oxygen availability

Techniques de préservation



Statique



Machine

CŒUR BATTANT

CŒUR ARRÊTÉ

« We are committed to save lives »

Transplantation Rénale

Pr. Thierry Hauet

American Journal of Transplantation 2011; 11: 1845–1860
Wiley Periodicals Inc.

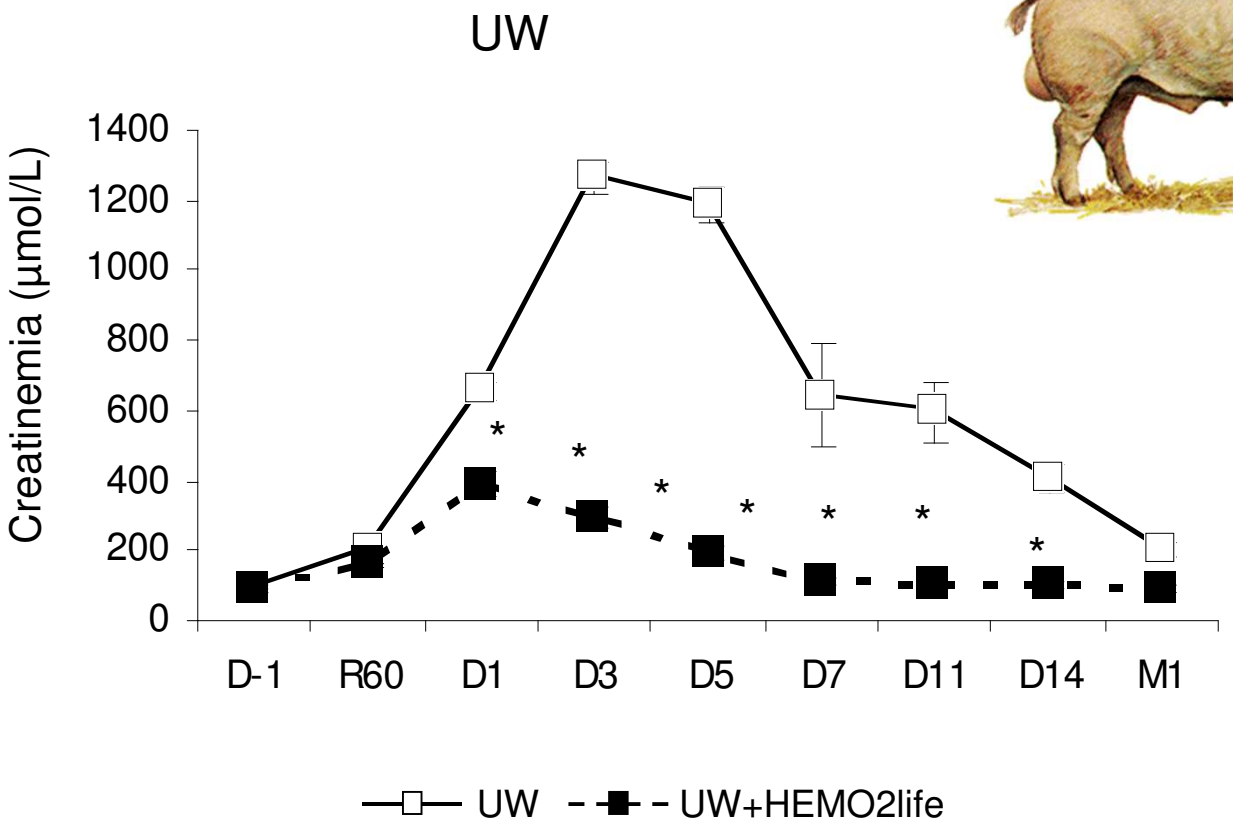
doi: 10.1111/j.1600-6143.2011.03614.x

Supplementation With a New Therapeutic Oxygen Carrier Reduces Chronic Fibrosis and Organ Dysfunction in Kidney Static Preservation

R. Thuillier[a,b,g,†], D. Dutheil[c,†], M. T. N. Trieu[a], V. Mallet[a,c], G. Allain[a], M. Rousselot[c], M. Denizot[e,f], J.-M. Goujon[a], F. Zal[c] and T. Hauet[a,b,d,g,*]

« We are committed to save lives »

HEMO$_2$life® - préclinique



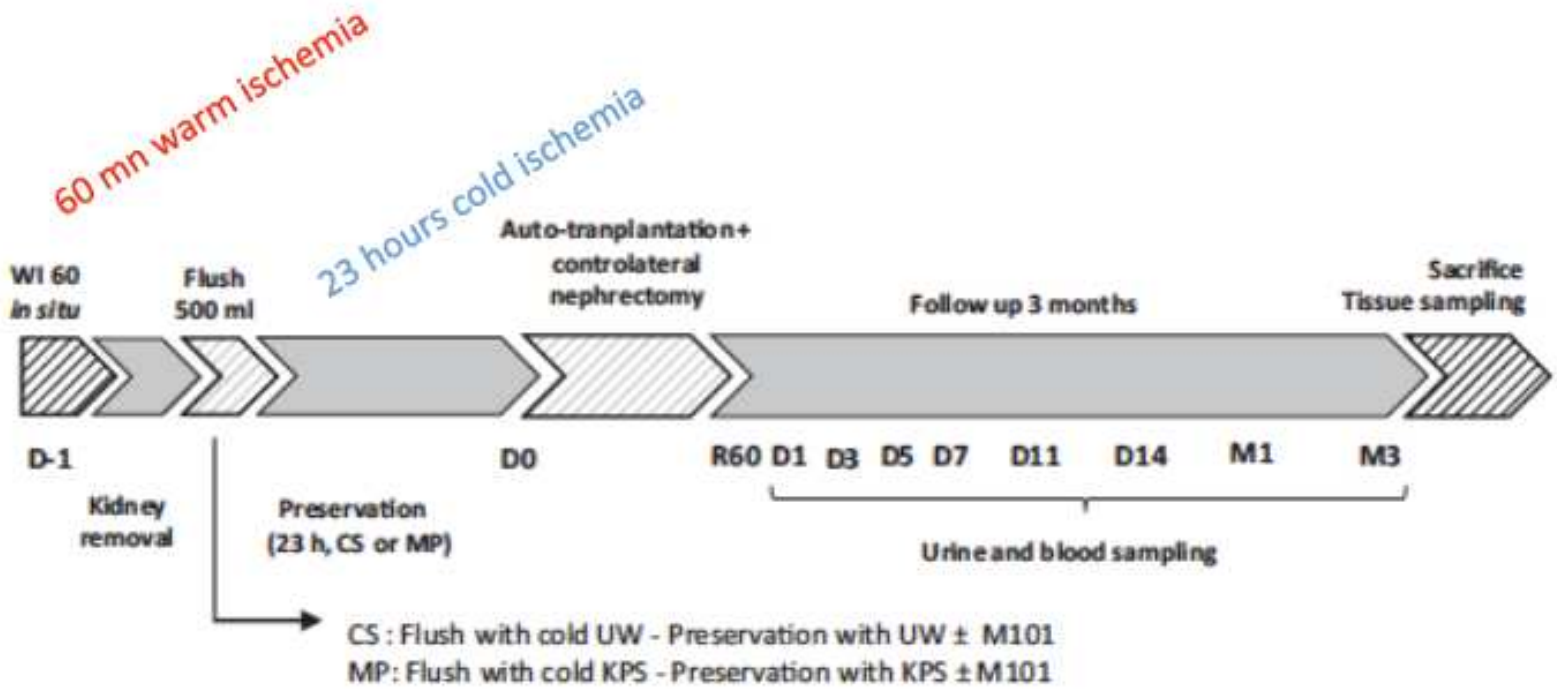
*: p<0.05 to UW

(Thuiller et al., AJT 2011)

HEMO$_2$life® - préclinique

Hemo2life® and DCD:

Pig kidney transplantation after 60 mn WIT and 23 hours CIT



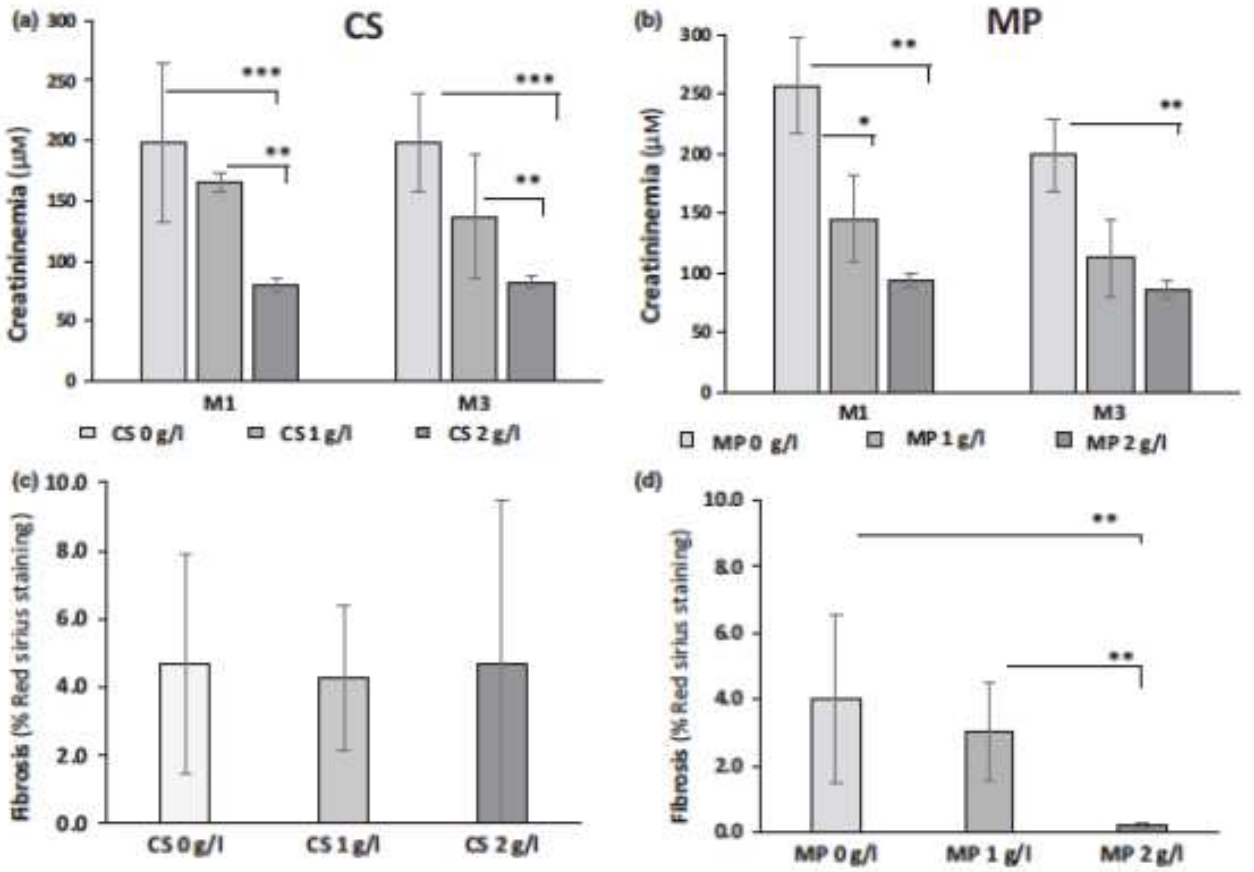
Kaminski J et al; Transpl Int. 2019 Sep;32(9):985-996

« We are committed to save lives »

HEMO$_2$life® - préclinique

Hemo2life® and DCD:

Pig kidney transplantation after 60 mn WIT and 23 hours CIT



Kaminski J et al; Transpl Int. 2019 Sep;32(9):985-996

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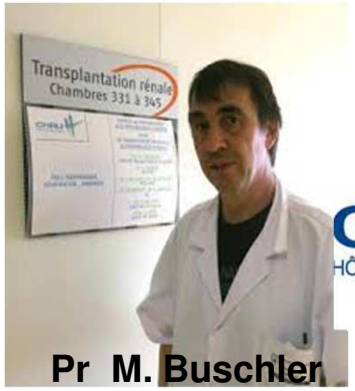
OXYGP

Pr Y. Lemeur

CHRU BREST
CENTRE HOSPITALIER REGIONAL UNIVERSITAIRE

Hôpitaux Universitaires Pitié Salpêtrière - Charles Foix

Pr B. Barrou



Pr M. Buschler

CHRU HÔPITAUX DE TOURS

Hospices Civils de Lyon

Pr L. Badet

Pr A. Thierry

CHU de Poitiers

CHU Centre hospitalier universitaire Limoges

Pr M. Essig

OXYOP : design of the study

- We checked this sample size was sufficient to **show a significant difference between the DGF rate in the HEMO2life® group and the contralateral group.**

  - We set :
    - Significance level **α to 0.05** and power **β to 0.8**, by convention,
    - **Reference value for the DGF rate:**
      - in the contralateral group comes from the literature **26,5%** (Moers et al, 2012 :)
      - for HEMO2life® group from the pre-clinical studies (DGF rate should drop by 15-20 points) : **7.5 %**
    - **Same sample size in both groups** as we use pairs of kidneys,

The minimal sample size per group is equal to 45 patients.
With 60 patients, we allow for 25% of lost to follow-up or excluded patients.

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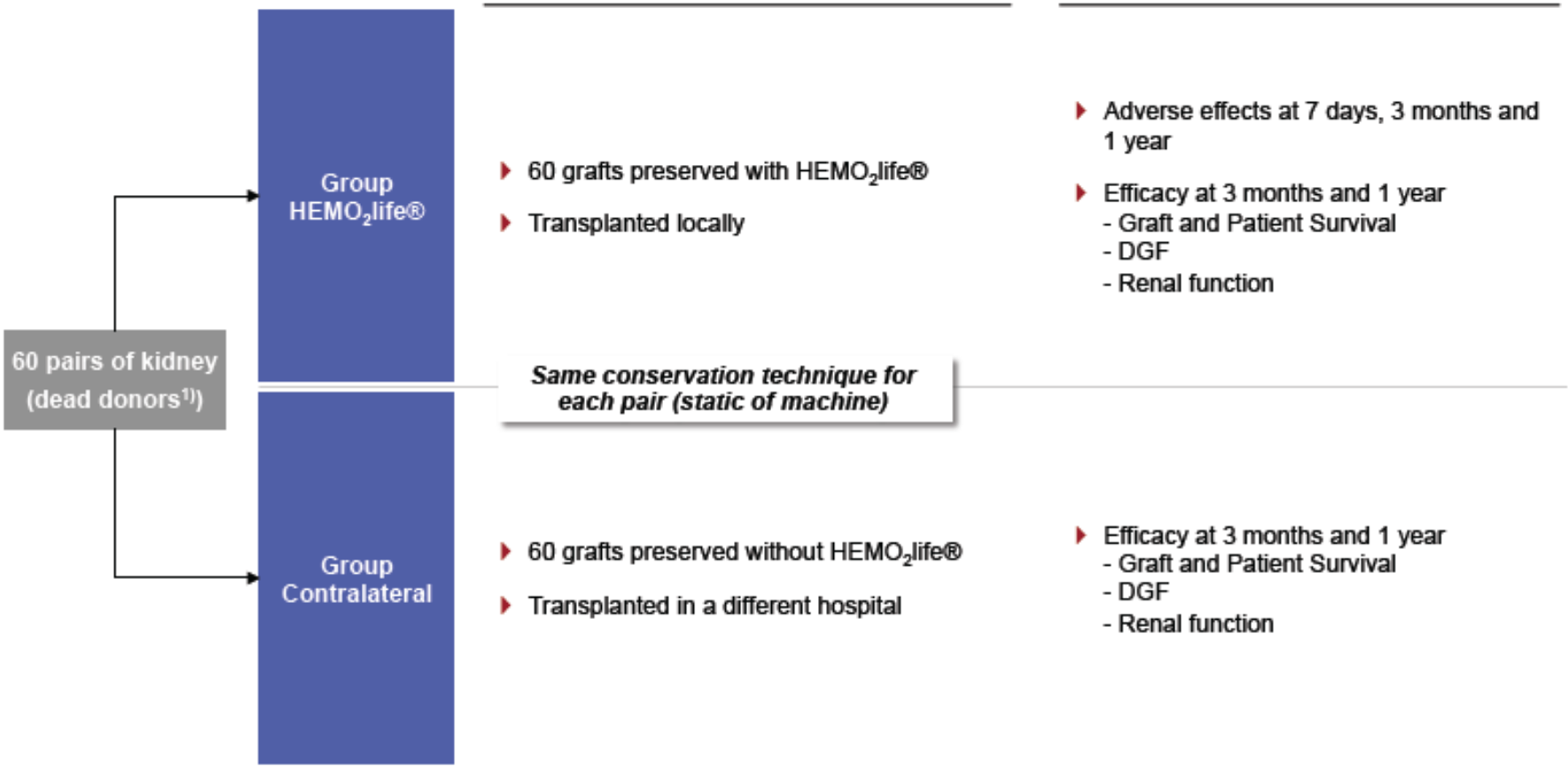
« We are committed to save lives »

HEMO2life® : OxyOp

2/3 Study Design: National multicentric open-labeled safety study on HEMO$_2$life® used in organ preservation solution

OXYOP



HEMARINA

« We are committed to save lives »

HEMO2life® : OxyOp

2 OxyOp: HEMO$_2$life® has been demonstrated to be 100% safe at clinical level

OXYOP

HEMO$_2$LIFE® CLINICAL STUDY – OXYOP – 3 MONTHS SAFETY RESULTS

60 kidneys included
58 transplantations in 58 recipients[1)]

Day 1
58 patients alive with a functioning kidney
0 death, 0 graft loss
0 lost to follow up

Day 7
58 patients alive, 57 with a functioning graft
0 death, 1 graft loss
0 lost to follow up

Month 1
58 patients alive, 56 with a functioning graft
0 death, 2 graft losses
0 lost to follow up

Month 3
58 patients alive, 56 with a functioning graft
0 death, 2 graft losses
0 lost to follow up

Patient Survival:
58 out of 58

Graft Survival:
56 functioning graft out of 58 after 3 months[2)]

No serious events, allergic reaction or hypersensitivity related to the products

HEMO$_2$life® is 100% safe

« We are committed to save lives »

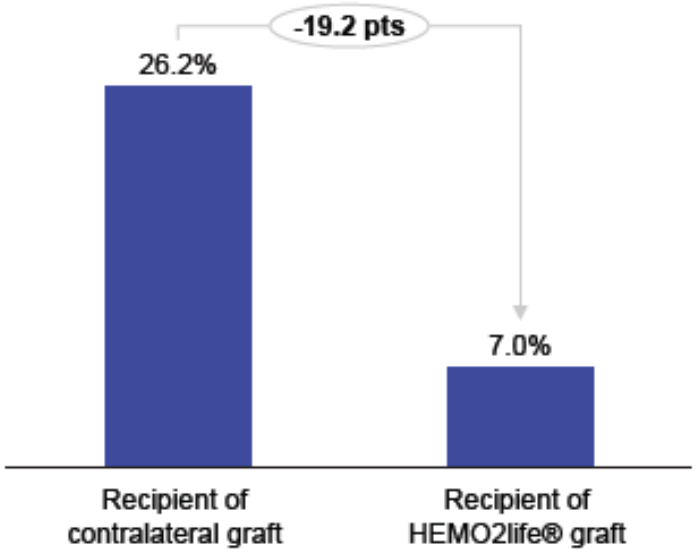
HEMO2life® : OxyOp

3 OxyOp: HEMO$_2$life® has significantly reduced delay in graft function recovery

OXYOP

HEMO$_2$LIFE® CLINICAL STUDY – OXYOP – 3 MONTHS EFFICACY RESULTS (1/2)

Effects of HEMO$_2$life® on function recovery: % of transplant with delay in graft function recovery[1)]



Impact of HEMO$_2$life®
Significant reduction of delayed graft function vs. contralateral group

- Delay in graft function recovery reduces significantly long-term graft survival rate

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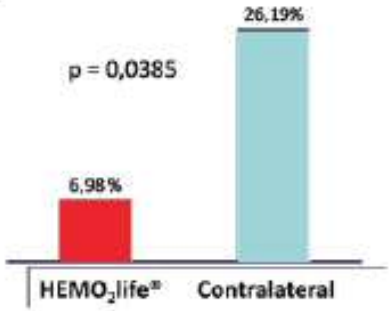
HEMO2life® : Clinical trial OxyOp

Oxyop: secondary efficacy end points M3

DGF: More than one HD session

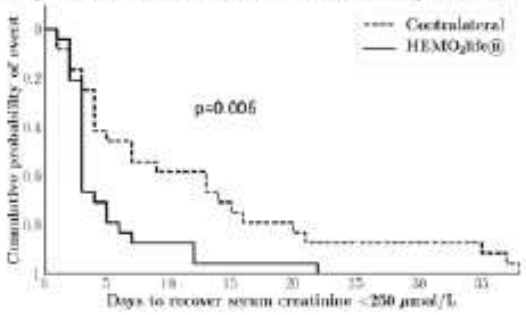


Paired analysis excluding preemptive transplantations: (n = 43)

Markers of DGF	HEMO$_2$life® n=43	Controlatéral n=43	p value
At least one HD session, %	10 (23.2)	14 (32.5)	0,4544
More than one HD session, %	**3 (6.9)**	**11 (26.1)**	0,0385 *
Number of dialysis sessions	0.47 +/- 1.18	1.33 +/- 2.86	0.008 *
Days for creatinine < 250µmol	6.9 +/- 9.1	13.1 +/- 13.8	0.0208 *

Kaplan-Meier estimate curves of cumulative probability to achieve creatinine < 250 µmol/l

Subgroup of cold storage n= 25 pairs



Multivariate Cox analysis

	Coef	Lower 0.95	Upper 0.95	P value
Group (HEMO$_2$life® versus contralateral)	-0.6823	-1.3604	-0.0042	0.0486
Recipient Age	-0.030	-0.320	0.259	0.8376
Recipient Sex	0.0734	-0.5419	0.6887	0.8151
Race	0.1199	-0.7906	1.0305	0.7963
Cold ischemia	-0.0014	-0.0022	-0.005	0.0026

HEMO$_2$life® reduces DGF independently of CIT

OXYOP

Le Meur Y, Am J Transplantation in revision

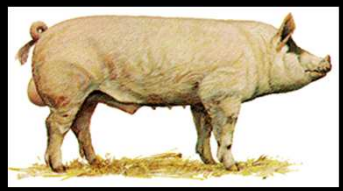
Pr. Edouard Sage

HOPITAL FOCH

Pr. Marcelo Cypel

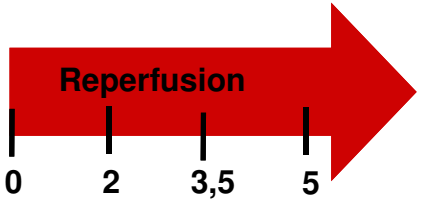
UHN
Toronto General
Toronto Western
Princess Margaret
Toronto Rehab

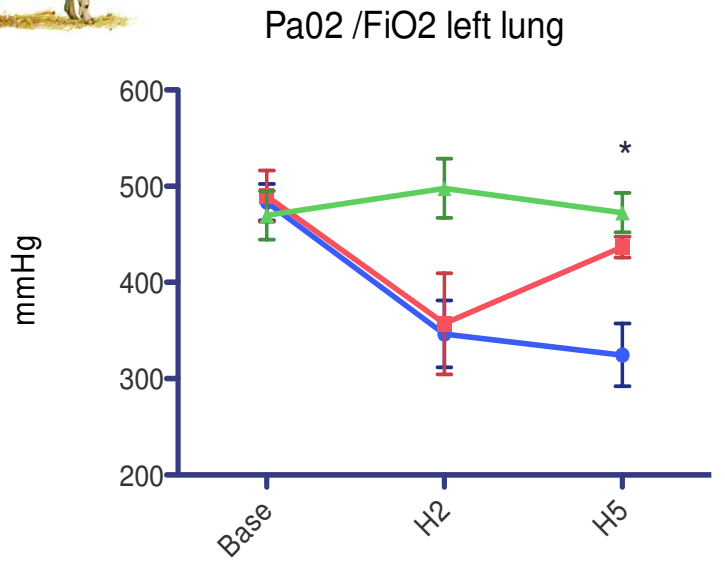
Préservation Pulmonaire

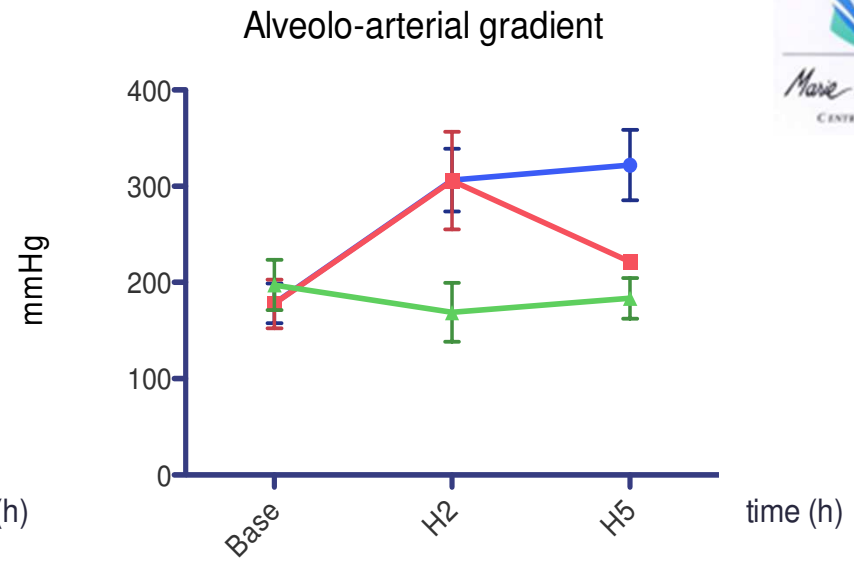


HEMO$_2$life® : poumon

- **Hématoses : poumon gauche**







* : Perfadex vs Hemarina : p<0,05

perfadex n=5
Hemo2life® n=4
Sham n=5

ANOVA 2 Way for repeated measures
Bonferroni post test

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HEMO$_2$life® : poumon

1 Lung: HEMO$_2$life® improves post-transplant reperfusion after 48 hours of pulmonary preservation

Two-Day Lung Preservation Followed by Lung Transplantation in a Large Animal Model Using Novel Extracellular Oxygen Carrier.

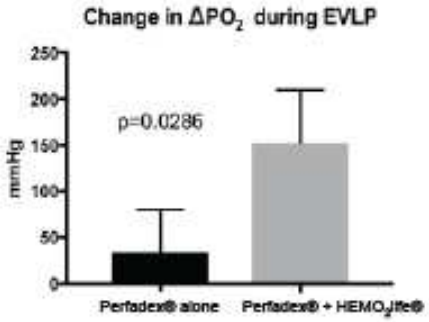
Ali *et al.* and M. Cypel (University Health Network, Toronto General Hospital Research Institute).

J Heart Lung Transplant. April 2018; Volume 37, Issue 4, Supplement, Pages S123–S124.

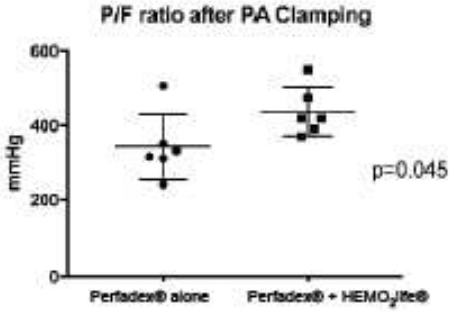
- Extended cold static preservation (CSP) of lungs in a swine model
- Supplementation by HEMO$_2$life® of Perfadex® preservation solution
- **48h of pulmonary preservation:** 36h of CSP and 12h of normothermic *ex-vivo* lung perfusion (EVLP)
- Lung transplant followed by 4h of reperfusion

MAIN RESULTS

Effects of HEMO$_2$life® on graft oxygenation ratio during EVLP



Effects of HEMO$_2$life® on graft oxygenation ratio after transplantation



Impact of HEMO$_2$life®

Successful in minimizing lung injury during cold static storage and attenuating ischemia-reperfusion injury after 48h of pulmonary preservation

Pr. Karim Boudjema

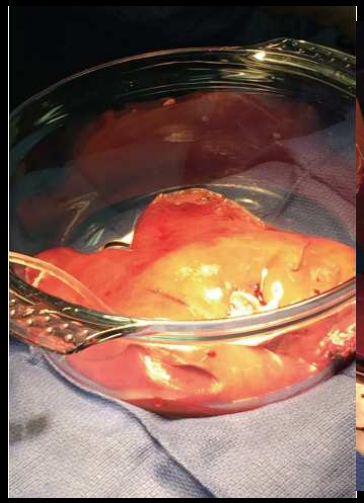
CHU Rennes

Pr. René Adam

Hôpitaux universitaires Paris-Sud

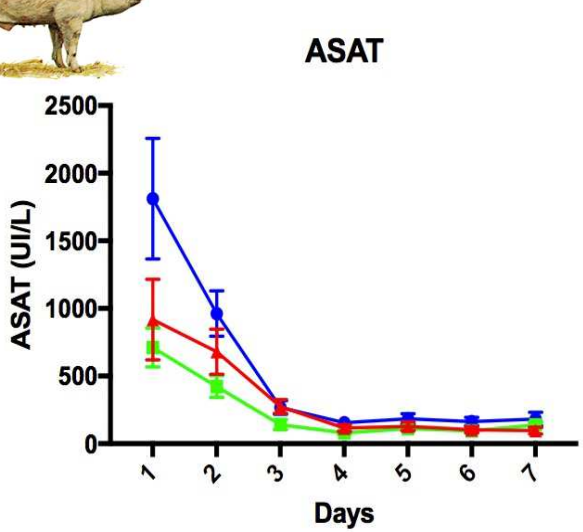
Antoine-Béclère Bicêtre Paul-Brousse

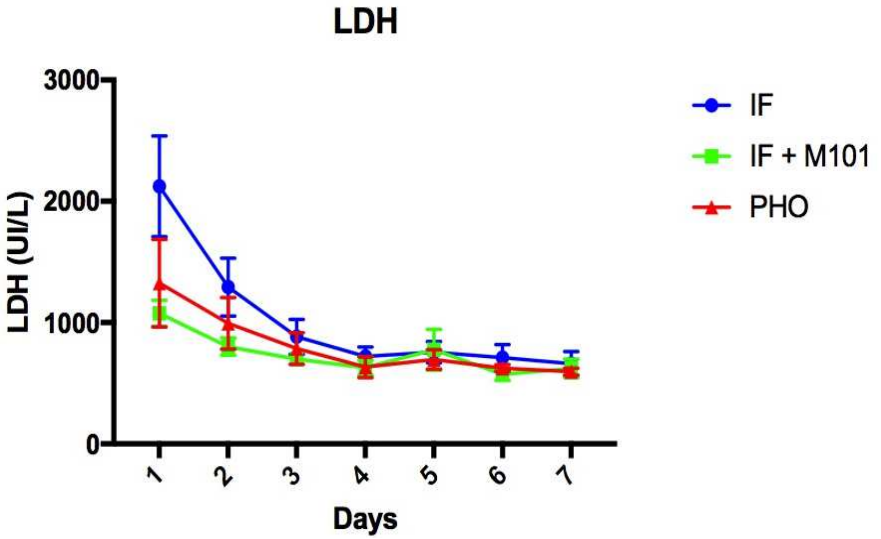
Préservation Hépatique

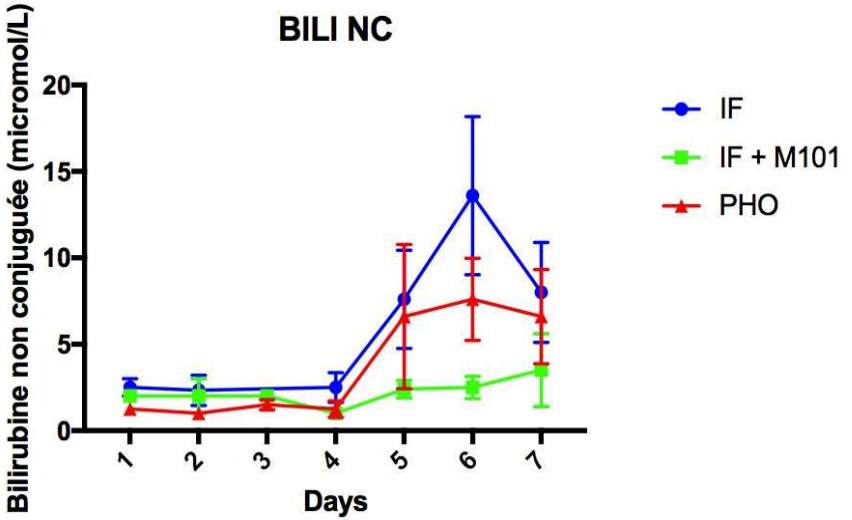


« We are committed to save lives »

HEMO$_2$life® : foie





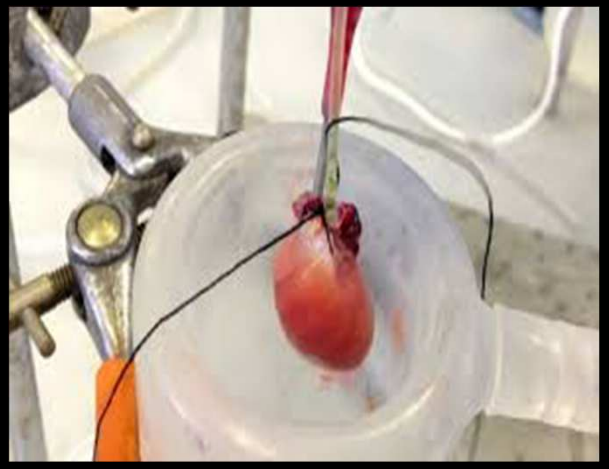


Boudjema *et al.* en préparation

HÔPITAUX UNIVERSITAIRES PARIS OUEST
Hôpital européen Georges-Pompidou

Pr. Philippe Menasché

Préservation Cardiaque



Les Hôpitaux Universitaires de STRASBOURG

Pr. Michel Pinget

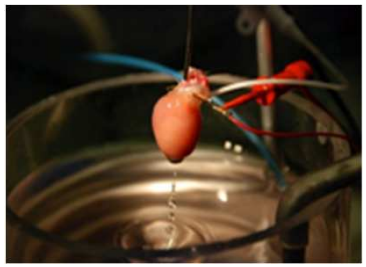
Préservation Pancréatique

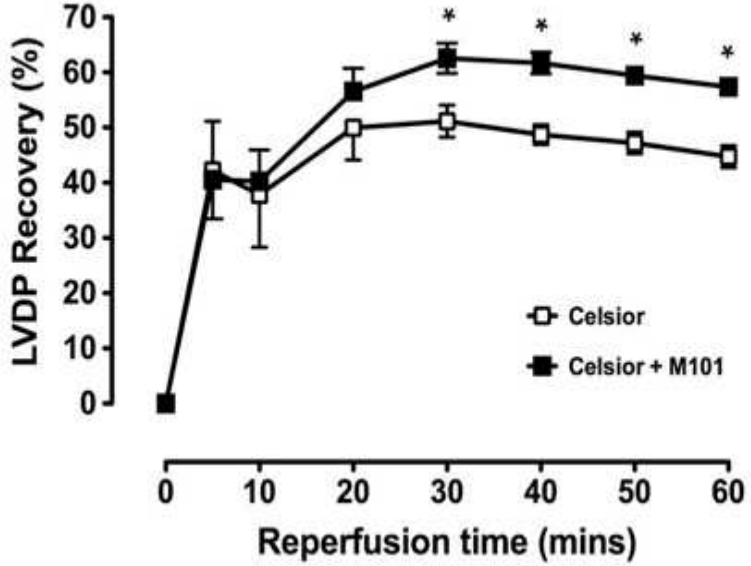
« We are committed to save lives »

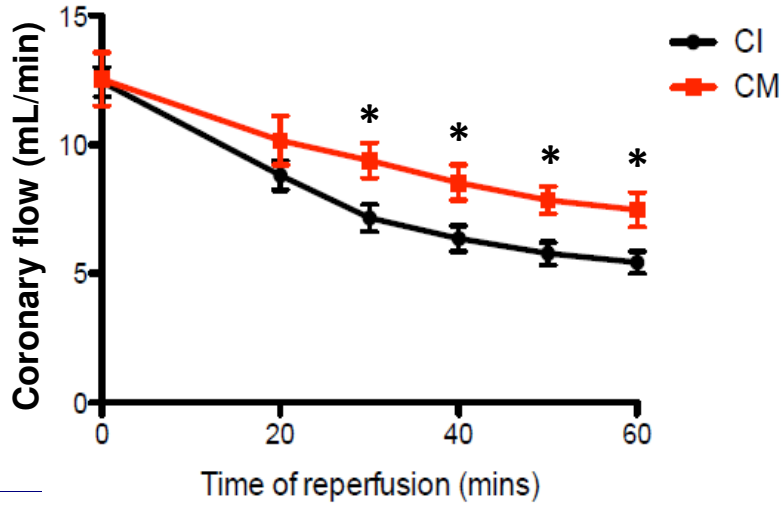
HEMO$_2$life® : Coeur

Ex *vivo* isolated perfused heart model (Langendorff model)

- Collaboration with cardio-thoracic surgery of Rayne Institute, King College of London; and Pr Ménasché (Hôpital Européen Georges Pompidou - Paris)
- Evaluation of the benefits of the supplementation by HEMO2life® of Celsior® preservation solution
- Cold static preservation of rat heart during 8h

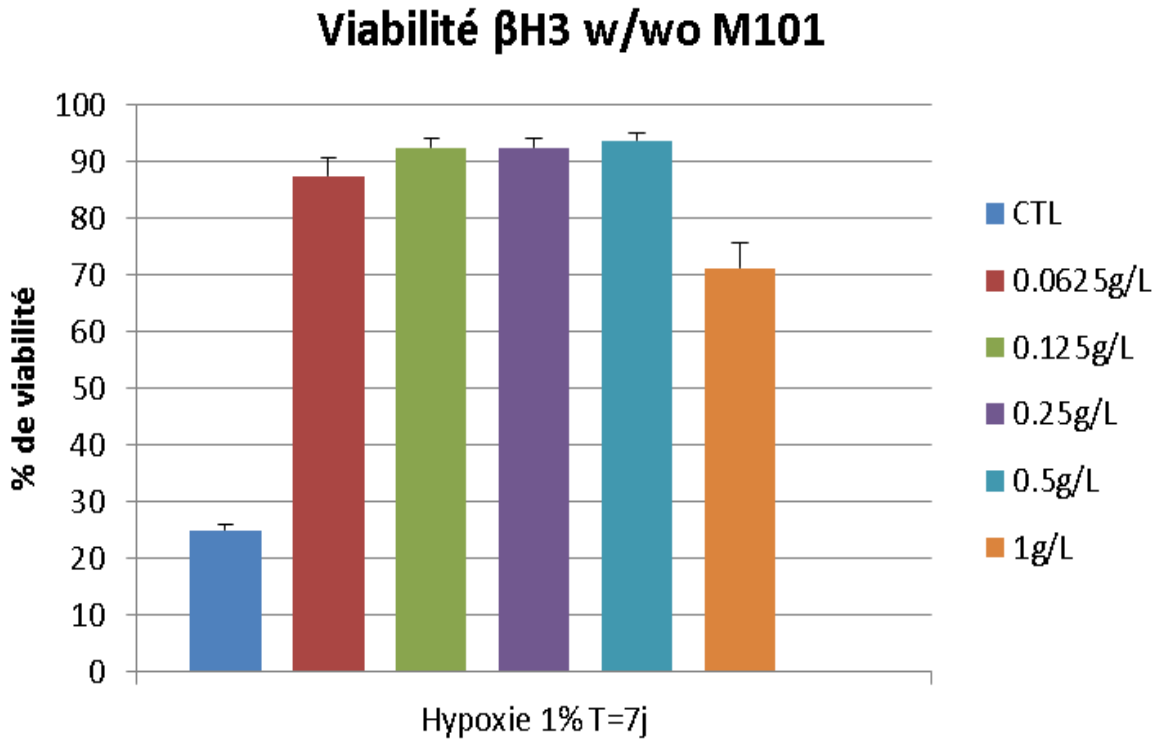






HEMO$_2$life® : langherans islets

Effets-dose sur la viabilité cellulaire (BetaH3) en 1% pendant 7 jours



Collaboration with the CEED - Strasbourg

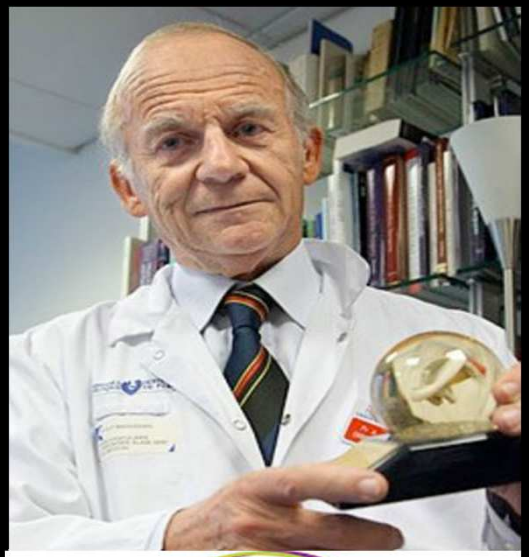
Greffe de la face

Pr. Laurent Lantieri

HÔPITAUX UNIVERSITAIRES PARIS OUEST

Hôpital européen Georges-Pompidou


Vendredi, 13 Février 2019
13 mois après
“La vie est belle”



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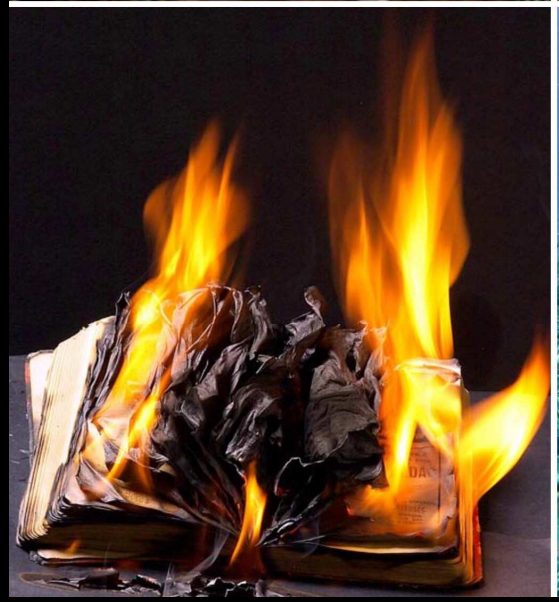
Pr. Alain Carpentier
Cœur artificiel CARMAT

« Il y aura eu deux événements majeurs dans le domaine de la greffe d'organes : Les immuno-suppresseurs qui nous ont permis de transplanter et HEMO2Life, votre innovation, qui va nous donner du temps et des organes de meilleur qualité »

Hemarina lauréat du 1er prix du Concours des Technologies Médicales Innovantes



« Regarde vers la nature, c'est là qu'est ton futur…"

Léonard de Vinci