

XXIII Encuentro de Cooperación Farma-Biotech

28 de noviembre de 2023

NIL10: a novel nanotechnological compound to reduce inflammation and preserves heart function after acute myocardial infarction



Carlos Zaragoza



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2. The Product
 - a) Target Indications
 - b) Innovative mechanisms of action
 - c) Differential features facing the market
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 - e) IPR protection
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3. Partnering Opportunities

1.The institutions



CARDIOLOGY DEPARTMENT.

- IMAGING
- CORNARY
- HEMODYNAMICS
- ARRHYTHMIAS
- HEART FAILURE
- VALVULAR PATHOLOGY
- **RESEARCH**

HEAD OF THE RESEARCH UNIT CARDIOLOGY DEPARTMENT

- | | LAB COMPOSITION |
|---------------------------------|------------------------|
| - 2 LAB TECHNICIANS | |
| - <u>4 PREDOCTORAL FELLOWS</u> | |
| - <u>4 POSTDOCTORAL FELLOWS</u> | |
| - 2 CARDIOLOGY FELLOWS | |

1.The institutions



Universidad
Francisco de Vitoria
UFV Madrid

SCHOOL OF MEDICINE

- PROFESSOR OF PHYSIOLOGY
- PROFESSOR OF CARDIOLOGY

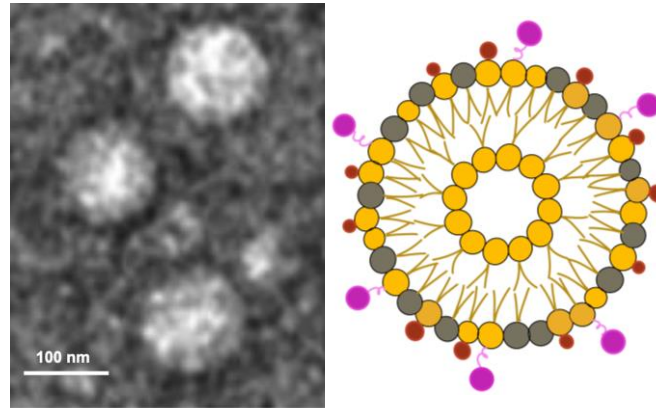
SCHOOL OF BIOMEDICINE

- PROFESSOR OF CARDIOLOGY

MASTER PROFFESOR

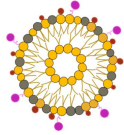
2. The Product

NIL10



NIL10: A NANOPARTICLE TARGETING IL10 RECEPTOR IN CARDIAC ISCHEMIA/REPERFUSION

2. The Product



NIL10

a) Target Indications

A1.NIL10 INDUCES CARDIAC PROTECTION IN RESPONSE TO ACUTE MYOCARDIAL INFARCTION

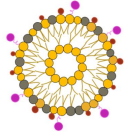
A2.NIL10 INDUCES CARDIAC PROTECTION IN EARLY HEART FAILURE

A3. NIL10 INDUCES CARDIAC PROTECTION THROUGH ADMINISTRATION OF AUTOLOGOUS “MODULATED MONOCYTES”.

A4. IN PROGRESS: PREVENTION OF ATHEROSCLEROSIS.

A5. IN PROGRESS: CARDIOTOXICITY INHIBITION IN RESPONSE TO TREATMENT WITH ANTHRACYCLINES

2. The Product



NIL10

b) Innovative mechanisms of action

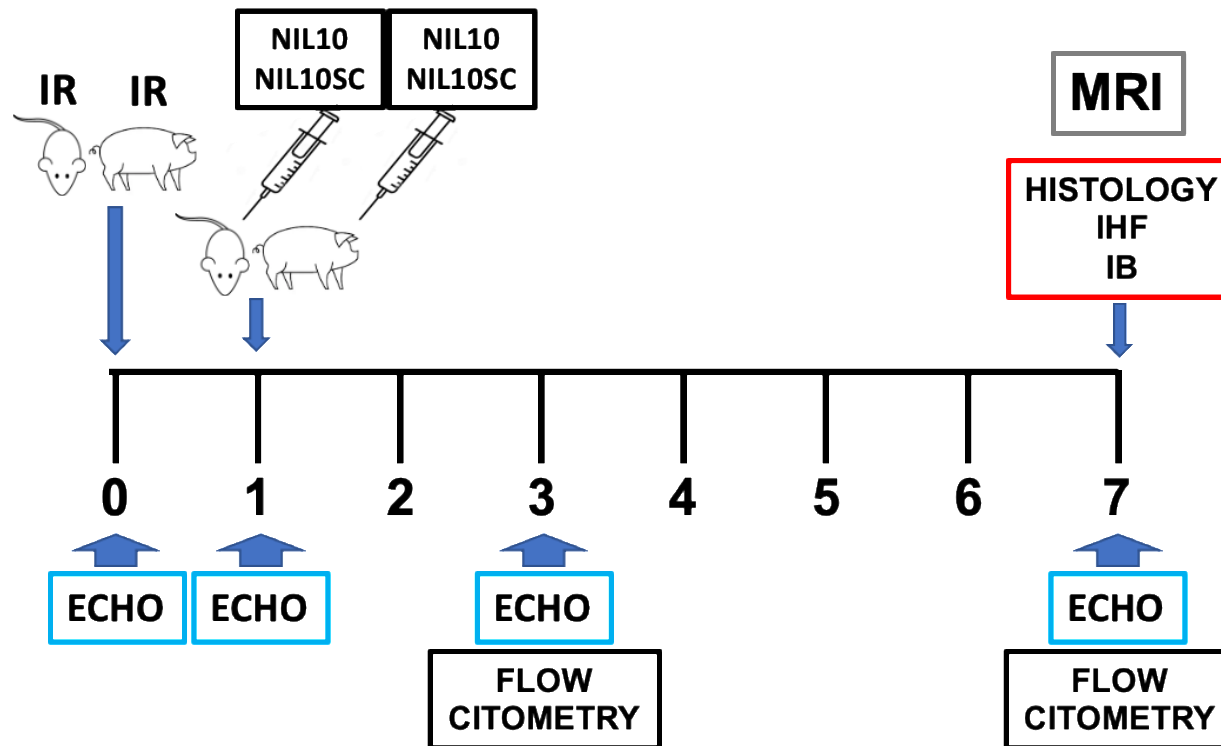
NIL10 INDUCES:

- MACROPHAGE POLARIZATION TOWARDS RESOLUTION OF INFLAMMATION BY ACTIVATING IL10 RECEPTOR THROUGH STAT3 MOLECULAR SIGNALING PATHWAY AND
- STAT-3 DEPENDENT PRO-INFLAMMATORY TRANSCRIPTION FACTOR INHIBITION OF NF-KB.

2. The Product

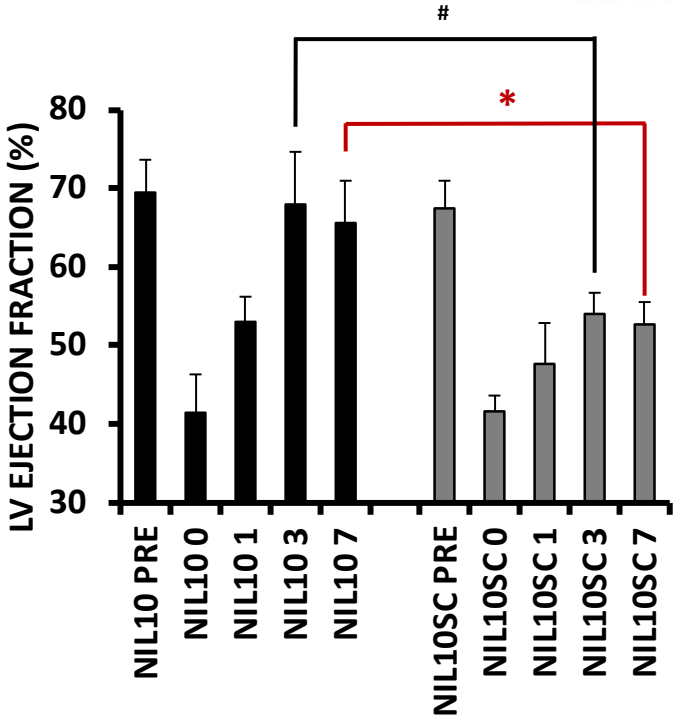
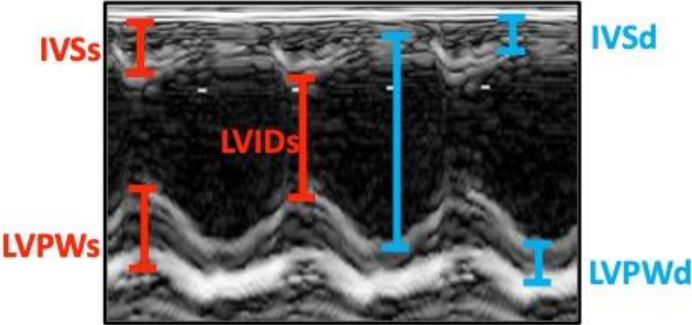
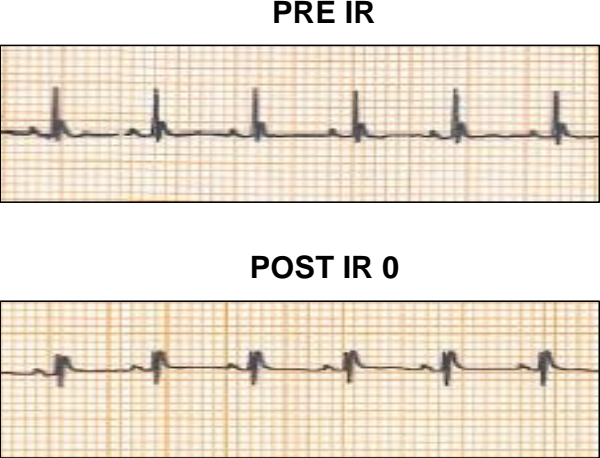


b) Innovative mechanisms of action



TARGETING IL10 IN CARDIAC IR

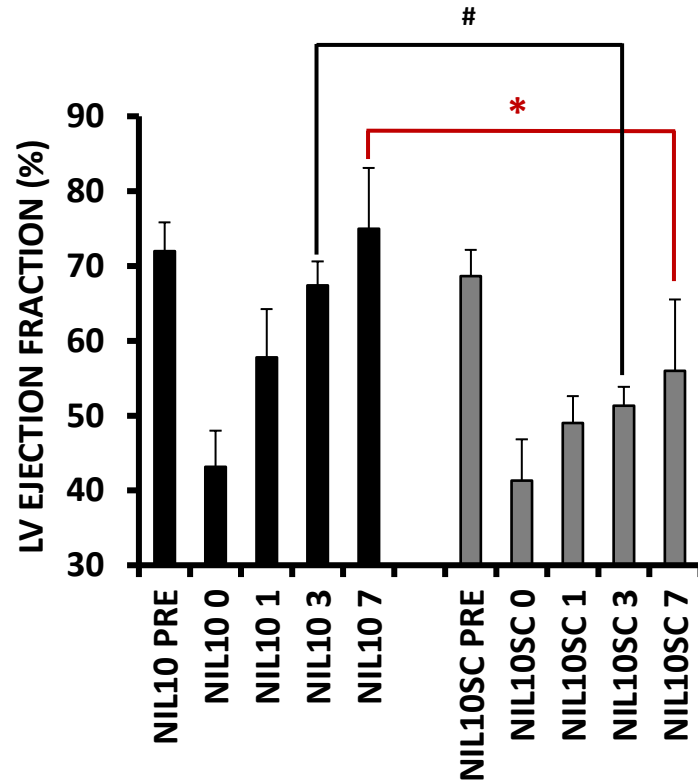
NIL10 improves cardiac function in mice subjected to cardiac IR



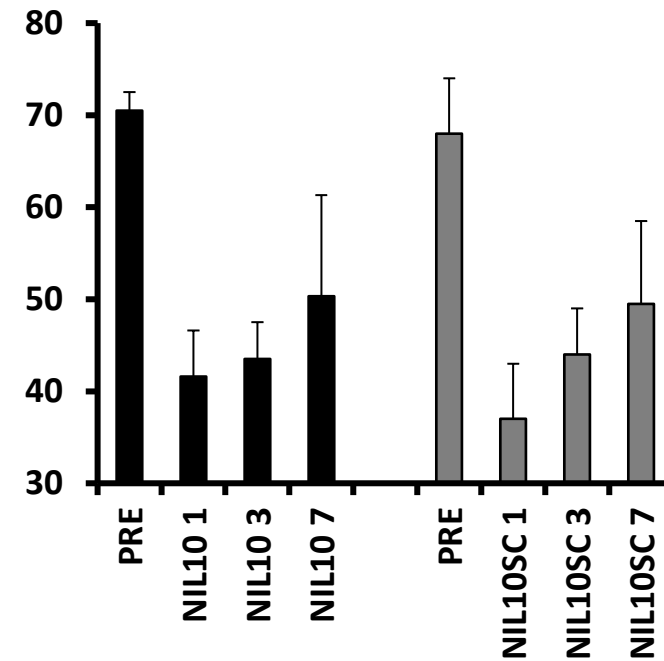
TARGETING IL10 IN CARDIAC IR

NIL10 improves cardiac function in mice subjected to cardiac IR

IL-10 NULL MICE

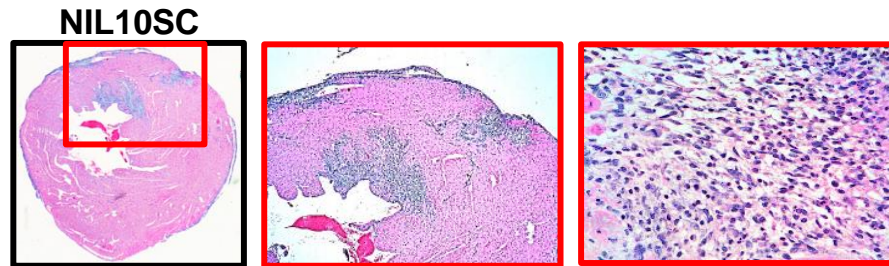
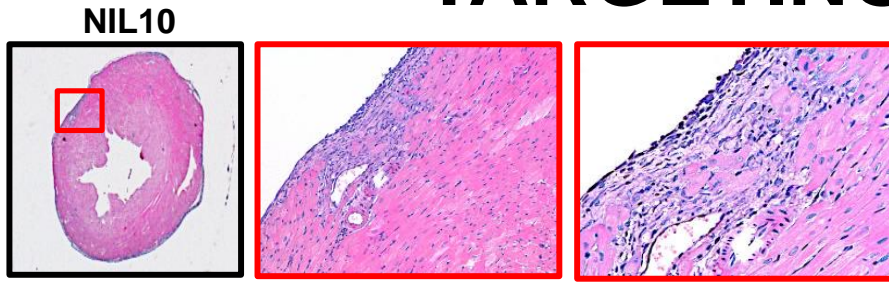


IL-10R NULL MICE

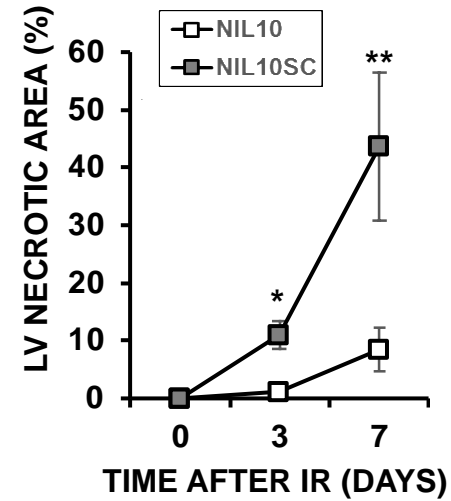
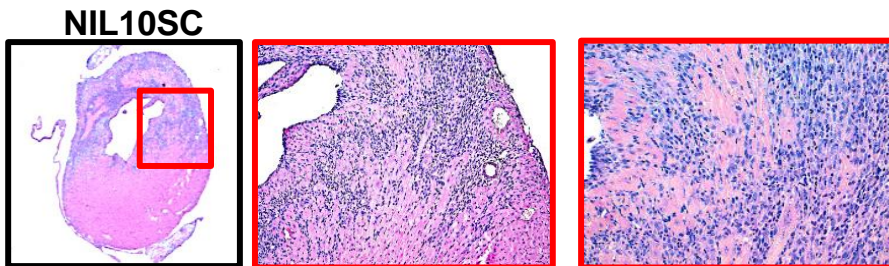


TARGETING IL10 IN CARDIAC IR

HEMATOXILIN/EOSIN DAY 3 POST IR

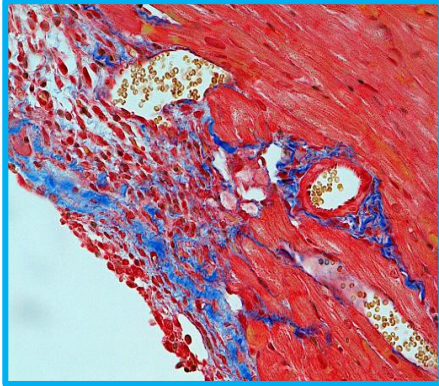


HEMATOXILIN/EOSIN DAY 7 POST IR

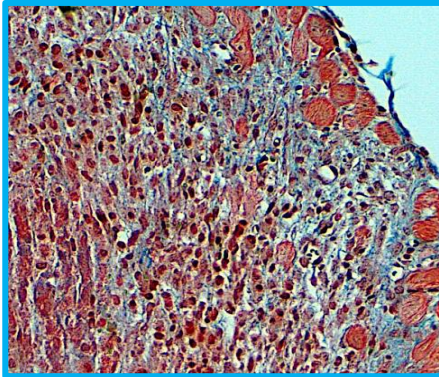
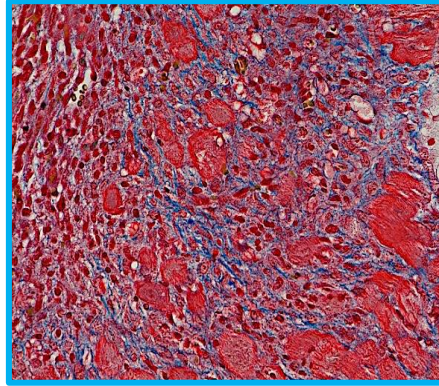


TARGETING IL10 IN CARDIAC IR

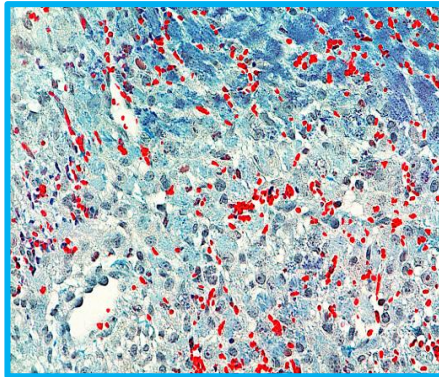
NIL10 D3



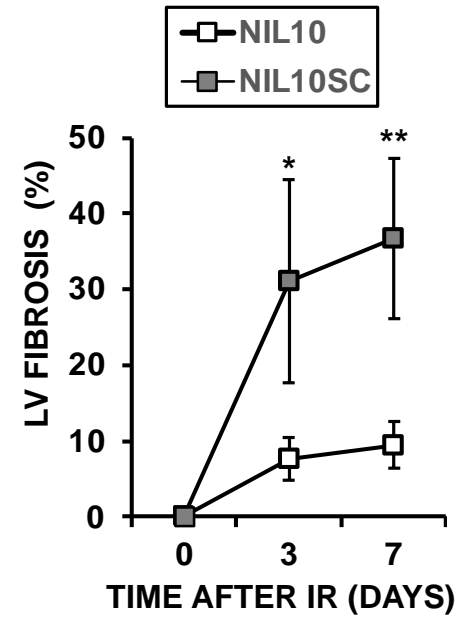
NIL10SC D3



NIL10 D7



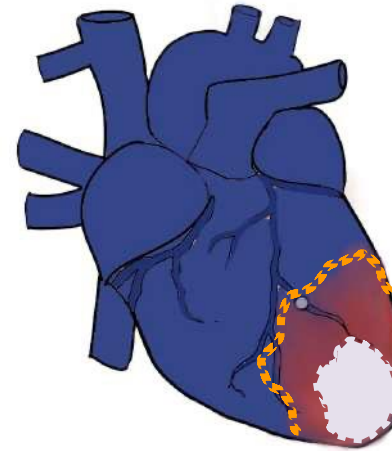
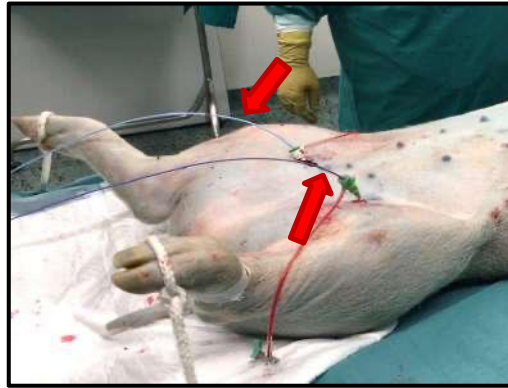
NIL10SC D7



TARGETING IL10 IN CARDIAC IR

ANGIOPLASTY
BALLOON
CATHETER

PIGTAIL
CATHETER

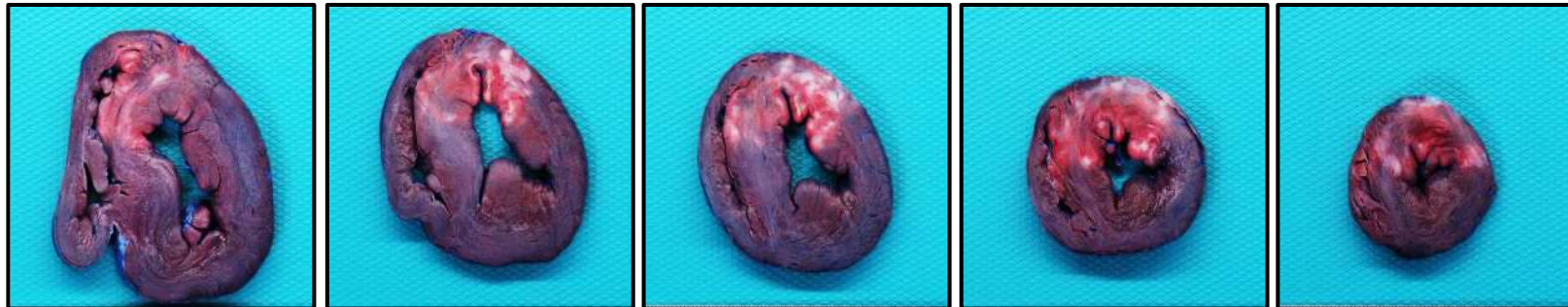


HEALTHY
AREA AT RISK
NECROTIC AREA

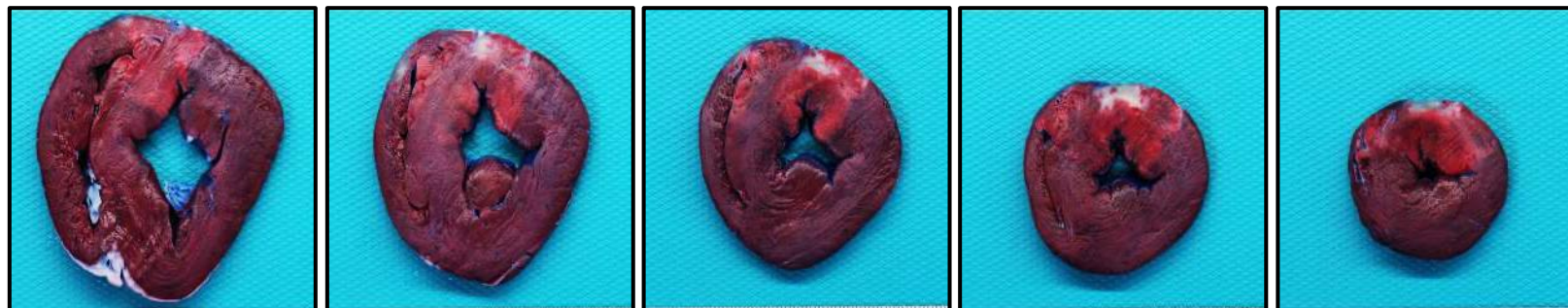
BASE

APEX

NIL10SC

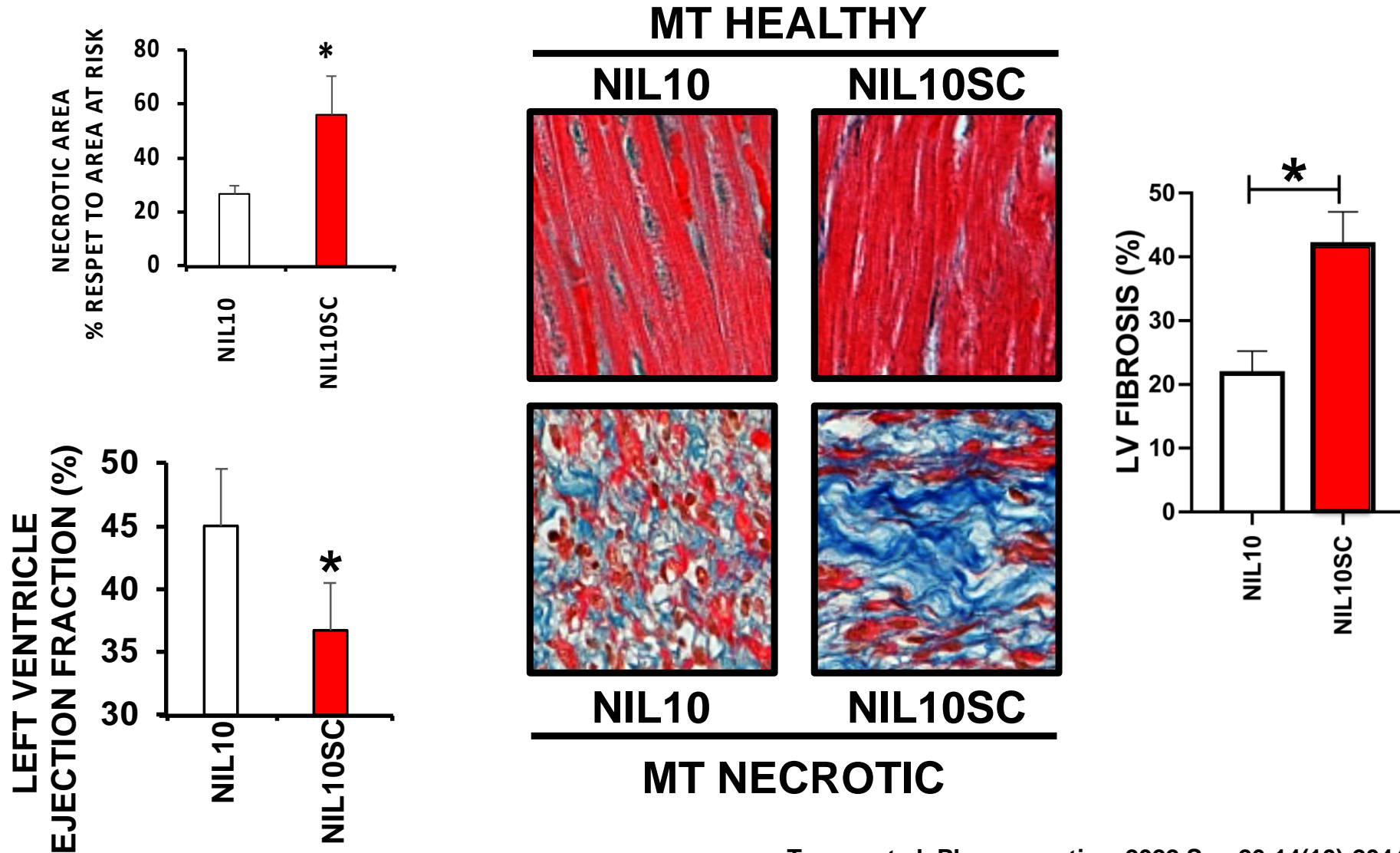


NIL10



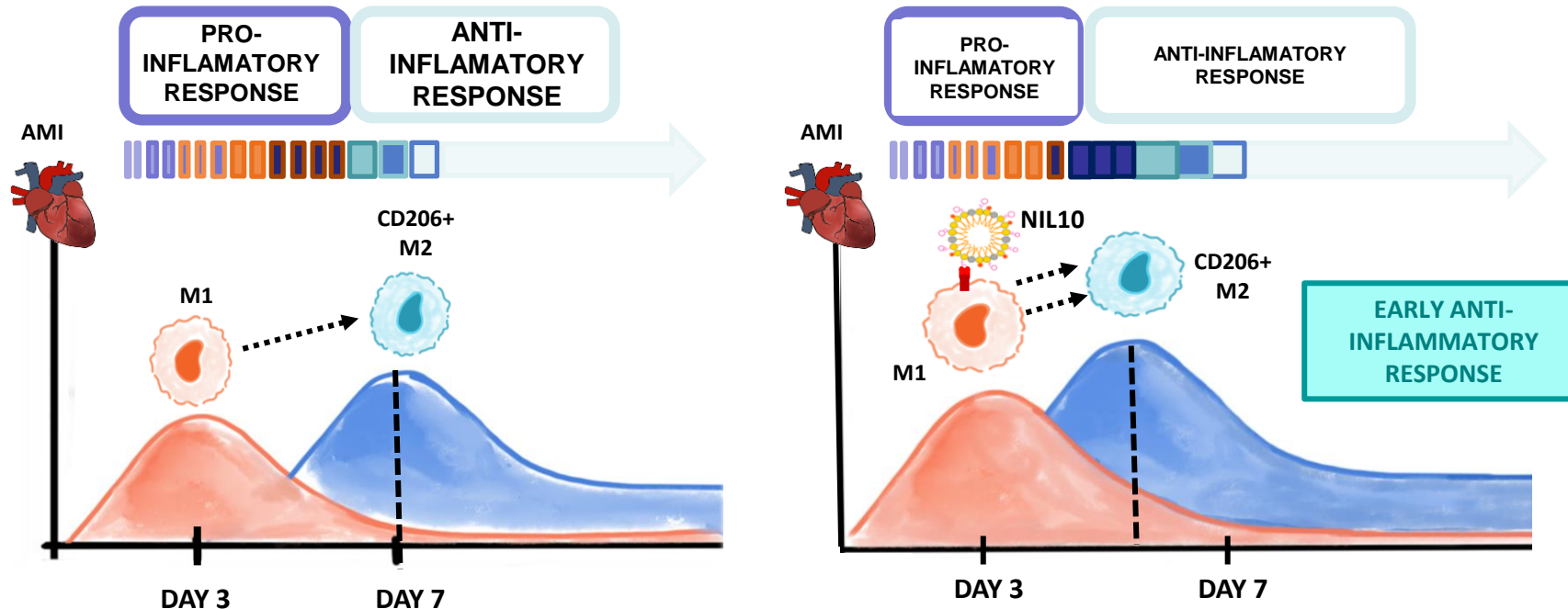
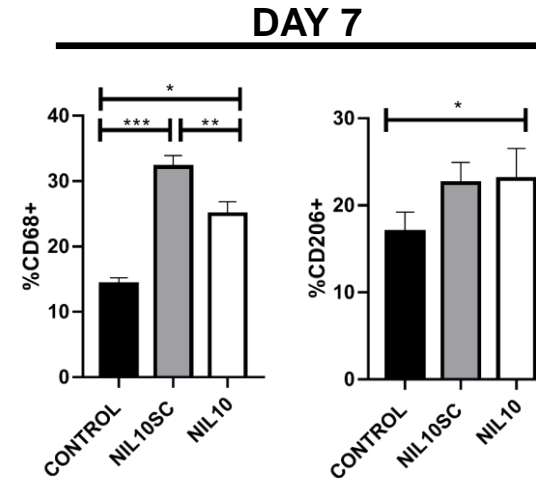
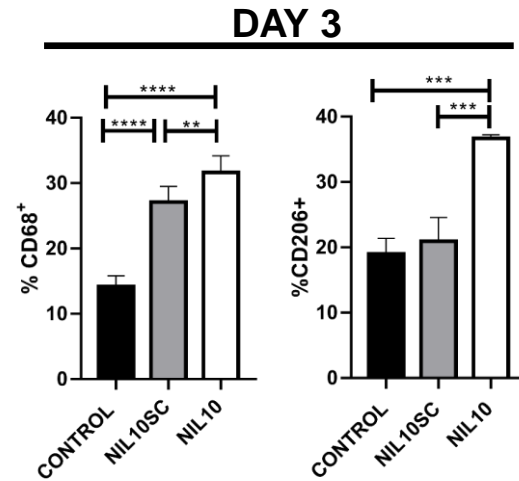
TARGETING IL10 IN CARDIAC IR

NIL10 IMPROVES CARDIAC FUNCTION AND REDUCES CARDIAC NECROSIS IN PIGS SUBJECTED TO CARDIAC IR



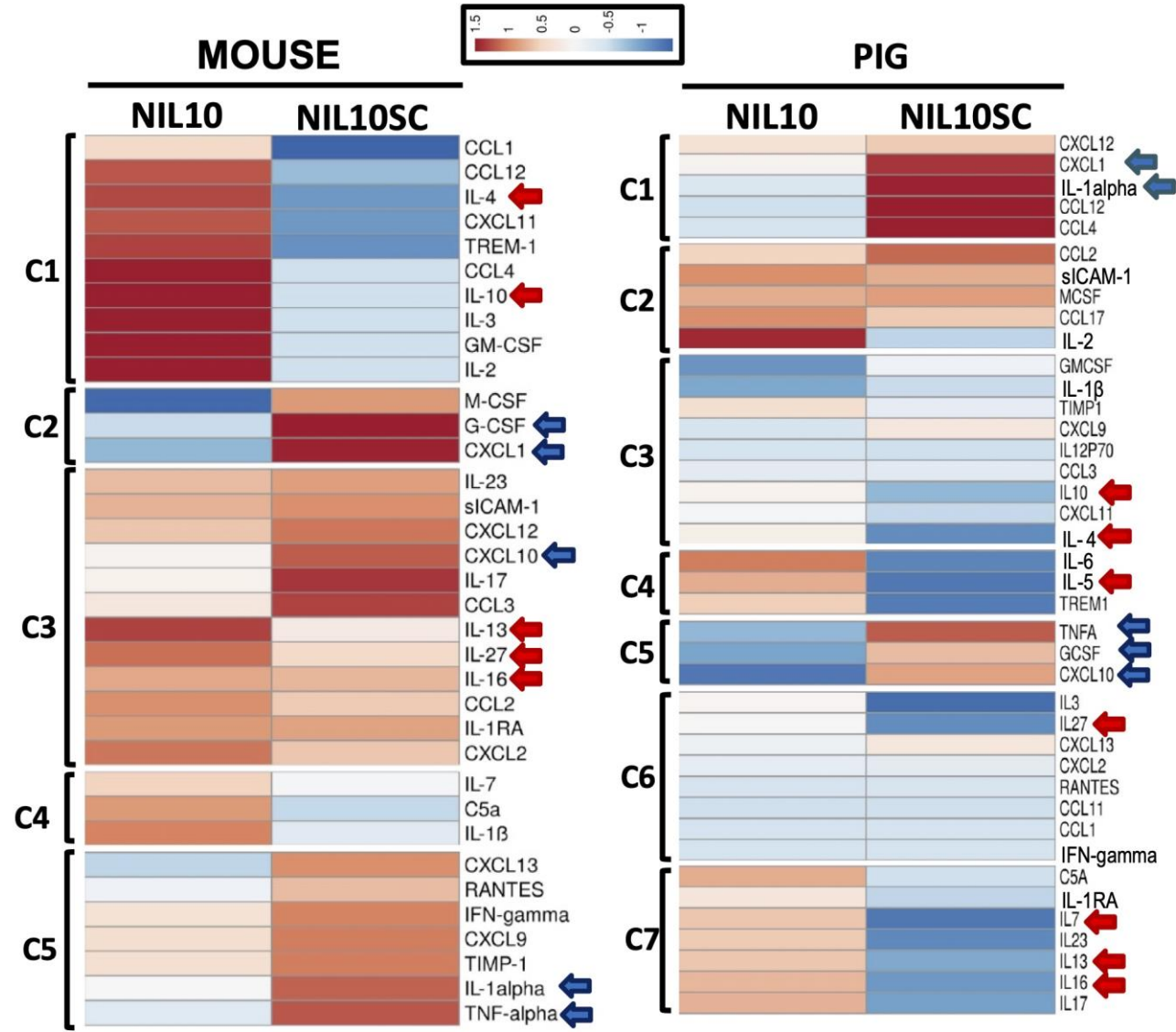
TARGETING IL10 IN CARDIAC IR

NIL10 SPEEDS INFLAMMATION RESOLUTION IN PIGS SUBJECTED TO IR



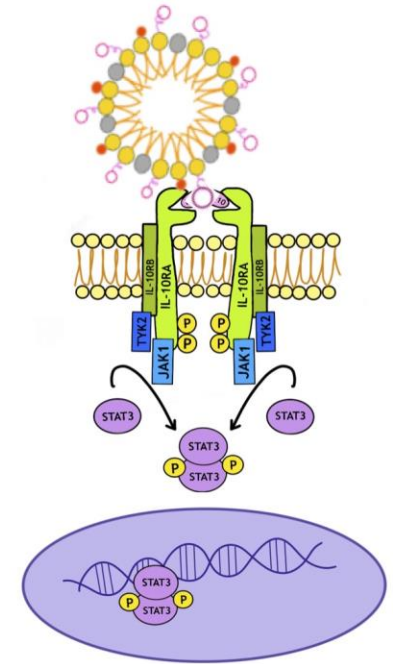
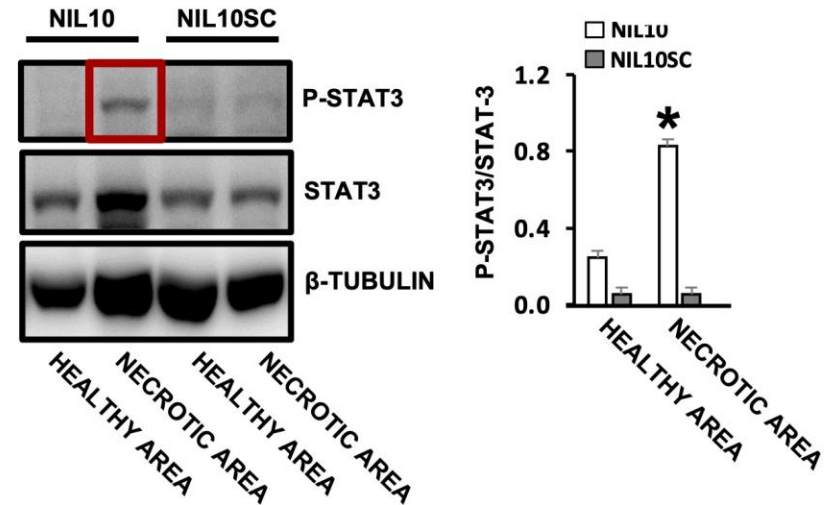
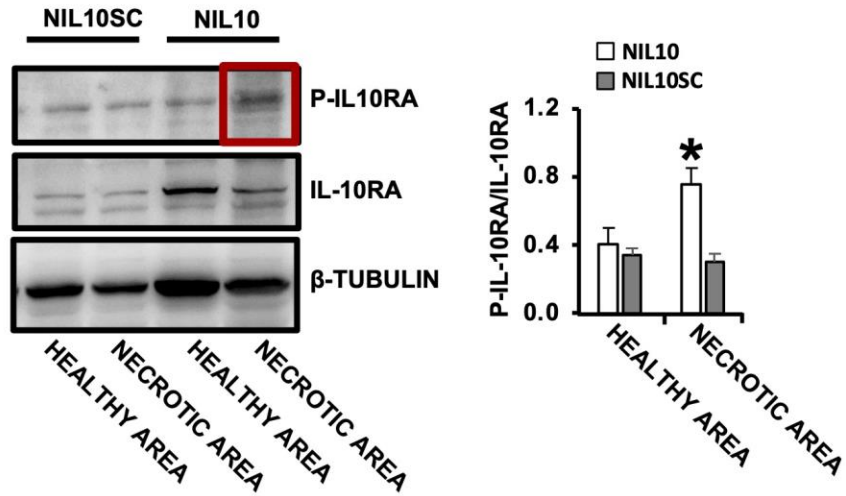
TARGETING IL10 IN CARDIAC IR

NIL10 CREATES A SYSTEMIC ANTI-INFLAMMATORY RESPONSE IN MICE AND PIGS SUBJECTED TO IR



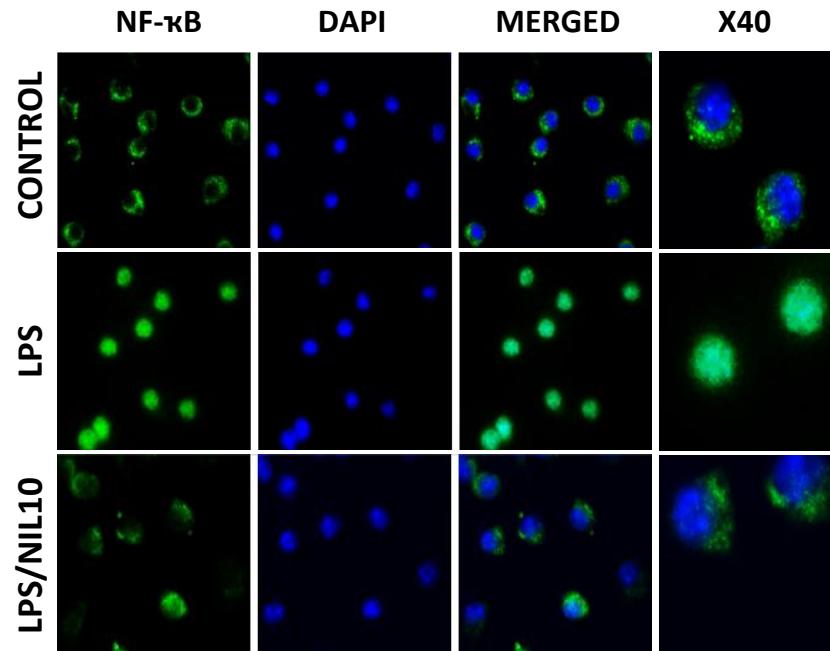
TARGETING IL10 IN CARDIAC IR

NIL10 INDUCES ACTIVATION OF THE IL10R/STAT3 DOWNSTREAM PATHWAY

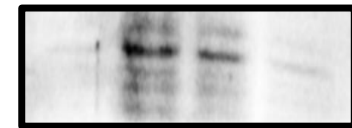


TARGETING IL10 IN CARDIAC IR

NIL10 PREVENTS NF κ B NUCLEAR TRANSLOCATION IN MACROPHAGES



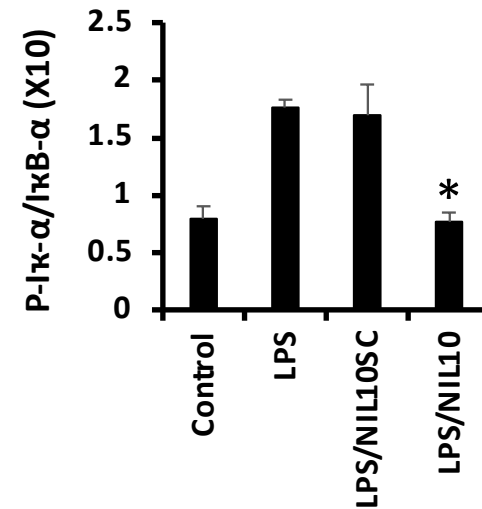
LPS	-	+	+	+
NIL10	-	-	-	+
NIL10SC	-	-	+	-



P-I κ B- α

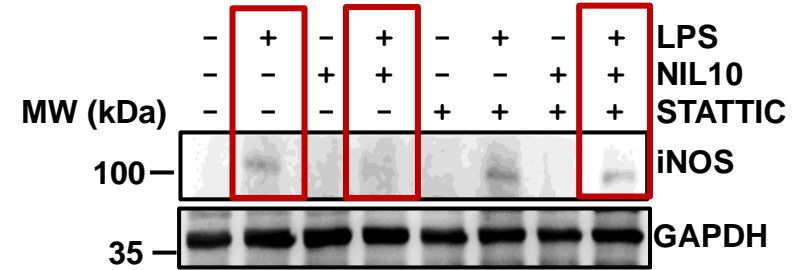
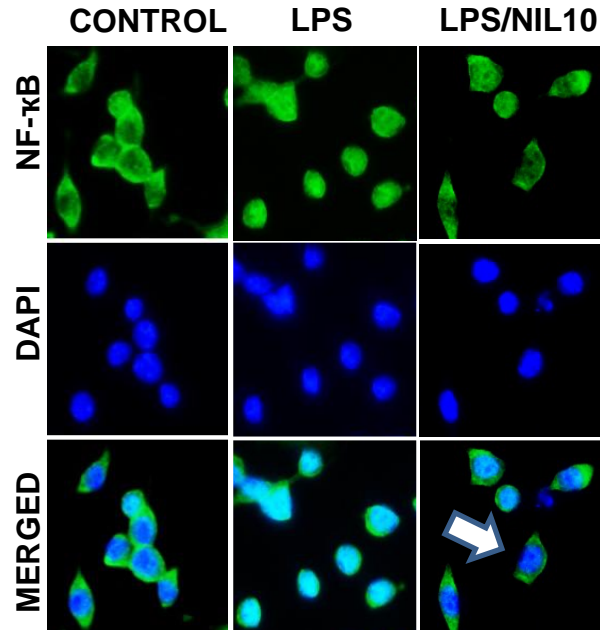


β -TUBULINA

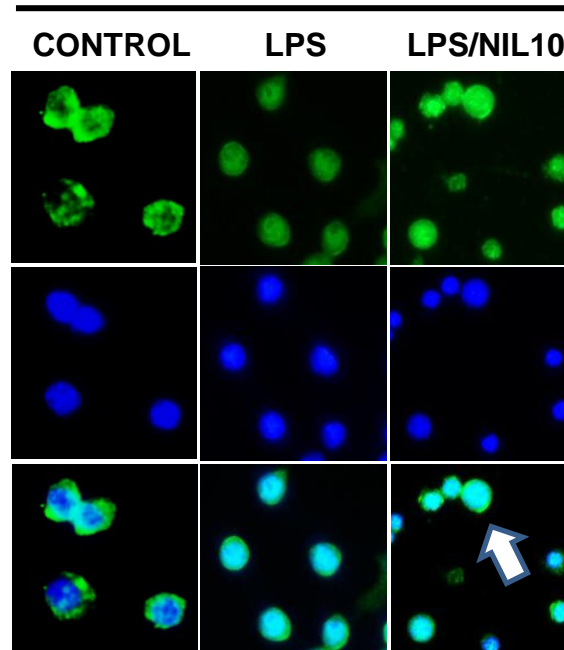


TARGETING IL10 IN CARDIAC IR

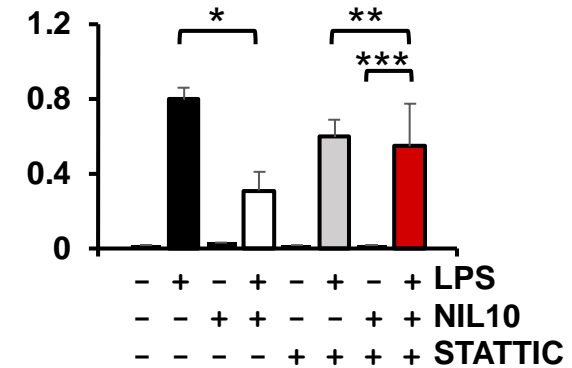
NIL10 INHIBITS STAT3 DEPENDENT NFκB ACTIVITY IN MACROPHAGES



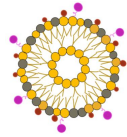
STAT3C



EXPRESSION OF iNOS



2. The Product

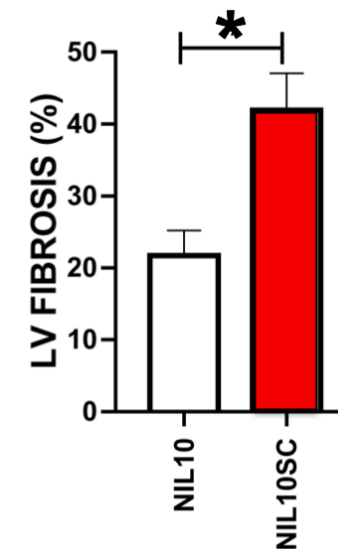
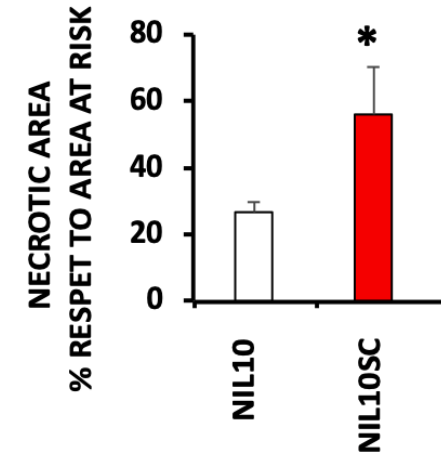


NIL10

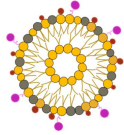
c) Differential features facing the market

By injecting one single shot of NIL10:

- 1. NIL10 PREVENTS CARDIAC NECROSIS AFTER ACUTE MYOCARDIAL INFARCTION WITHIN THE FIRST 7 DAYS**
- 2. NIL10 PREVENTS CARDIAC FIBROSIS AFTER ACUTE MYOCARDIAL INFARCTION WITHIN THE FIRST 7 DAYS**



2. The Product



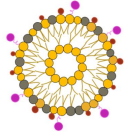
NIL10

c) Differential features facing the market

By injecting a second shot of NIL10:

- 1. NIL10 PREVENTS CARDIAC NECROSIS BY DAY 28
AFTER ACUTE MYOCARDIAL INFARCTION**

2. The Product

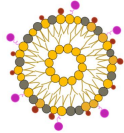


NIL10

c) Differential features facing the market

- **NIL10 IS A NANOPARTICLE: UNIQUE CAPABILITY TO ACCESS MICROVASCULATURE, ALLOWING FOR EFFICIENT PERFUSION INTO TISSUES.**
- **NO SIDE-EFFECTS REPORTED IN ANIMAL MODELS.**
- **NO CARDIAC RENAL, AND LIVER, TOXICITY.**

2. The Product



NIL10

d) Current status of development

**NIL10 WAS ALREADY TESTED IN MURINE AND PORCINE MODELS
OF ACUTE MYOCARDIAL INFARCTION**

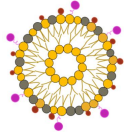
NIL10 EXPERIMENTS WERE REPRODUCED BY USING GMP-LIKE CONDITIONS

TECHNOLOGICAL READINESS LEVEL TRL:

6: MODELO DE SISTEMA EN UN ENTORNO RELEVANTE

7: DEMOSTRACIÓN DE SISTEMA EN UN ENTORNO REAL

2. The Product

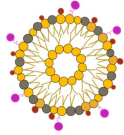


NIL10

e) IPR protection

Carlos Zaragoza, Laura Tesoro, Ignacio Hernandez, Rafael Ramirez-Carracedo, Laura Botana, Javier Díez-Mata, Marco Filice, Karina Ovejero, **PCT/EP2022/067242**. PREVENTION AND/OR TREATMENT OF CARDIAC DAMAGE.

2. The Product

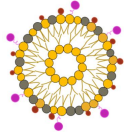


NIL10

e) Pitfalls & Risks to be considered

1. LONG TERM SIDE EFFECTS OF MULTIPLE ADMINISTRATION OF NIL10
2. GLP REPRODUCIBILITY
3. TOXICITY IN HUMANS

3. Partnering Opportunities

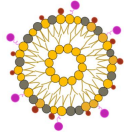


NIL10

**PHARMA INDUSTRY
GOVERNMENT**

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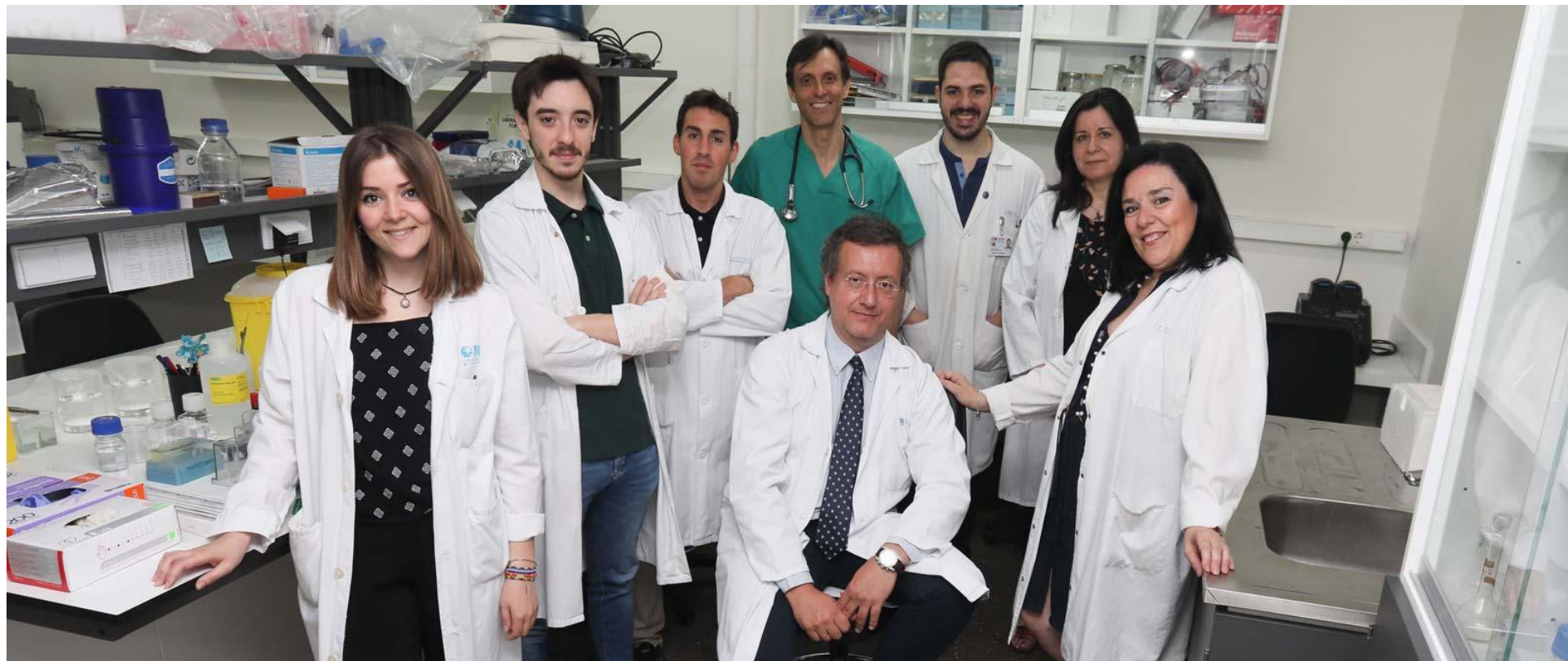
RESEARCH FUNDING



NIL10

1. **PDC2021-121817-I00.** VALORIZACION PARA LA TRANSFERENCIA A LA INDUSTRIA DE NIL10: UNA NUEVA NANOPARTICULA CREADA PARA REDUCIR LA INSUFICIENCIA CARDIACA AGUDA POSTINFARTO (SAF2017-87342-R). **PLAN ESTATAL MICINN. PROYECTOS PRUEBA DE CONCEPTO.** € 150000. INVESTIGADOR PRINCIPAL.
2. **SAF 2020. PID2020-118371RB-I00.** PREVENCIÓN DE LA INSUFICIENCIA CARDIACA AGUDA, MEDIANTE EL USO NO INVASIVO DE NANOTECNOLOGIA FRENTE AL REMODELADO ADVERSO, EN MODELOS ANIMALES CON POTENCIAL TRASLACION CLINICA. **Plan Estatal Retos. MICINN.** (Hospital Universitario Ramón y Cajal). 01/09/2021- 30/08/2024. 157.000 €. INVESTIGADOR PRINCIPAL.
3. NON-INVASIVE MOLECULAR IMAGING OF CARDIAC INFLAMMATORY REGRESSION IN RESPONSE TO ACUTE MYOCARDIAL INFARCTION, BY USING NANOPARTICLES TARGETING MACROPHAGE POLARIZATION IN A PORCINE MODEL OF CORONARY ISCHEMIA/REPERFUSION. **Fundación BBVA. Ayudas a 6 equipos de investigación traslacional.** (Hospital Universitario Ramón y Cajal). 01/01/2018- 31/12/2021. 125.000 €. INVESTIGADOR PRINCIPAL
4. **SAF2017-87342-R,** Control de la remodelación cardiaca, mediante de nanotecnología aplicada la regulación de la respuesta inflamatoria en el corazón de modelos animales de isquemia/reperfusión Ministerio de Educación, Política Social y Deporte. **Plan Estatal MINECO.** (Hospital Universitario Ramón y Cajal). 01/01/2018- 31/12/2020. 145.200 €. INVESTIGADOR PRINCIPAL.
5. **DTS16/00229,** Nanotecnología aplicada a la imagen molecular por resonancia para la visualización no invasiva de marcadores de síndrome coronario agudo y su contribución como herramienta terapeutica **Instituto de Salud Carlos III.** Investigación en salud con base tecnológica. (Hospital Universitario Ramón y Cajal). 01/01/2017- 31/12/2018. 99.550 €. INVESTIGADOR PRINCIPAL.

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THANK YOU!