HEMO2life®

« We are committed to save lives »

- Design général
  - Etude biomédicale organe
  - Etude de sécurité
  - Obligatoire pour dépôt de demande de marquage CE
- Centres participants

- Conseil scientifique : 12 membres (6 Nephr. + 6 Chir.)
- Coordinateur médical: Y Le Meur; Coordinateur Chirurgical: B Barrou
- Comité de surveillance (iDSMB) : 3 experts P Merville, C Legendre, A Le Moine

HEMARINA

« We are committed to save lives »

HEMO2life® : OxyOp

- **<u>Excellente nouvelle</u>** : après le « Stop » prévu au 10ème patient, le « Go » a été donné fin Juillet par le Comité Scientifique indépendant.

- **HEMO$_2$life® peut continuer** de sauver et améliorer la vie d'autres patients (31 patients depuis la reprise de l'essai)

- Les chiffres des 10 premiers patients sont conforment aux attentes et **les paramètres biologiques sont identiques au modèle animal**.

- Un commentaire de l'investigateur principal : « **A ce stade, nous pouvons déjà dire que le produit est totalement safe** »

HEMARINA

« We are committed to save lives »

HEMO2life® : OxyOp

- 1) **Evolution de la créatine et comparaison avec l'étude préclinique :**

La slide 1 prouve que les résultats obtenus avec les patients HEMO2life® sont tout à fait superposables aux résultats obtenus chez l'animal. Tu as le commentaire sur chaque slide

- 2) **Evolution du débit de filtration glomérulaire** :

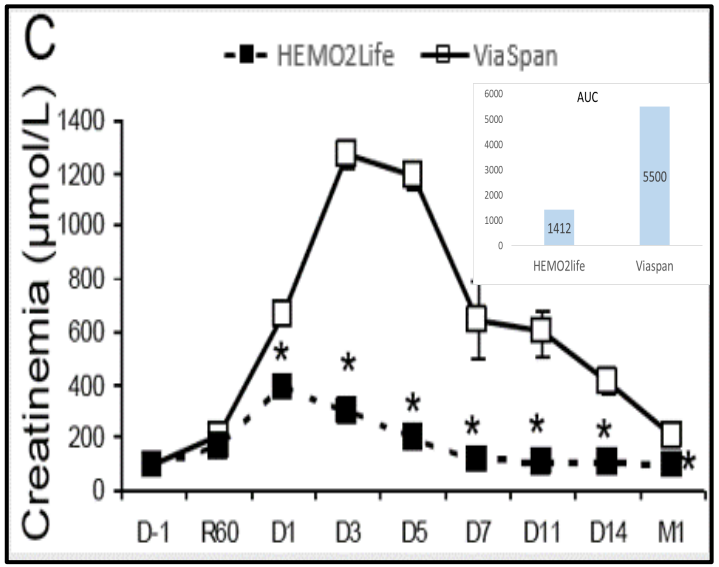
Là également OxyOp prouve que grâce à HEMO2life®, la reprise de filtration est spectaculaire, en forte corrélation avec les taux de créatine ce qui est prédictif pour la survie à long terme des greffons (il ne faut pas oublier que maintenant des patients sont à la 4ème greffe alors que nous manquons de greffons...)

OXYOP

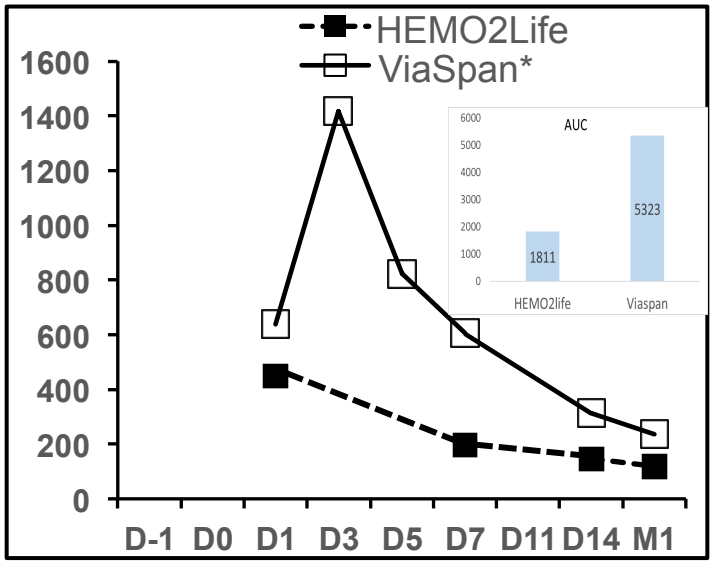
HEMARINA

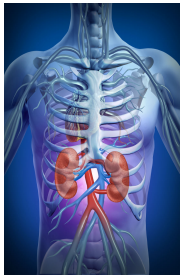
« We are committed to save lives »

HEMO2life® : OxyOp



Etude auto-transplantation rénale chez le porc Large White (Thuiller et al., 2011)





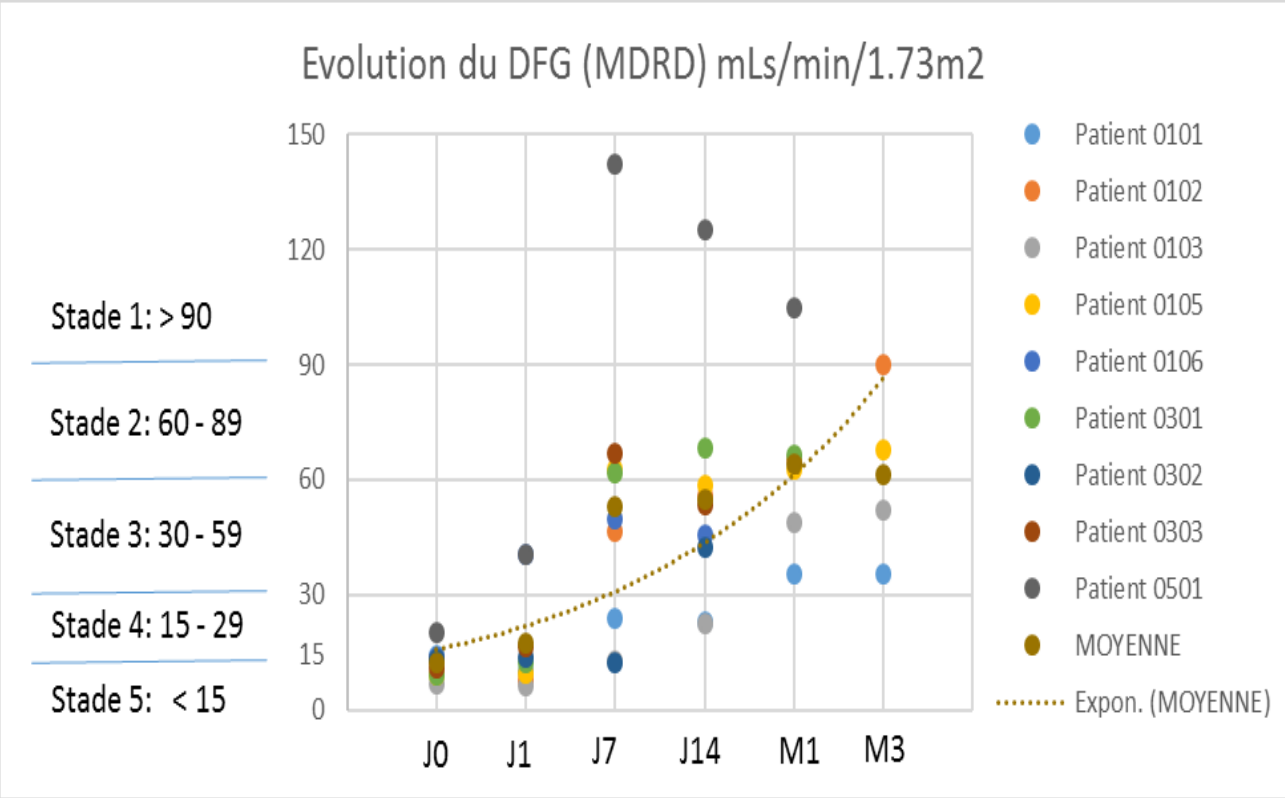
Etude OXYOP (données préliminaires, *comparaison avec données historiques ViaSpan)

- Même profile de réponse sur la créatinine sanguine entre l'étude préclinique (gauche) et l'étude OXYOP (droite)
  → étude préclinique prédictive
- La décroissance de la créatinine survient de façon plus précoce et le retour à une valeur normale intervient plus rapidement
  → reprise de fonction plus rapide, meilleur pronostic à long terme

OXYOP

« We are committed to save lives »

HEMO2life® : OxyOp



- Reprise rapide de filtration glomérulaire avec $HEMO_2$life avec une amélioration d'au moins 2 stades fonctionnels après uniquement 14 jours
- Forte corrélation avec les taux de créatininémie en fortes baisses après les premiers jours
- DFG – le critère le plus prédictif pour la survie à long terme (C.R. Lenihan et al. , *Renal Failure,* 30:345–352, 2008)

HEMARINA

« We are committed to save lives »

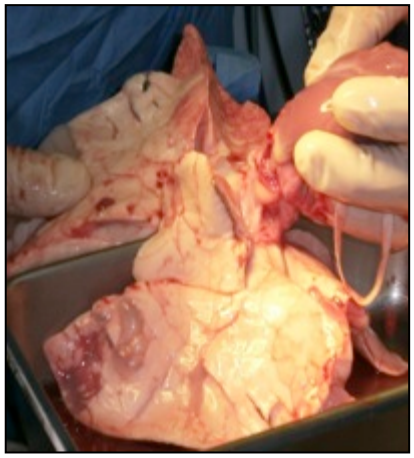
HEMO2life® for Lung preservation

- Porcine allotransplantation model: cold static preservation of lungs during 24h
- Supplementation by $HEMO_2Life$® of Perfadex® preservation solution
- Collaboration with Marie Lannelongue Center (Le Plessis Robinson, France) and Foch Hospital (Surènes, France)

HOPITAL FOCH

Marie Lannelongue
CENTRE CHIRURGICAL





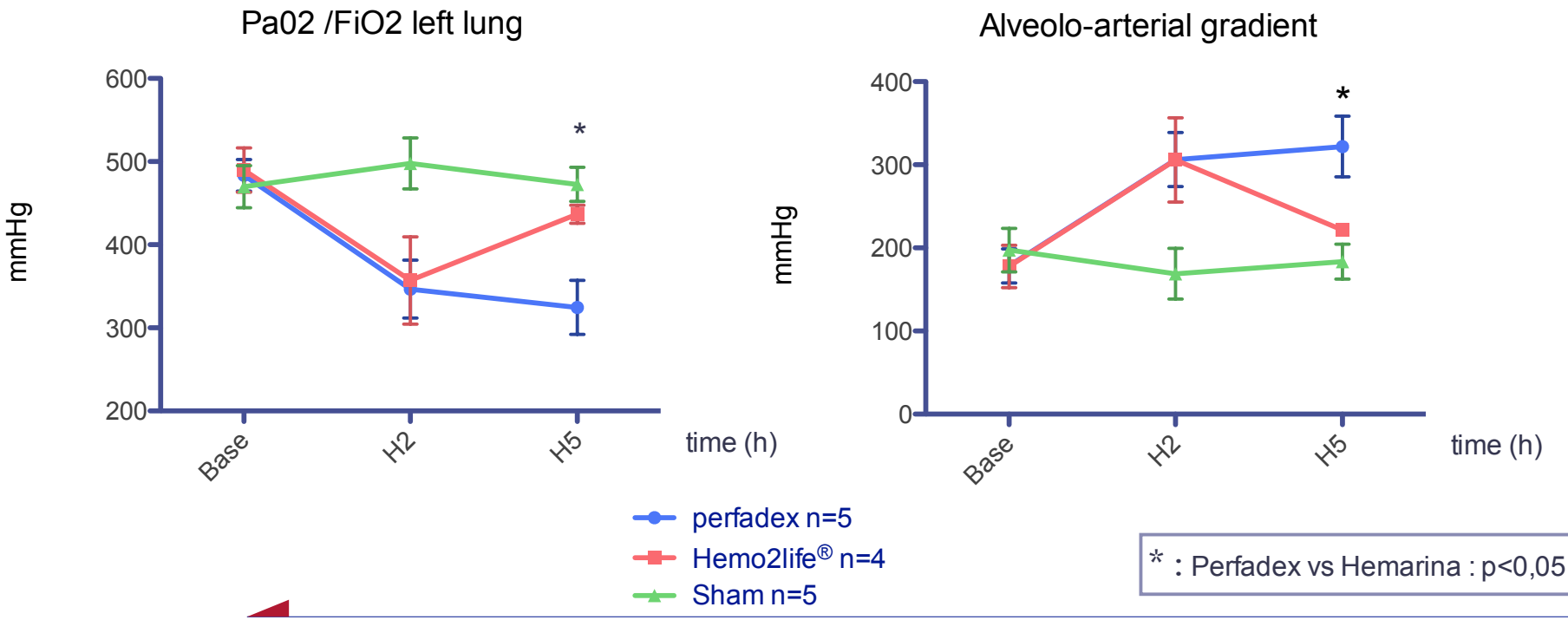

HEMARINA

« We are committed to save lives »

HEMO2life® for Lung preservation

- Porcine allotransplantation model: cold static preservation of lungs during 24h
- Supplementation by $HEMO_2Life$® of Perfadex® preservation solution
- Collaboration with Marie Lannelongue Center (Le Plessis Robinson, France) and Foch Hospital (Surènes, France)

❑ HEMATOSIS LEFT LUNG (Graft)



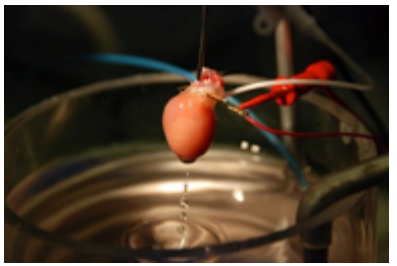
Sham control group: anesthesia + surgery

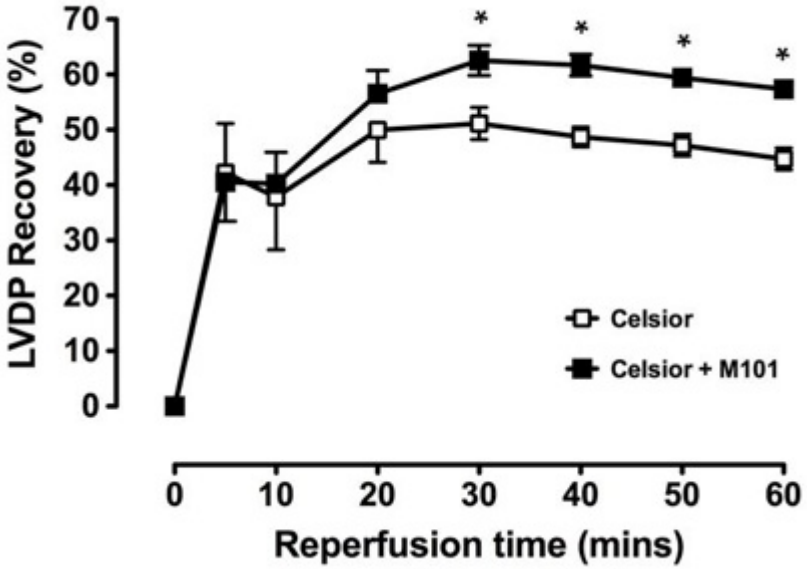
HEMO2life® for heart preservation

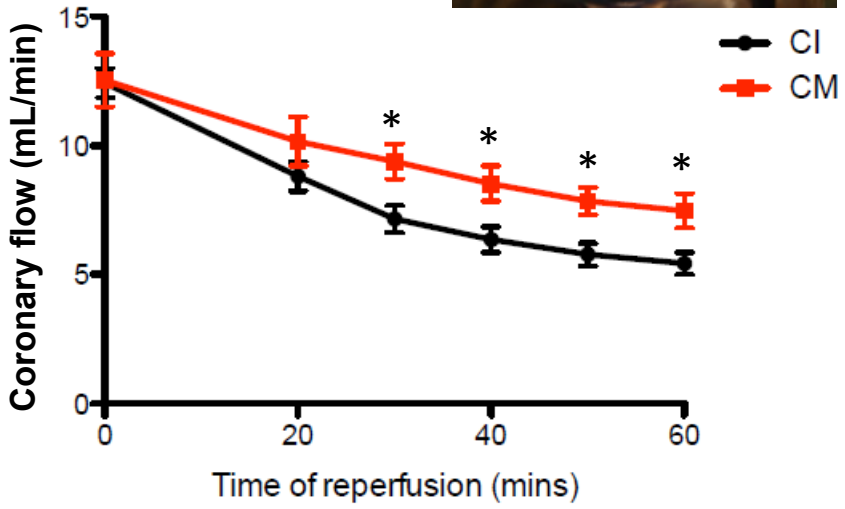
« We are committed to save lives »

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







HEMO2life® for liver preservation

Greffons Hépatiques

Pr Karim Boudjema (Rennes)

Wound Healing

HEMARINA

« We are committed to save lives »

HEMHealing®

It has been shown in numerous clinical studies that typical wound partial pressures of oxygen are markedly reduced and may be the rate limiting process in wound repair. Supplemental oxygen has been shown to enhance healing dependent on dose and frequency,however, excessive or continuous oxygen may impair the normal healing process.

Although numerous topical medications and gels are promoted for ulcer care, relatively few have proved to be efficient. Topical antiseptics, such as povidone-iodine, are usually considered to be toxic to healing wounds. Generally, a warm, moist environment that is protected from external contamination is most conducive to wound healing. This can be provided by a number of commercially available special dressings, including semipermeable films, foams, hydrocolloids, and calcium alginate swabs.

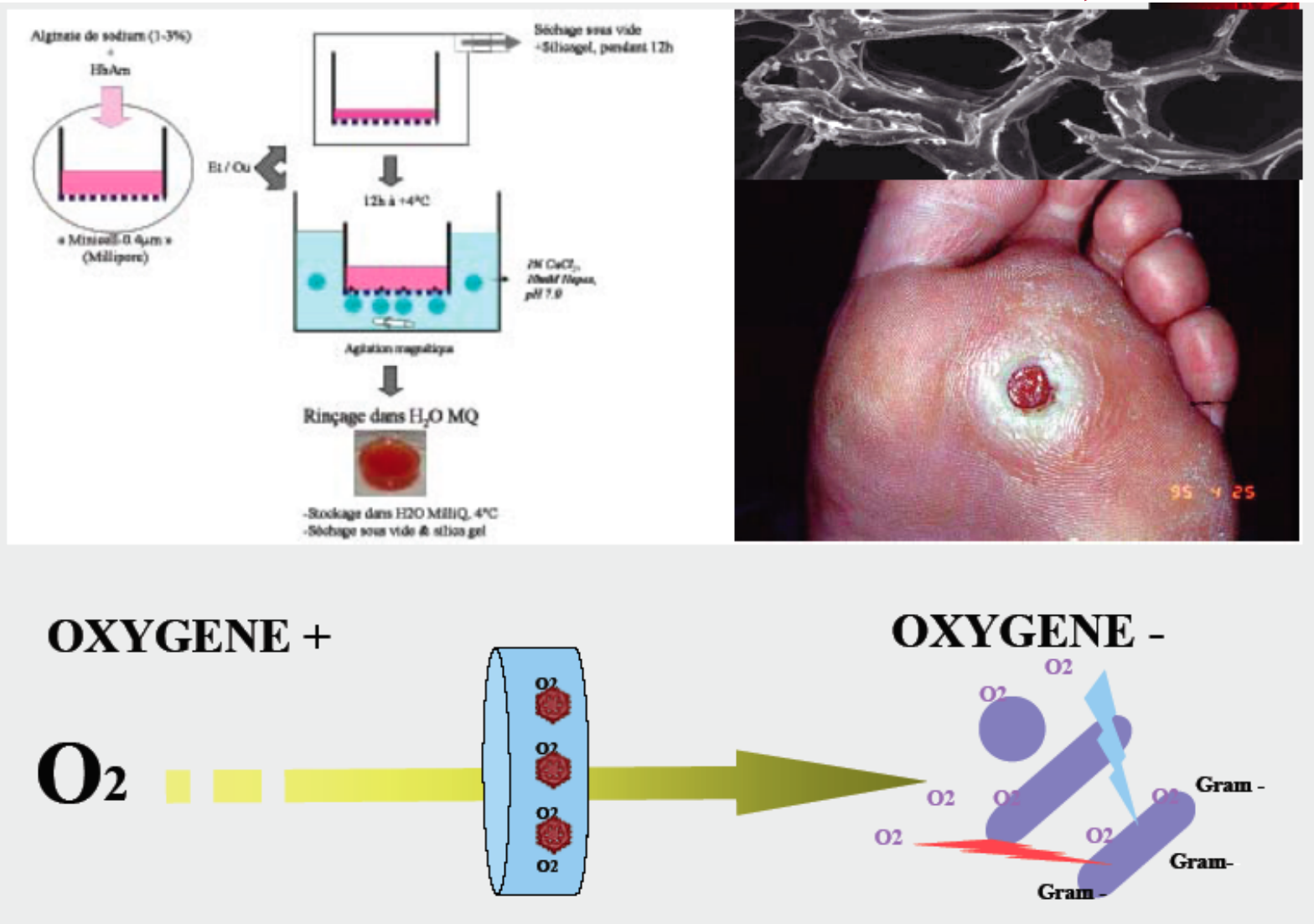
Any of this treatment is able to provide oxygen to the cell of the wound

Patented technology

HEMARINA

« We are committed to save lives »

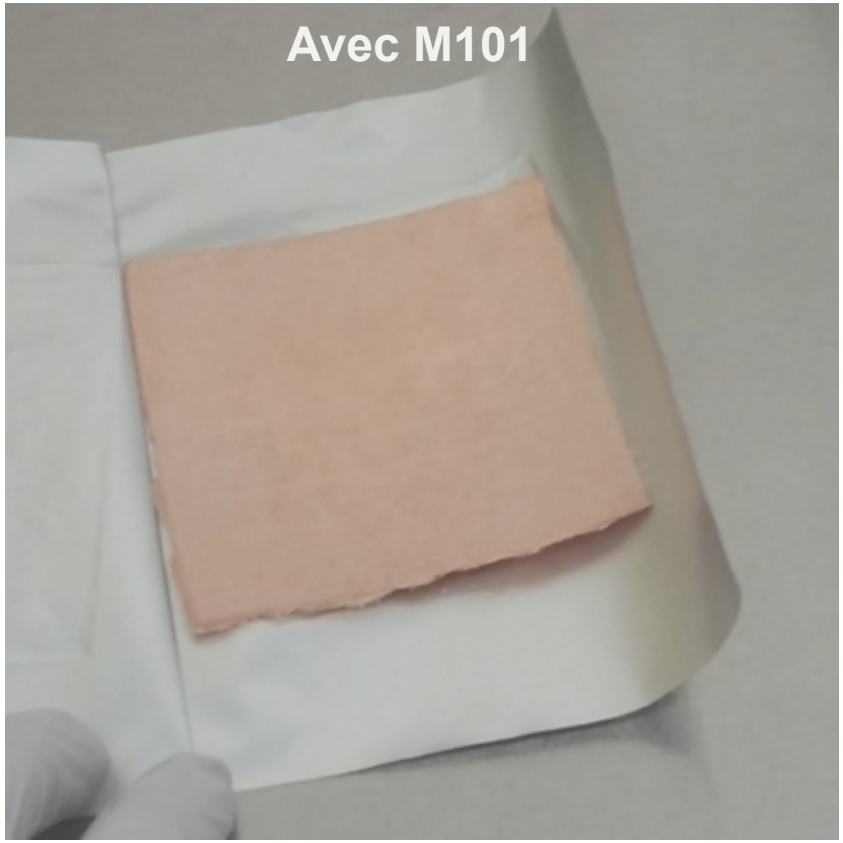
HEMHealing®



Patented technology

HEMHealing®

Sans M101



Efficacité démontrée *in vitro* et *in vivo* avec un industriel

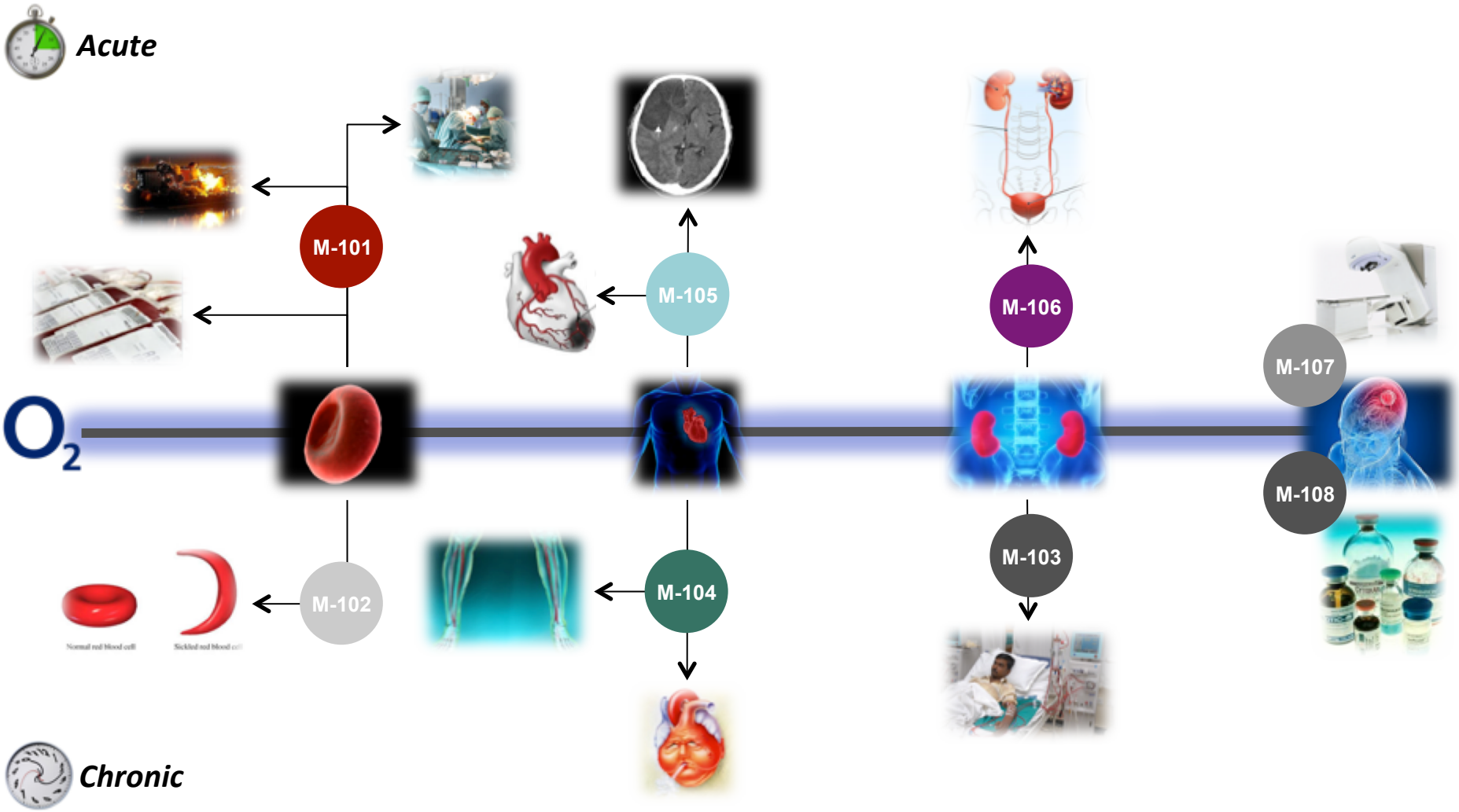
Patented technology

Blood Oxygen Transporter

HEMARINA

« We are committed to save lives »

HEMOXYCarrier®



HEMOXYCarrier® - Safety

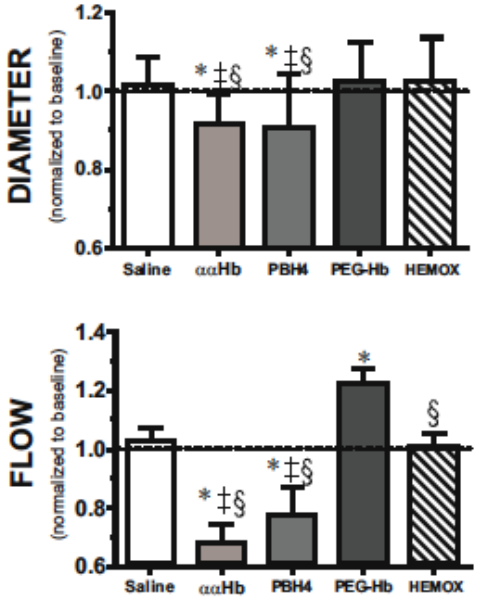


Fig. (4). Summary of diameter and flow (Q) response at the microvascular level with molecular hemoglobins in hamster model. The smaller molecular Hbs (ααHb and PBH4) caused arteriolar constriction leading to reduced microvascular perfusion compared to PEG-Hb and HEMOXYCarrier®. Both HEMOXYCarrier® and PEG-Hb did not change arteriolar diameter compared to baseline and saline. However, increased arteriolar blood flow levels were achieved with PEG-Hb, while HEMOXYCarrier® had unchanged levels. ααHb and PBH4 induced reduced arteriolar blood flow levels. Blood flow data (Q) is presented as mean ± sem. Parameters are presented relative to baseline, thus no change from baseline would be denoted as 1, while 1.05 would mean a 5% increase from baseline. *, $p < 0.05$ relative to saline; ‡ , $p < 0.05$ relative to HEMOX; § , $p < 0.05$ relative to PEG-Hb.

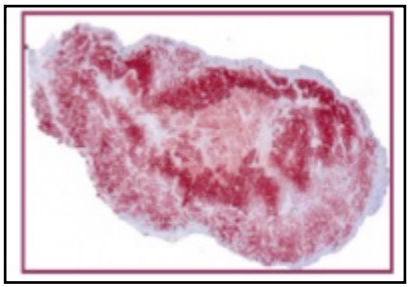
Tsai et al., CDD, 2012

« We are committed to save lives »

HEMOXYCarrier® - Efficacy

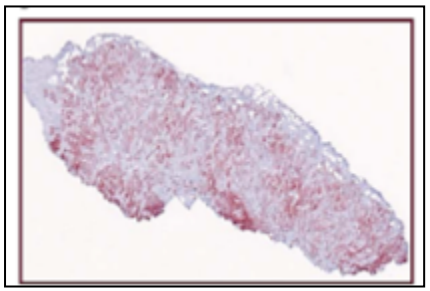
- **Tissue Oxygenation potency – radiotherapy adjuvent**
  - Human subcutaneous tumor model in mice (strong tissue hypoxia)
  - IV treatment with HEMOXYCarrier® (60, 600 and 1200 mg/kg)
  - Evaluation of tumoral tissue hypoxia (Glut-1 labelling)

Hypoxic Tumoral Tissue



- Poor oxygenation
- Necrotic areas

Tumoral Tissue 1h after the treatment



Increase of tissue oxygenation

- Increase of tissue oxygenation after the treatment with HEMOXYCarrier® *(Submitted Publication)*
- Applications in radiotherapy and chemotherapy: increase of the sensibility of solid tumors to treatment *(Patented)*

Le Gall et al., J. Biotech 2014

HEMOXYCarrier® - Efficacy on Trauma Brain Injury

US Navy collaborative research agreement

Scheduled:

- Trauma brain injury model (TBI)
  - Efficiency study on rat model
  - Survival increasing vs control
  - Evaluation of Tissue oxygenation
  - Evaluation of inflammation and oxydative stress

- Plan further studies of TBI and hemorrhagic models in large animals

Moon et al. (2015) Cerebral vasoactivity and oxygenation with oxygen carrier M-101 in rats

« We are committed to save lives »

HEMOXYCarrier® - Efficacy on Trauma Brain Injury

US Navy collaborative research agreement

- Dose ranging safety study on healthy rat

Pharmacodynamics evaluation: blood pressure, heart rate, microvasoconstriction

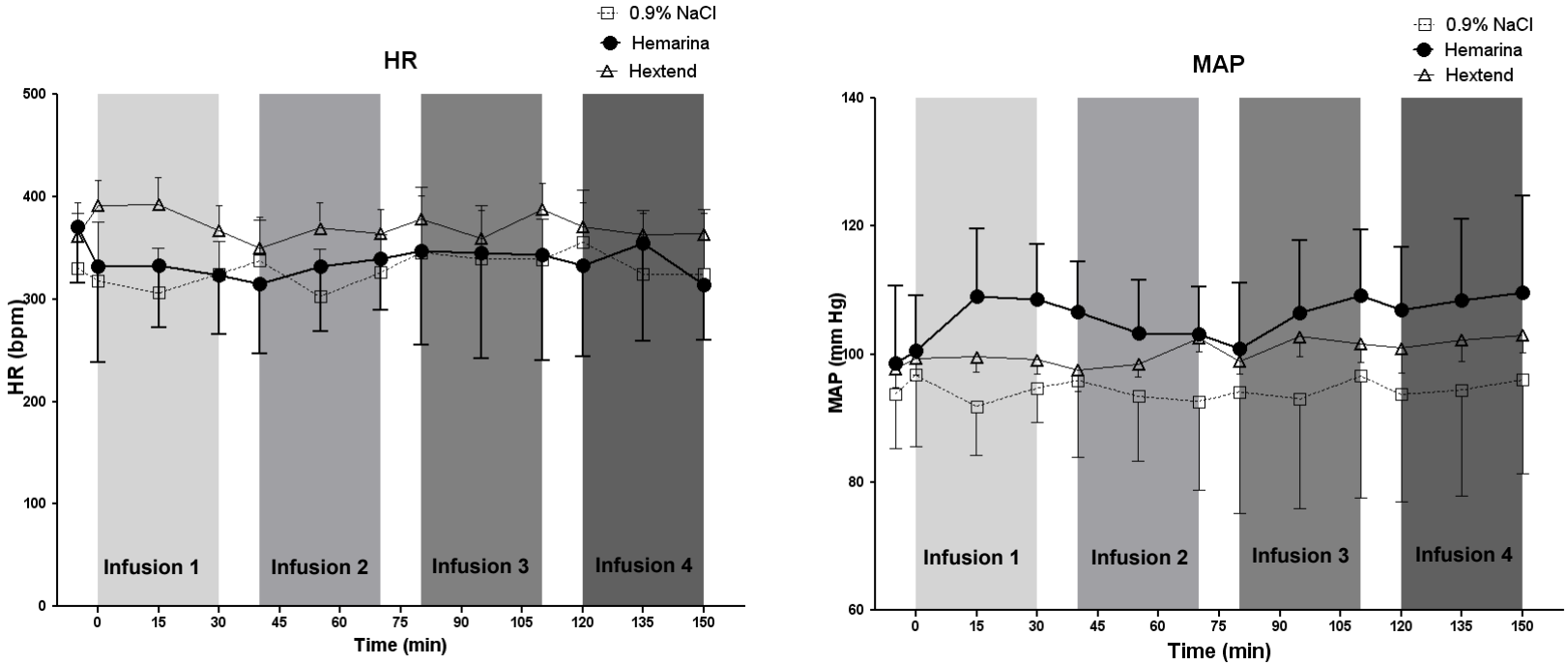
Moon et al. (2015) Cerebral vasoactivity and oxygenation with oxygen carrier M-101 in rats

HEMOXYCarrier® - Safety

US Navy collaborative research agreement

- Dose ranging safety study on healthy rat

Pharmacodynamics evaluation: blood pressure, heart rate, microvasoconstriction

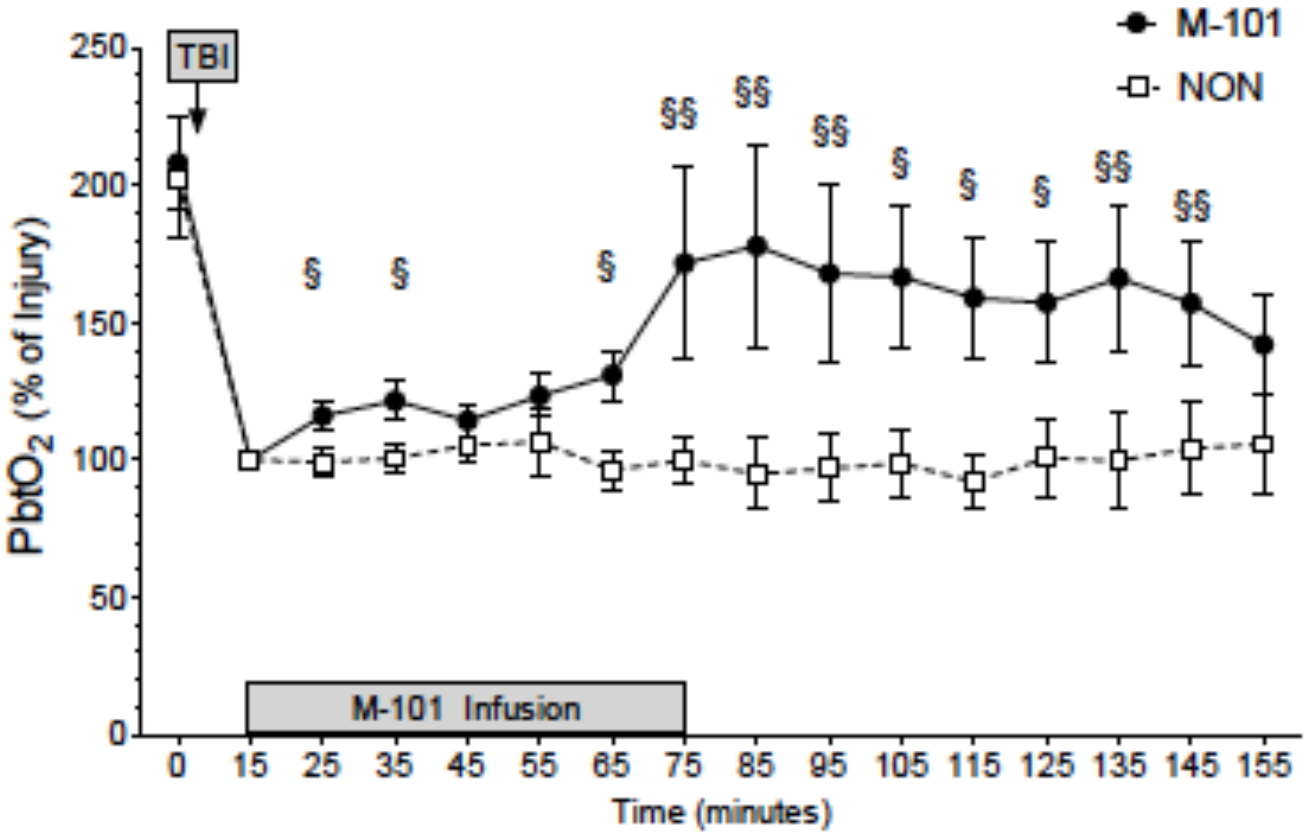


- HR changes with Hemarina-M101 similar to the ones of control groups (Maximal decrease of HR of about 13-15% compared to baseline values)
- Maximum increase of MAP of about 10% compared to baseline values (T15 min)

Moon et al. (2015) Cerebral vasoactivity and oxygenation with oxygen carrier M-101 in rats

HEMOXYCarrier® - Efficacy on Trauma Brain Injury

US Navy collaborative research agreement



Moon et al. (2015) Cerebral vasoactivity and oxygenation with oxygen carrier M-101 in rats

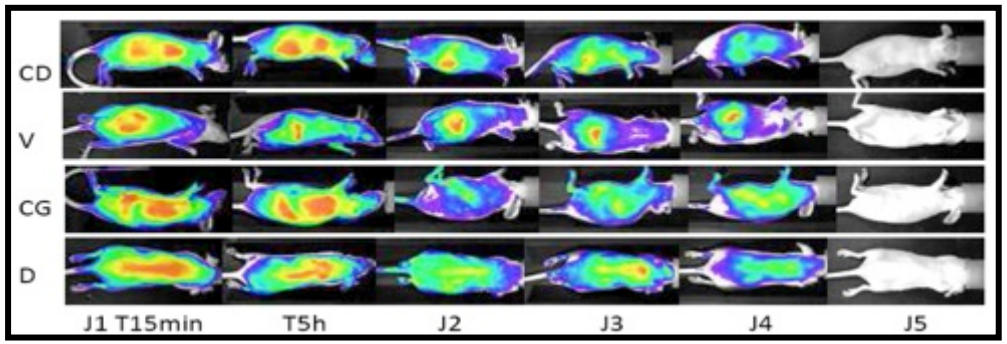
HEMARINA

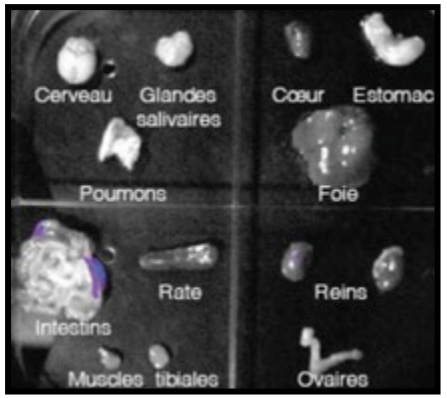
« We are committed to save lives »

HEMOXYCarrier® - Pharmacokinetic/ Biodistribution

In vivo biodistribution by fluorescence imaging *(Article submitted)*

- Mice model
- IV administration of HEMOXYCarrier® (200 mg/kg)
- Quantification of the fluorescence:
  - Whole body until 4 days after treatment
  - Isolated organs





D4

- Whole body distribution: liver, kidney, ovaries, brain, lungs and heart
- Absence of accumulation
- Complete elimination 4 days after the injection

Plate-forme IBiSA « SynNanoVect »
Unité INSERM 613

Inserm IBiSA SynNanoVect

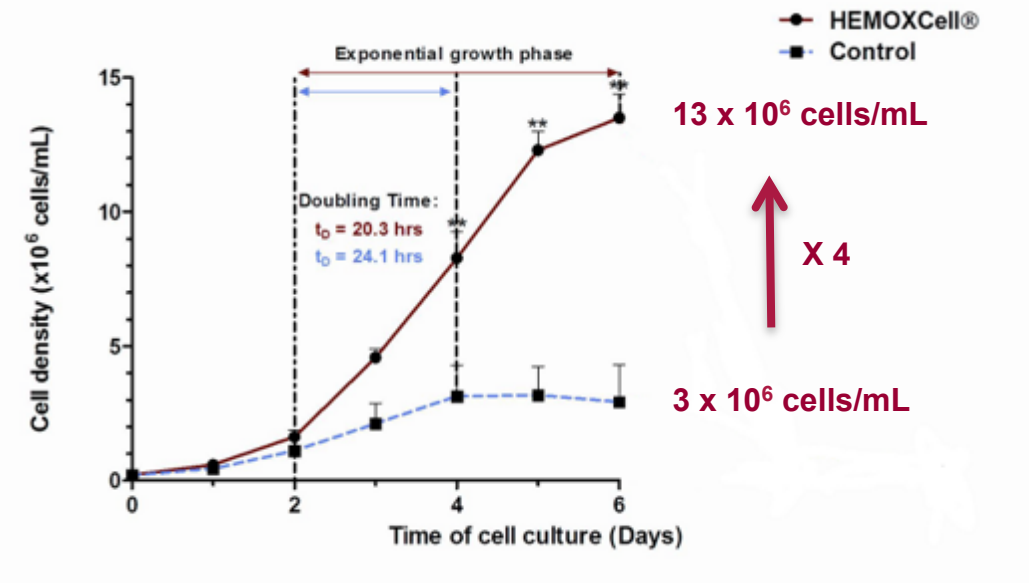
Le Gall et al., J. Biotech 2014

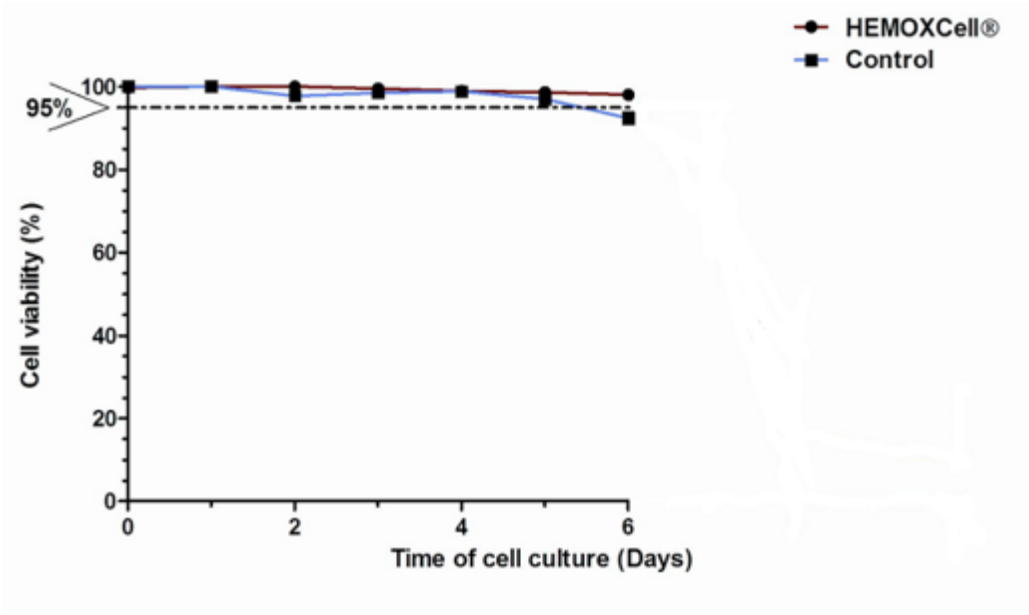
Cell media - Up-stream Process

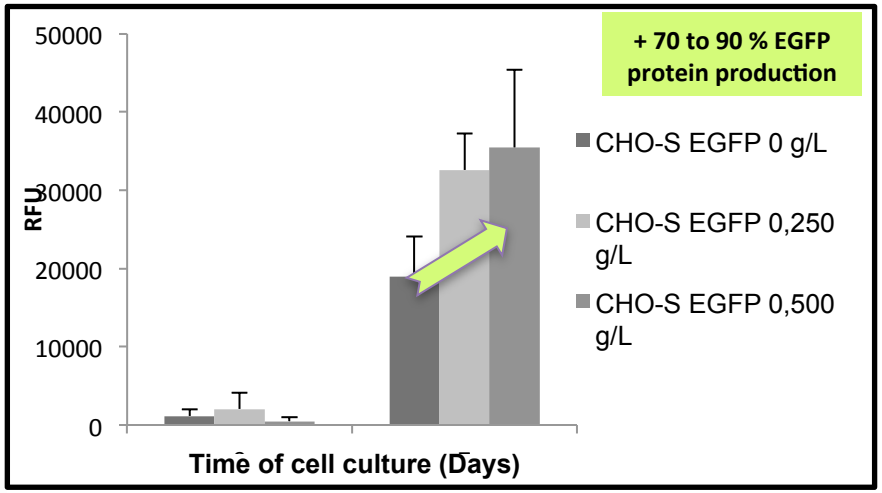
HEMARINA

« We are committed to save lives »

HEMOXCell®







Le Pape et al., Art. Cell, 2015

www.hemarina.com