

Neurovascular Research Lab was created within the Neurology Service at HUVH in 2001 **focused in Stroke research** from a basic and translational point of view. The lab. is nowadays is composed by a motivated group of 20 researchers: neurologists, biologists, technicians, neuropsychologists and nurses.

Vall Hebron Research Institute, Mediterranean building
1st floor, laboratories 106, 110, 120 and 123

PIs: Pilar Delgado, Mar Hernandez, Olga Maisterra, Anna Rosell, (Joan Montaner).



PREVENTION

- Non-invasive vascular markers of post-stroke cognitive impairment
- Diagnostic and prognostic markers in mixed dementias (Alzheimer's and cerebrovascular disease)

NEUROPROTECTION & BIOMARKERS

- Brain damage biomarkers
- Blood biomarkers to explore stroke subtypes
- Neuroprotection in cerebral ischemia
- Blood biomarkers as companion diagnostics in stroke

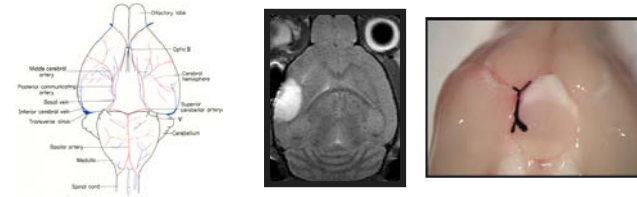
NEUROREPAIR

- Progenitor Cells for Neurorepair
- Nanomedical products for stroke treatments
- New molecular targets of neurorecovery
- Rehabilitation and biomarkers for stroke recovery

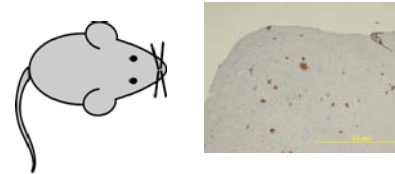
CEREBRAL AMYLOIDOSIS

- Search of new biomarkers for the diagnosis of Cerebral Amyloid Angiopathy
- Study of the mechanisms involved in the cerebral beta-amyloid deposition

- Multiple pre-clinical models of Stroke/Cerebral Ischemia

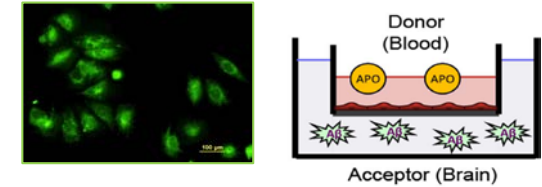


- Transgenic mouse models of cerebral beta-amyloidosis



- In vitro cell and tissue culturing including vascular models and progenitor cells.

- Blood, brain and CSF Biomarkers. Multicenter trials infrastructure

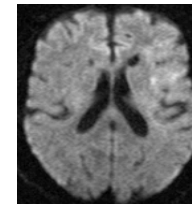
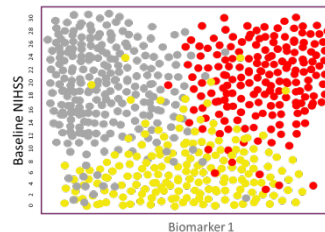


- Arrays of proteins performance and analysis



- Co-development of rapid POC tests

- Structural and functional brain imaging



Risk of cognitive impairment after small vessel stroke (P17/02222)

PI: Pilar Delgado

COHORT:

- AT LEAST 3 MONTHS AFTER LACUNAR STROKE
- LONGITUDINAL STUDY (BASELINE AND AFTER 2-YEARS FOLLOW-UP)
- BP variability (24 hours, circadian)
- Arterial stiffness (office and 24 hours moitoring)
- Cognitive markers (neuropsychological assessment)
- Plasma biomarkers (inflammation, stiffness, amyloid pathology, neurodegeneration)

NEXT STEPS (if granted, PI22): INCREASE SAMPLE SIZE (AND CENTERS), INCLUDE DEEP HEMORRHAGIC STROKE (COMBIVICS STUDY)

Other Ongoing Studies: Plasma and CSF markers of mixed dementia (AD plus cerebrovascular disease)



Horizon 2020
European Union funding
for Research & Innovation

A HUB-Lab for Stroke Surrogate Biomarkers



RESSTORE
Regenerative Stem Cell Therapy for Stroke

Videos

Sample preparation for biomarker studies



TOLLMark



Study of biomarkers to differentiate the etiology of stroke. Specifically, we have focused on the study of biomarkers to identify **atrial fibrillation (AF)** and understand its pathophysiology and relationship with cerebrovascular pathology within the framework of different projects.

- **AFRICAT: Atrial Fibrillation Research in CATalonia**

Biomarcadores de FA en pacientes asintomáticos para el uso en estrategias de *screening* poblacional.

(Palà et al, Front Neurology 2019; Abellana et al, Eur J Clin Invest 2021)



- **CRYPTO-FA**

Biomarcadores de FA en pacientes con ictus criptogénico monitorizados durante un mes.

(Palà et al, Eur J Neurol 2021; Pagola et al, Transl Stroke Res 2021; Palà et al, Int J Cardiol Heart Vasc 2022)



- **PARIAS**

Biomarcadores de infartos cerebrales silentes (y otras lesiones radiológicas) en pacientes con FA de bajo riesgo embólico.

(Escudero-Martínez, J Neurol 2020)

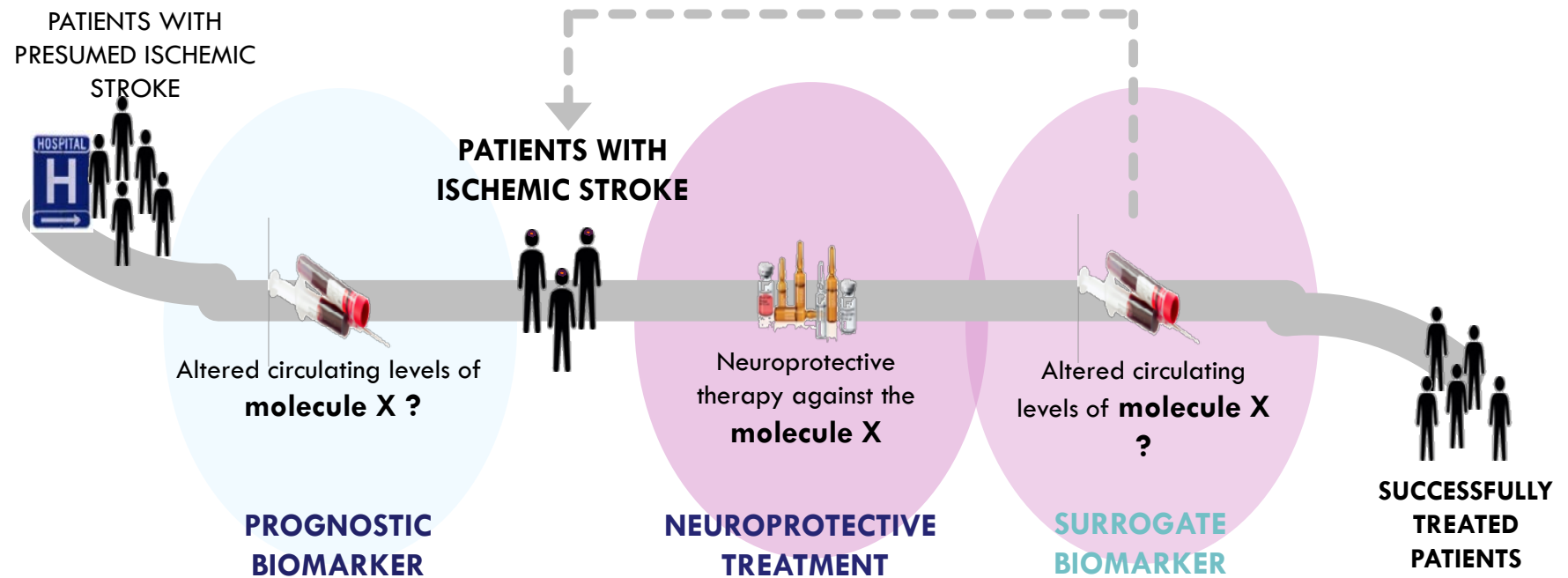


- **ODEA-TIA: Optimal DEtection of Atrial fibrillation in Transient Ischemic Attack**

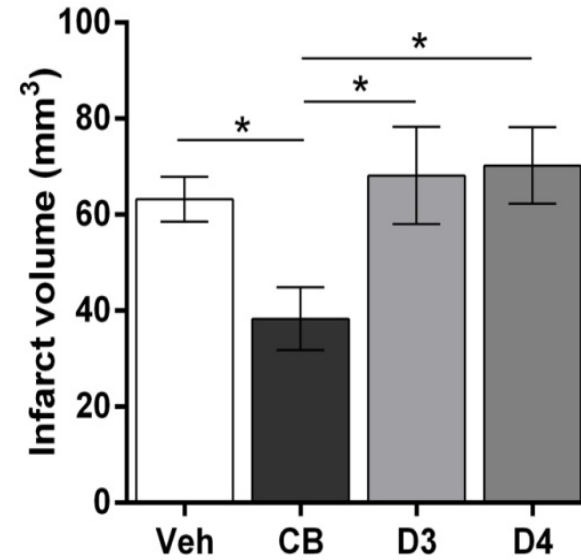
Biomarcadores de FA en pacientes con ataque isquémico transitório (AIT).



BIOTARGETS: May Stroke prognostic **biomarkers** also serve as therapeutic targets?



Neuroprotective drug combinations




Neurotherapeutics
<https://doi.org/10.1007/s13311-022-01203-0>

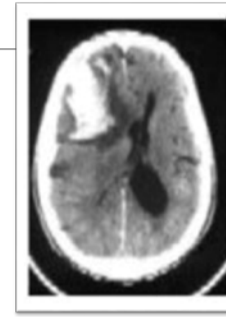
ORIGINAL ARTICLE



Ceruletide and Alpha-1 Antitrypsin as a Novel Combination Therapy for Ischemic Stroke

Alba Simats¹ · Laura Ramiro¹ · Raquel Valls² · Helena de Ramón¹ · Paula García-Rodríguez¹ · Cyrille Orset³ · Laura Artigas² · Teresa Sardon² · Anna Rosell¹ · Joan Montaner^{1,4,5} 

Accepted: 15 February 2022
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PI: Mar Hernández Guillamon

1: Biological, genetic and imaging markers of CAA

Why novel biomarkers are needed?

- To improve the present diagnostic criteria (to differentiate CAA from other SVDs and A β -associated pathologies) and the prognosis of the disease, in terms of stroke recurrence and cognitive decline.
- To underscore the molecular pathways associated with CAA, to suggest new therapeutic candidates and to monitor the efficacy of future treatments.
- To identify pre-symptomatic patients and to classify patients receiving treatments, such as anticoagulants or anti-A β antibodies.

2: Therapeutic strategies (Tg CAA models)

Role of apolipoproteins in CAA

- To study the effect of human ApoJ/ Clusterin on CAA progression (CMB, amyloid deposition)
- To study the effect of ApoA-I-Milano variant to reverse the vascular function associated with AD/CAA



PI14/01134, PI17/00275, PI20/00465 (ISCIII)



Instituto de Salud Carlos III

COHORT: patients with suspected CAA

Inclusion criteria:

- Patients > 55 years old
- To undergo a brain MRI
- To present at least one lobar hemorrhagic lesion or the presence of cSS (without any deep hemorrhagic lesion), or, to present CAA pathological confirmation from brain biopsy
- Not receiving anticoagulant treatment
- To obtain a blood sample at least 2 months after the last ICH
- To agree to participate in the study

Achievement: N=105

Spanish participant centers:

1. Hospital Universitario Vall d'Hebron, Barcelona: Dr. David Rodríguez-Luna, Dra. Olga Maisterra
2. Hospital Son Espases, Palma de Mallorca: Dra. Silvia Tur
3. Hospital de la Verge de Cinta, Cardona: Dr. Moisés Garcés
4. Hospital Universitario de Basurto, Bilbao: Dra. María del Mar Freijo
5. Hospital Universitario Virgen de la Macarena, Sevilla: Dra. Soledad Pérez, Dra. Sara Eichau
6. Hospital Universitario Virgen del Rocío de Sevilla: Dra. Lucía Lebrato
7. Hospital Universitario Donostia: Dra. Maite Martínez
8. Hospital Universitario Ramón y Cajal, Madrid: Dra. Rocío Vera
9. Hospital Arnau de Vilanova de Lleida: Dr. Francisco Purroy
10. Hospital Universitario de Bellvitge, Hospitalet del Llobregat, Barcelona: Dr. Pere Cardona
11. Hospital Clínico Universitario de Valladolid: Dr. Juan Arenillas.
12. Hospital de la Santa Creu i Sant Pau, Barcelona: Dr. Joan Martí Fàbregues
13. Hospital Germans Trias i Pujol, Badalona: Dra. Anna Ramos



Article

Comparison of Plasma Lipoprotein C in Cerebral Amyloid Angiopathy and

Anna Bonaterra-Pastra¹, Sofia Fernández-de-Retana¹, Andrea Riv. Olalla Pancorbo³, David Rodríguez-Luna³, Francesc Pujadas⁴, Mar Maite Martínez-Zabaleta⁷, Pere Cardona Portela⁸, Rocío Vera⁹, Luc Juan F. Arenillas^{11,12}, Soledad Pérez-Sánchez¹³, Joan Montaner^{1,14} and Mar Hernández-Guillamon^{1,5}



Article

Circulating AQP4 Levels in Patients with Cerebral Amyloid Angiopathy-Associated Intracerebral Hemorrhage

Paula Marazuela¹, Anna Bonaterra-Pastra¹, Júlia Faura¹, Anna Penalba¹, Jesús Pizarro¹, Olalla Pancorbo², David Rodríguez-Luna², Carla Vert³, Alex Rovira³, Francesc Pujadas⁴, M. Mar Freijo⁵, Silvia Tur⁶, Maite Martínez-Zabaleta⁷, Pere Cardona Portela⁸, Rocío Vera⁹, Lucía Lebrato-Hernández¹⁰, Juan F. Arenillas¹¹, Soledad Pérez-Sánchez¹³, Joan Montaner^{1,13,14}, Pilar Delgado¹ and Mar Hernández-Guillamon^{1,5}

Marazuela et al. *Acta Neuropathol Commun* (2021) 9:154
<https://doi.org/10.1186/s40478-021-01257-9>

Acta Neuropathologica
Communications

RESEARCH

Open Access

MFG-E8 (LACTADHERIN): a novel marker associated with cerebral amyloid angiopathy

Paula Marazuela¹, Montse Solé¹, Anna Bonaterra-Pastra¹, Jesús Pizarro¹, Jessica Camacho², Elena Martínez-Sáez², H. Bea Kulperl³, Marcel M. Verbeek^{3,4}, Anna M. de Kort³, Floris H. B. M. Schrauder³, Catharina J. M. Klijn³, Laura Castillo-Ribelles⁵, Olalla Pancorbo⁶, David Rodríguez-Luna⁶, Francesc Pujadas⁷, Pilar Delgado¹ and Mar Hernández-Guillamon^{1,5}

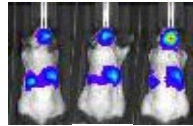
SCIENTIFIC DATA 2022

Main Research Interest: Neurorepair in the context of Stroke

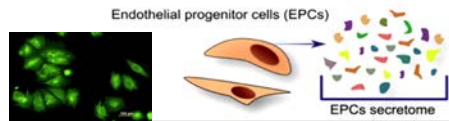
PI: Anna Rosell

Research lines: repair mechanisms, molecular targets, advanced therapies & clinical studies in stroke recovery.

Projects & Know-How: Preclinical models



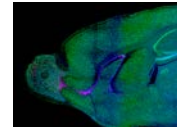
Progenitor cells



Biomarker studies in stroke cohorts



Neurovascular remodelling



Nanomedicine platforms



Nanocapsule (NC)

Identification of biomarkers and therapeutic targets for neurorepair during neurorehabilitation after stroke.

Funded by ISCIII (PI13, PI16 and PI19) to identify markers of functional recovery and new therapeutic targets in multicentric studies in stroke patients under rehabilitation. **Coordinated Multicentric Observational Clinical Study (SMARRTS)** with 7 participants (HUVH, Taulí, La Fe, Gorliz, A Coruña, Pere Virgili, HUGTiP) to create a cohort in post-stroke rehabilitation with a sub-cohort follow-up at 5 years. The projects also aims to model the rehabilitation/recovery phase in pre-clinical models.



| Centro Participante SMARRTS-II | Intensiva (≥3h/día) | No Intensiva (≤2 h/día) | Controles | Estudio Neuroimagen |
|--|---------------------|-------------------------|-----------|---------------------|
| H.Universitario Vall d'Hebron | Si | | Si | Si |
| Hospital Mútua de Terrassa | Si | | Si | Si |
| H. Parc Taulí- Sabadell | Si | | Si | - |
| Hospital Universitari i Politècnic La Fe | Si | | Si | Si |
| Consorci Socio-sanitari Pere Virgili | | Si | Si | - |
| H. Universitari Manresa | | Si | Si | - |
| H.Marítimo de Oza- A Coruña | | Si | Si | - |
| H.Universitario Marqués de Valdecilla | | Si | Si | Si |
| H. Universitari Germans Trias i Pujol | | Si | Si | Si |
| H. de Gorliz-Bizkaia | | Si | Si | - |

TABLE 1 | Baseline characteristics of the control and stroke cohorts.

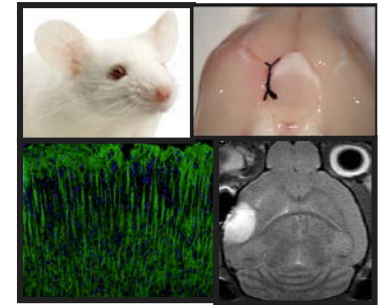
| Stroke cohort | Control cohort |
|---------------|----------------|
| n = 62 | n = 43 |

TABLE 2 | Baseline characteristics of the IRT vs. NO-IRT cohorts.

| IRT | NO-IRT |
|--------|--------|
| n = 45 | n = 17 |

Biomarkers/ Identification of therapeutic targets.

Translation into pre-clinical models.



ORIGINAL RESEARCH
published: 25 November 2021
doi: 10.3389/fneur.2021.767494



Functional Recovery and Serum Angiogenin Changes According to Intensity of Rehabilitation Therapy After Stroke

Nicolás García-Rodríguez^{1,2}, Susana Rodríguez², Pedro Ignacio Tejada², Zuberoa Maitte Miranda-Artieda¹, Natalia Ridao¹, Xavi Buxó¹, Maria Engracia Pérez-Mesquida¹, Maria Rosario Beseler^{1,3}, Juan B. Salom^{4,5}, Laura M. Pérez^{1,6}, Marco Inzitari^{6,7,8}, Sergio Otero-Villaverde¹, Rosa Martín-Mourelle¹, Mercedes Mollada¹, Manuel Quintana¹, Marta Olivé-Gadea¹, Anna Penalba¹ and Anna Rosell^{1*}

Angiogenin in the Neurogenic Subventricular Zone After Stroke

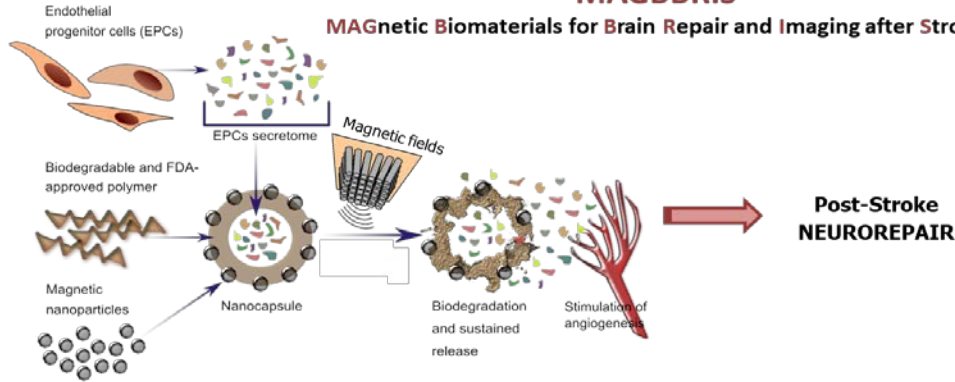
Marina Gabriel-Salazar¹, Ting Lei¹, Alba Grayston¹, Carme Costa², Esperanza Medina-Gutiérrez¹, Manuel Comabella¹, Joan Montaner¹ and Anna Rosell^{1*}

MAGBRRIS: New MAGnetic Biomaterials for Brain Repair and Imaging after Stroke.

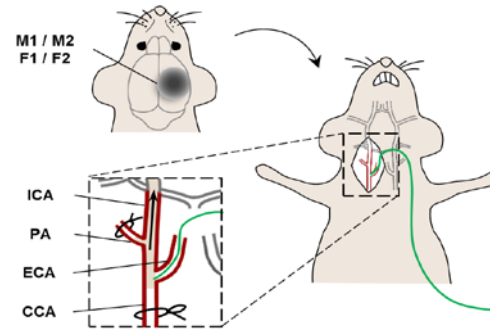
Euronanomed Programm *Consortia Coordinator of an european consortia with academic, clinical and private partnership.*
We have been working in the use of biodegradable and biocompatible PLGA nanocapsules (an FDA-approved polymer for the medical use) capable of encapsulating endothelial progenitor cells secretome and magnetized with SPIONs for brain magnetic targeting and neurorepair.

MAGBRRIS

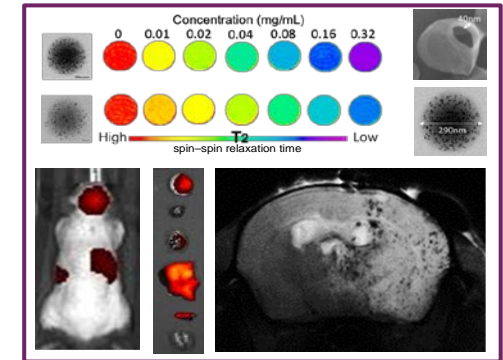
MAGnetic Biomaterials for Brain Repair and Imaging after Stroke



Endovascular Delivery



Multimodal NC for imaging and specific brain targeting after stroke



Grayston et al. JCBFM. 2022

3D-printed supra aortic vascular model testing intraarterial delivery

Endovascular approach to infuse PLGA-NanoCapsules towards middle cerebral artery vascular territory to test the retention effect of a focused magnet prototype for the human use.

Dr. Anna Roig Lab
at ICMAB-CSIC (UAB)



PLGA NC-SPION-CY5
< 300 nm diameter

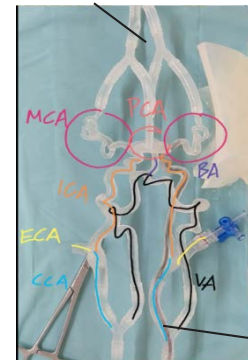
Dr. Kopkansky Lab
at ISI-SAS (Kosice) &
GIAMAG



Gold-coated
40 mm diameter

Collaboration with Dr. Ribó at the HUVH

SUPRAAORTIC HUMAN CEREBRAL ARTERIAL ANATOMY



Imaging of the NC-Cy5

