

2016-2017

**PLAN DE INVESTIGACIÓN DE LA
UNIVERSIDAD DE NAVARRA**

INDICE

RESUMEN EJECUTIVO	7
ESCUELA DE ARQUITECTURA	8
<i>Producción de uniones de Madera Estructural con nuevas tecnologías automatizadas (NUEVO)</i>	9
<i>Cabrero Ballarín, José Manuel</i>	
<i>Manual de criterios de diseño urbano y sostenibilidad (NUEVO)</i>	11
<i>Orgeig Corgini, José María</i>	
<i>Diseños en H. aportaciones del grupo Huarte al diseño español del S. XX (PRÓRROGA)</i>	13
<i>García Alonso, Marta</i>	
FACULTAD DE CIENCIAS	15
<i>Optimización de la codigestión anaerobia de residuos agroalimentarios de la industria navarra (PRÓRROGA)</i>	16
<i>Fernández Rodríguez, Juana</i>	
<i>El cilio primario como factor de pronóstico clínico en meduloblastomas (PRÓRROGA)</i>	18
<i>Saez Castresana, Javier</i>	
<i>Respuesta al estrés en el hígado fibrótico: papel de variantes de la nox no fagocíticas y de inductores fisiológicos de estrés del retículo (PRÓRROGA)</i>	25
<i>Iraburu Elizalde, María</i>	
<i>Interacciones entre especies exóticas invasoras y nativas amenazadas en áreas fluviales protegidas (PRÓRROGA)</i>	27
<i>Miranda Ferreiro, Rafael</i>	
<i>Mecanismos implicados en la génesis de las neoplasias mieloproliferativas crónicas con mutaciones en CALR: desarrollo de un modelo experimental en Caenorhabditis elegans (PRÓRROGA).</i>	29
<i>Vizmanos Pérez, José Luis</i>	
FACULTAD DE COMUNICACIÓN.....	31
<i>Mythmaking y héroe: la creación de mitos y héroes a través de los relatos y de las narrativas mediáticas (PRÓRROGA)</i>	32
<i>Gutiérrez Delgado, Ruth</i>	

FACULTAD DE DERECHO	36
<i>La aportación del modelo de la reciprocidad a la superación de la discriminación por razón de género (NUEVO)</i>	37
<i>Aparisi Miralles, Ángela</i>	
<i>Derecho y vivienda (NUEVO)</i>	39
<i>Velarde Queipó de Llano, Caridad</i>	
<i>Propuestas sobre las medidas cautelares en el arbitraje interno e internacional y en el concurso de acreedores (PRÓRROGA)</i>	41
<i>Sánchez Pos, M^a Victoria</i>	
FACULTAD ECLESIAÍSTICA DE FILOSOFÍA.....	44
<i>La relación entre las ciencias y la teología en el S. XXI: una propuesta de articulación filosófica (PRÓRROGA)</i>	45
<i>Sánchez Cañizares, Javier</i>	
FACULTAD DE EDUCACIÓN Y PSICOLOGÍA	49
<i>La transición a la vida adulta de jóvenes de la comunidad gitana en Navarra. Perfil de competencias y propuestas de mejora (NUEVO)</i>	50
<i>Arellano Torres, Araceli</i>	
<i>Estudio de la eficacia de un sistema de enseñanza-aprendizaje de la Lengua en Primaria, que integra la enseñanza del pensamiento y el trabajo cooperativo: variables cognitivas y no-cognitivas (PRÓRROGA)</i>	51
<i>Lara Ros, Sonia</i>	
FACULTAD DE ENFERMERÍA.....	55
<i>Narrativas y práctica reflexiva: un programa para el desarrollo de competencias profesionales en enfermería (NUEVO)</i>	56
<i>Choperena Armendáriz, Ana</i>	
<i>El cuidado en el domicilio de la persona con enfermedad avanzada: conociendo la experiencia de la familia</i> <i>Narrativas y práctica reflexiva: un programa para el desarrollo de competencias profesionales en enfermería (NUEVO)</i>	58
<i>Saracibar Razquin, M^a Isabel</i>	
FACULTAD DE FARMACIA	60
<i>Multiexposición y toxicidad combinada de micotoxinas en el hombre y animales de granjas (NUEVO)</i>	61
<i>González Peñas, Elena</i>	

<i>Potencial terapéutico de inhibidores de HDAC5 y de Sirt2 en la depresión mayor (NUEVO)</i>	63
<i>Tordera Baviera, Rosa M^a</i>	
<i>Estudio de agentes inmuno-nucleares en oncología mediante plataformas preclínicas para desarrollar un modelo cinético-dinámico con carácter traslacional (PRÓRROGA)</i>	65
<i>Garrido Cid, M^a Jesús</i>	
<i>Modulación estructural sobre antitumorales selenados inductores de apoptosis y reguladores de la vía PI3K/Akt/Mtor (PRÓRROGA)</i>	67
<i>Sanmartín Grijalba, M^a Carmen</i>	
FACULTAD DE FILOSOFÍA Y LETRAS.....	70
<i>Cognition, Learning and Intergestural Coordination: Tracking the evolutionary learning of vocal tract coordination en route from novice to expert behavior in two subject groups (NUEVO)</i>	71
<i>Gibson, Mark</i>	
<i>La correspondencia del tercer viaje europeo de Charles S. Peirce (septiembre-noviembre de 1877) (NUEVO)</i>	73
<i>Nubiola Aguilar, Jaime</i>	
<i>Las freiras de la Orden del Hospital de San Juan de Jerusalén en la Edad Media en el reino de Navarra. Intervención arqueológica y estudio histórico-artístico del convento de Bargaota (NUEVO)</i>	74
<i>Pavón Benito, Julia</i>	
<i>Perfiles del centro político (1976-1986) (NUEVO)</i>	76
<i>Pérez López, Pablo</i>	
<i>Experiencia estética en la acción. Antoni Tàpies: una nueva perspectiva (NUEVO)</i>	78
<i>Piñero Moral, Ricardo</i>	
<i>Las elites sociales y políticas en Navarra durante la crisis del Antiguo Régimen: ¿continuidad o ruptura? (NUEVO)</i>	80
<i>Zabalza Seguin, Ana</i>	
<i>Unidad y pluralidad. Metafísica del logos en las líneas explicativas medievales de la racionalidad de la naturaleza (PRÓRROGA)</i>	82
<i>Soto Bruna, M^a Jesús</i>	
<i>Contractor State Group. Expansión del grupo de investigación internacional (PRÓRROGA)</i>	86
<i>González Enciso, Agustín</i>	

FACULTAD DE MEDICINA.....	90
<i>Desarrollo de herramientas computacionales para evaluación de incertidumbres y adaptación de tratamientos en radioterapia estereotáctica en cáncer de pulmón (NUEVO)</i>	<i>91</i>
<i>Azcona Armendáriz, Juan Diego</i>	
<i>Evaluación de las variaciones en la presión intraocular en el síndrome de apnea obstructiva del sueño (NUEVO)</i>	<i>93</i>
<i>Carnero González, Elena M^a</i>	
<i>A non-invasive liquid biopsy approach to evaluate the DNA methylation status in patients with NSCLC (NUEVO).....</i>	<i>95</i>
<i>De Andrea, Carlos Eduardo</i>	
<i>Evaluación de diversas formulaciones combinadas de ivermectina en dosis única para su potencial uso en el bloqueo de la transmisión de la malaria (PRÓRROGA)</i>	<i>97</i>
<i>Del Pozo, José Luis</i>	
<i>Papel de los ligando de los receptores HER en la acantólisis del pénfigo vulgar en un modelo murino (PRÓRROGA).</i>	<i>99</i>
<i>España Alonso, Agustín</i>	
<i>Péptidos antimicrobianos para el control de biofilms asociados a implantes médicos (PRÓRROGA).....</i>	<i>101</i>
<i>Martínez de Tejada, Guillermo</i>	
<i>Electroporación irreversible con adyuvantes inmunológicos para el tratamiento percutáneo de tumores sólidos (PRÓRROGA).....</i>	<i>103</i>
<i>Vivas Pérez, Isabel</i>	
<i>Estudio multicéntrico de factores genéticos implicados en la hipermetropía infantil (PRÓRROGA)</i>	<i>104</i>
<i>Barrio Barrio, Jesús</i>	
<i>Transmisión GABAérgica desde los ganglios basales a los núcleos pedunculopontino y laterodorsal: dianas celulares de la proyección palidotegmental y receptores GABAérgicos implicados en el animal control (PRÓRROGA)</i>	<i>106</i>
<i>Mengual Poza, Elisa</i>	
<i>Caracterización de los mecanismos de heterogeneidad clonal y quimiorresistencia primaria en Leucemia Mieloblástica Aguda: una aproximación integradora fenotípico-molecular basada en estudios de Enfermedad Mínima Residual (PRÓRROGA).</i>	<i>108</i>
<i>Merino Roncal, Juana M^a</i>	

<i>Evaluación de una intervención para mejorar la convivencia con la enfermedad de parkinson de pacientes y familiares (PRÓRROGA)</i>	<i>110</i>
Riverol Fernández, Mario	
<i>Caracterización fenotípica y filogenética productores de betalactamasas de espectro extendido aisladas en Navarra (PRÓRROGA).....</i>	<i>113</i>
Vitas Pemán, Ana Isabel	
FACULTAD DE TEOLOGÍA	115
<i>Conciencia y verdad en el John Henry Newman anglicano (1825-1845). (PRÓRROGA)</i>	<i>116</i>
Alonso García, Juan	
LÍNEAS ESPECIALES	119
<i>SIGLO DE ORO.....</i>	<i>120</i>
<i>PENSAMIENTO CLÁSICO.....</i>	<i>121</i>

RESUMEN EJECUTIVO

FACULTAD	Nº PROYECTOS	PRESUPUESTO
Arquitectura	3	43.300,00 €
Ciencias	5	61.800,00 €
Comunicación	1	5.400,00 €
Derecho	3	15.700,00 €
Ecles. De Filosofía	1	7.500,00 €
Educación	2	13.900,00 €
Enfermería	2	7.250,00 €
Farmacia	4	55.900,00 €
Filosofía y Letras: <ul style="list-style-type: none">• Proyectos• Líneas Especiales• Proyectos Especiales	8 2 1	60.146,00 € 410.050,00 € 5.000,00 €
ICF <ul style="list-style-type: none">• Proyectos Especiales	2	6.000,00 €
Medicina / CUN	12	178.900,00 €
Teología	1	4.100,00 €
TOTALES:	47	874.946,00 €

Presupuesto para el curso 2016/2017

ESCUELA DE ARQUITECTURA



CABRERO BALLARÍN, JOSÉ MANUEL

Título: Producción de uniones de Madera Estructural con nuevas tecnologías automatizadas

Presupuesto: 32.000,00 euros

Palabras Clave: Madera; Polímeros; Fabricación aditiva; Diseño estructural; Uniones estructurales; Ensayos experimentales; Modelos de elementos finitos; Modos de rotura; Reglas de diseño.

Periodo: 2016-2019

Resumen:

Por costo y seguridad, las uniones son críticas en cualquier estructura, no sólo en las de madera:

- Son **caras**: se fabrican artesanalmente con placas y conectores metálicos a medida.
- Son **inseguras**: como el acero es mucho más rígido que la madera, restringe su movimiento y produce concentración de tensiones. Esto último ha sido causa de numerosos colapsos estructurales en Europa. Lo que es más importante, los modelos normativos del Eurocódigo 5 no logran prevenir este tipo de rotura frágil.

Además, las uniones actuales con elementos metálicos tienen otros problemas: corrosión, puentes térmicos, elevado peso, baja estabilidad al fuego...

Este proyecto propone desarrollar uniones más seguras, mediante el uso de polímeros como alternativa al acero, y más baratas, al aplicar nuevas tecnologías de fabricación, pultrusión y fabricación aditiva.

Así, el proyecto PROMETEO desarrolla y caracteriza uniones estructurales más seguras, baratas y eficientes con elementos mecánicos poliméricos. Obtendrá reglas de diseño y modelos precisos para controlar su resistencia, rigidez y modo de rotura. Las reglas desarrolladas garantizarán un modo dúctil de fallo en la unión.

Los polímeros son resistentes a la corrosión, ligeros y con un excelente balance entre propiedades mecánicas estáticas y dinámicas (resistencia, rigidez, tenacidad...). Como demuestran los resultados preliminares del equipo investigador, hay una sinergia positiva entre la madera y los polímeros. La unión resultante es dúctil y eficiente.

Los objetivos del proyecto se resumen en los siguientes puntos:

- Obtener una solución alternativa competitiva, viable y eficiente, a las uniones con componentes metálicos en estructuras de madera.
- Analizar el empleo de dos tecnologías de producción de elementos estructurales poliméricos, pultrusión y fabricación aditiva.
- Desarrollar y caracterizar las uniones estructurales de madera con dichos elementos y proponer modelos completos de las mismas.
- Trasladar al ámbito industrial los beneficios obtenidos, generando para ello la documentación base necesaria para el desarrollo de posteriores proyectos de investigación a nivel europeo, en los que participe la industria. El proyecto está respaldado por tres empresas líderes: en la pultrusión, FIBER PROFIL; en la fabricación aditiva, OPTIMUS3D; y en la construcción en madera, CBS LIFTEAM.
- Difundir a la sociedad los resultados de esta investigación en diversos ámbitos. En el científico, con publicaciones en congresos, revistas con alto índice de impacto, y la presentación de los resultados en la acción COST FP 1402. En el normativo, presentando los resultados a comités normativos españoles y europeos. Y en el técnico y docente, con una completa documentación sobre el diseño y comportamiento mecánico de uniones en madera.
- Posicionar a la Universidad de Navarra como pionera en el empleo estructural de elementos poliméricos por fabricación aditiva.

El equipo investigador cuenta con experiencia previa en las áreas de trabajo y está suficientemente cualificado para el desarrollo de la investigación y consecución con éxito de los objetivos propuestos: uniones estructurales de madera optimizadas, eficientes, seguras y a un precio competitivo.



ORDEIG CORSINI, JOSÉ MARÍA

Título: Manual de criterios de diseño urbano y sostenibilidad

Presupuesto: 2.700,00 euros

Palabras Clave: Sostenibilidad en Diseño Urbano, Diseño urbano, Planeamiento Urbano, Criterios de forma urbana, regeneración urbana, intervención urbana.

Período: 2016-2019

Resumen:

El objetivo general del proyecto MANUAL-D-USO es el estudio de criterios morfológicos de diseño urbano y de sostenibilidad con la finalidad principal es la elaboración de un manual que proporcione una base adecuada para la proyectación y regeneración de la ciudad. Es imprescindible añadir que por criterios morfológicos se entiende no una mera cuestión formal, sino la manera en que las necesidades sociales y la estructura territorial (las dos vertientes claves del urbanismo) condicionan la configuración formal de la ciudad. Criterios morfológicos que llegan a su detalle a través de conceptos de sostenibilidad.

El proyecto se muestra relevante si nos atenemos a cuatro consideraciones. En primer lugar el momento en el que se plantea este trabajo, pues nos encontramos en un punto de inflexión entre el mayor desarrollo urbanístico de la historia de la segunda década del siglo XX y el crecimiento exponencial de la ciudades que se prevé en los próximos años. En segundo lugar la escasez de estudios de este tipo en los últimos cincuenta años, y especialmente en el campo de criterios de diseño urbano sostenible. En tercer lugar, la trayectoria académica en el Área de Urbanismo de la ETSAUN, los años de experiencia en docencia y las líneas de investigación centradas en la historia del diseño urbano, que revelan una suficiente madurez como para acometer un proyecto de este tipo. En cuarto lugar, saber que esos criterios no intentan abarcar toda la disciplina urbanística: ni en sus contenidos históricos, ni en las derivaciones necesarias hacia las disciplinas con las que está relacionada, ni en los instrumentos legales a los que la práctica profesional debe hacer referencia; sino que se centran en lo más importante, desde el punto de vista proyectual, según se explica más adelante.

El resultado más importante que se espera es la publicación del manual elaborado durante el proyecto de investigación. Ahora bien, también se

espera el impacto siguiente como consecuencia de la publicación del Manual que gira en torno a tres ámbitos complementarias e importantes. En primer lugar se prevé un impacto considerable en el ámbito académico mediante la trasmisión del conocimiento: se espera un alto grado de aplicabilidad a la docencia de los criterios obtenidos, sobre todo a través de las asignaturas vinculadas con la disciplina urbanística. En segundo lugar se espera un elevado potencial de divulgación y difusión en el ámbito investigador a través de publicaciones en revistas indexadas a nivel internacional dando a conocer las líneas de investigación del Área. Y en tercer lugar, se espera una repercusión vinculada al ámbito profesional: una buena acogida de la investigación en cuanto al establecimiento de pautas y criterios tanto para la regeneración urbana, actualmente tan reclamada, como para el planteamiento de nuevos desarrollos urbanos.



GARCÍA ALONSO, MARTA

Título: Diseños en H. aportaciones del grupo Huarte al diseño español del S. XX

Presupuesto: 8.600,00 euros

Palabras Clave: Diseño Industrial, Diseño Gráfico, Publicidad, Diseño de Interiores, Prefabricación, Diseño Constructivo, Escenografía, Grupo Huarte, Huarte y Cía, Hmuebles, H Decoración, X Films, Sala Hisa, Operación H, Sedí, Exco, Nueva Forma, Oteiza.

Período: 2014-2017

Summary:

Entitled Diseños en H and for the first time in Spain, a furniture store was advertised in the cinema in the sixties. It was HMuebles, a brand of Huarte Corporation interested in furnishing the Spanish homes in modern code. The research project presented paraphrases the title of the ad, because it expresses very well the approach developed in this research project studying the contributions of Huarte Corporation about Design.

The research will focus on a specific aspect of the intensive work of patronage Huarte family developed for some of the avant-garde movements. This research will not analyze the sponsorship through the collection of some of the work of most renowned figures of Spanish art. The study will focus on observing the contribution of Huarte Corporation on the design of objects. These objects sent the company a parallel spirit to the work they were developing those artists whose works acquired. Reproducibility of industrial objects promoted by the group together with chained operations (advertisements, exhibitions, specific stores) to make visible their products, multiply the social dimension of the patronage of the Huarte. Thanks to these designs achieved they introduce modern culture in Spain and complement the ambitious vision of the company business. In short, it defines the character of the family, his role as generators of wealth, industry and also culture.

The project proposes the study of objects designed for mass production and analysis of advertising from different companies of the group. In this sense provides the ability to delve into the graphic design of the time and is an opportunity to study national and international references on this topic. The

presence of these products in exhibitions like EXCO or SEDI was part of the same diffusion strategy. They also convened novel design competitions to who attended some of the most important architects and artists of the time. We must not forget the spirit has been behind the different spaces of the group (HISA, HMuebles, etc.) in relation to its projection in society. These spaces were intended for holding cultural events (exhibitions at SALA HISA, Architecture Review Session in HMuebles store). Just inside the SALA HISA, Oteiza ordered different pieces generated in Huarte Corporation of industries to shape OPERATION H. This short film, following a script made by Nestor Basterretxea, was performed with the purpose of promoting the work of its companies and the production of X Films opens.

The research project aims raised thus unfold its action in two areas: first, the study of industrial products of the Huarte Corporation, relating them to the Spanish twentieth century design and renovation taking place on those dates. On the other hand, the study of diffusion, the transmission strategy of the new design to the population by analyzing advertising group and other actions that can be framed within this informative will.

From all this, it will be a catalog of both the products and the information actions. The interest and scope of the contributions of Huarte Corporation in the field of industrial design and promotional determine the relevance of the results to derive a possible exhibition project.

Difusión de resultados:

Lucía C. Pérez Moreno publicó el pasado año los resultados de su tesis centrados en la revista Nueva Forma, en la publicación "Fullaondo y la revista Nueva Forma. Aportaciones a la construcción de una cultura arquitectónica en España (1966-1975)", financiada por el Museo Oteiza y el Colegio de Arquitectos Vasco Navarro, delegación Navarra y que se centra en la revista que el grupo Huarte dedicó a la difusión de la cultura y el diseño. La publicación este año ha sido galardonada con el premio en el campo de DIVULGACIÓN dentro de la XXIII Bienal española de arquitectura y urbanismo.

La IP, Marta García Alonso ha publicado en Proyecto, progreso, Arquitectura núm. 14 Ciudades paralelas, en mayo de 2016, el artículo titulado "Pamplona otra: el escenario de los Encuentros 72" en el que se da difusión a lo acaecido en aquellos días repasando de forma paralela los lugares y los carteles de gran valor visual, que los organizadores diseñaron para el evento que convirtió Pamplona en la capital de la cultura en aquel inicio de verano.

FACULTAD DE CIENCIAS



FERNÁNDEZ RODRÍGUEZ, JUANA

Título: Optimización de la codigestión anaerobia de residuos agroalimentarios de la industria navarra

Presupuesto: 10.300,00 euros

Palabras Clave: Digestión anaerobia, co-digestion, residuos agroindustriales, industria navarra, biogás, metano, optimización, reactor de tanque agitado, reactor de lecho fluidizado.

Período: 2015-2018

Summary:

In this project, the anaerobic digestion or biomethanation of agro-industrial waste generated in Navarre is proposed. The main industrial wastes can contain an important lignocellulosic fraction as asparagus or artichokes. Organic wastes are a source of environmental pollution if not properly managed, they can alter the quality of air and water, especially the quality of groundwater. But the potential environmental impact of wastes is not the only justification for treating them, likewise can be used as raw material in new processes for recoverable materials. In this sense the current law on wastes proposes biologic treatment, for example composting and biomethanization, as an alternative to landfill.

The anaerobic digestion process is the degradation of organic compounds in the absence of oxygen conducted by anaerobic microorganisms. These microorganisms convert biodegradable organic material into a gas enriched in methane, energetic recoverable, called biogas. The process consists of various microbiological stages from the hydrolysis of macromolecules of the wastes until methane. In addition to biogas rich in methane, a semisolid suitable for composting organic material is obtained. In short, as a result of anaerobic process, the pollutant potential of organic wastes is decreased while recoverable by-products is minimized are obtained.

The control of the process includes: temperature, agitation and the technology used. The operating temperature conditions the reactor equilibria. In this project two different temperatures will be tested:

mesophilic (optimum at 35°C) and thermophilic range (optimal at 55°C). Anaerobic stirred tank reactor will be used in the first part of the project with the objective of finding the optimal mixtures to proceed codigestion and potential inhibitors. After that, a more effective treatment for industrial organic wastes, anaerobic upflow anaerobic bioreactor, will be designed and the operation with this system will be proceed.

Monitoring provides important information on the evolution of the process. The following parameters will be analysed: pH, alkalinity, biogas production and composition, volatile fatty acids, the chemical oxygen demand (COD) and solids, both total as volatile.

In this project the following objectives are proposed:

- Studying individual digestion of organic waste produced in agricultural industries in Navarra.
- Studying the combination (co-digestion) to find several potential nutritional deficiencies and improve process efficiency.
- Studying the effect of temperature (thermophilic 55°C and mesophilic 35 °C) in the anaerobic digestion of different wastes and co-digestion.
- Designing and operating a fluidized bed reactor with the best conditions obtained.

The results will be analyzed in terms of physico-chemically, and microbiologically, obtaining the main kinetic parameters to highlight the best operating conditions and, consequently, the optimization process.

Difusión de resultados:

Hasta el momento, estos estudios realizados han sido divulgados en la Jornada de Investigación Científica de la Universidad de Navarra (17 de marzo de 2016) con una comunicación titulada "Study of anaerobic digestion on local agricultural wastes", así como en seminarios organizados por el Departamento de Química de la Universidad de Navarra, con las siguiente comunicaciones: "Introducción a la Digestión Anaerobia de Residuos Agroalimentarios: Producción de Biogás" (17 de diciembre de 2015), "Digestión anaerobia de aguas residuales de la industria de bebidas alcohólicas: Pacharán y Cerveza" (19 de mayo de 2016) y "Tratamiento de residuos industriales por biometanización" (22 de junio de 2016). Asimismo, como resultado de las investigaciones llevadas a cabo se están elaborando un par de artículos, que se pretenden enviar a revistas de alto impacto en el campo de trabajo y cuyos títulos provisionales son: "Study of anaerobic digestion on local agricultural wastes: effect of nutrients, substrate, temperature and co-digestion" y "Stabilization of wastewaters from the alcoholic drinks industry through anaerobic digestion: sloe and malt".



SÁEZ CASTRESANA, JAVIER

Título: El cilio primario como factor de pronóstico clínico en meduloblastomas.

Presupuesto: 13.000,00 euros

Período: 2015-2018

Resumen:

El meduloblastoma (MB) es un tumor embrionario del cerebelo, que representa el 4-6% de todos los tumores intracraneales primarios. Es el tumor intracraneal maligno más frecuente en niños, representando el 15-30% de todos los tumores pediátricos cerebrales, con un 85% de MB diagnosticados en pacientes menores de 18 años de edad. El MB es raro en adultos y representa menos del 1% de las neoplasias malignas intracraneales primarias, por lo que la mayor parte de los estudios se han realizado sobre MB infantiles.

Histológicamente, los MB se clasifican en cinco tipos [1]: clásico, desmoplásico, anaplásico, de células grandes y MB con extensa nodularidad y diferenciación neuronal avanzada (también denominado, este último, neuroblastoma cerebeloso). Estos subtipos histológicos son muy heterogéneos y exhiben un comportamiento clínico muy variable, con los subtipos anaplásico/células grandes típicamente asociados a los MB de peor pronóstico, seguidos del clásico y del desmoplásico/nodular, que se correlacionan con una mejor supervivencia global. Hoy en día, se reconoce al MB como una enfermedad heterogénea, no sólo a nivel histopatológico, sino también a nivel molecular.

Los MB aparecen en diferentes grupos de edad: 21% en menores de 3 años, 67% en niños de entre 3 y 16 años, y 12% mayores de 16 años. La edad media es de 7,3 años.

Los principales grupos moleculares de MB se denominan: Wnt, Shh, grupo 3, y grupo 4. El grupo 4 de MB es el más numeroso (34%), seguido por Shh (28%) y el grupo 3 (27%). Los MB Wnt son los más infrecuentes (11%). En lactantes y adultos los tumores Shh son más frecuentes y representaron más de la mitad de los casos, pero en niños se presentan con una frecuencia

menor (14%). Los MB Wnt son casi ausentes en los lactantes (1%) y la frecuencia del grupo 4 también es mucho menor en este grupo de edad (11%). El grupo 3 apenas se encuentra en los adultos (6%).

El grupo Wnt de MB es el mejor conocido debido a su buen pronóstico en comparación con otros grupos [2-9]. Los ratios de supervivencia superan el 90%. Los pacientes mueren debido a complicaciones del tratamiento o a neoplasias secundarias, más que por recidivas de los MB Wnt [10]. A nivel molecular destacan en este grupo las mutaciones en la línea germinal en el gen APC (Síndrome de Turcot), así como mutaciones somáticas en CTNNB1, que codifica la Beta catenina [11,12] y monosomía del cromosoma 6 [7].

Casi todos los MB del grupo Wnt presentan histología de MB clásico. Algunos tienen histología de MB anaplásico/células grandes. Pero aun así, éstos conservan un buen pronóstico. Los MB Wnt pueden darse a cualquier edad, pero son infrecuentes en niños menores de 3 años. Recientemente se ha descrito que los MB Wnt se producen a partir de células del labio rómbico inferior del cerebelo [13]. Como la mayor parte de los pacientes con MB Wnt sobreviven, está en discusión actualmente si sería interesante reducir la terapia para evitar someter a los pacientes a sobre-tratamientos.

El grupo Shh de MB presenta alteraciones en los diferentes reguladores de la vía sonic hedgehog (Shh). Así pueden darse a nivel germinal mutaciones en PTCH -receptor del ligando Shh-, como en el síndrome de Gorlin, que predispone al MB [14,15]. Las mutaciones de SUFU, igualmente, predisponen a MB infantil [16-19]. Las mutaciones somáticas de Ptch, Smo y Sufu, así como Gli1 y Gli2 se han detectado en MB esporádico [19-21]. Las deleciones del cromosoma 9q parecen estar limitadas al grupo Shh de MB, ya que PTCH se encuentra en 9q22 [7]. Por grupos de edad, este grupo es dicotómico, en el sentido de presentar alta frecuencia en menores de 3 años y en adultos (mayores de 16 años), y baja frecuencia en niños entre 3 y 16 años de edad. No está claro aun si los MB Shh de niños pequeños son similares genéticamente a los de adultos.

La mayor parte de los MB desmoplásicos/nodulares pertenecen al grupo Shh de MB. Sin embargo no es éste un marcador efectivo, ya que un 50% de los MB Shh no son desmoplásicos/nodulares. El pronóstico de los MB Shh es semejante al del grupo 4, e intermedio entre el de los grupos Wnt (bueno) y grupo 3 (malo). Recientemente se ha demostrado que pequeñas moléculas inhibitoras de Smo son efectivas contra los MB Shh, por lo que es urgente ahondar en la genética del MB, en busca de marcadores eficaces sobre los que plantear nuevas terapias [22-24]. El grupo 3 de MB corresponde mayormente a MB del tipo histológico clásico, aunque en este grupo se encuentra la mayor parte de los MB anaplásicos/células grandes. Son frecuentemente metastásicos [7]. El grupo Shh presenta altos niveles de MYCN, mientras que el grupo 3 tiene sobreexpresión de MYC, y el grupo 4 sobreexpresión de los dos genes MYC y MYCN [6,7,25]. Se ha denominado al grupo 3 el grupo MYC [25]. Igualmente la amplificación de MYC (no de MYCN) aparece casi siempre limitada al grupo 3 [6,7,26]. La amplificación y

sobreexpresión del oncogén OTX2 parece restringida a los grupos 3 y 4 de MB [7,27-29]. El grupo 3 muestra ganancias del cromosoma 1q y/o pérdidas de los cromosomas 5q y 10q más frecuentemente que el grupo 4.

Se presentan en niños menores de 3 años y en el grupo de edad entre 3 y 16 años, pero apenas se dan en adultos (mayores de 16 años). El grupo 3 es el de peor pronóstico. Se ha demostrado [26] que un subgrupo de MB dentro del grupo 3, con amplificación de MYC se asocia a alto riesgo de recidiva y metástasis, mientras que el subgrupo carente de amplificación de MYC presenta una evolución clínica semejante a la del grupo 4 de MB. Ese interesante hallazgo merece confirmación por parte de otros grupos de investigación, a fin de definir la posible existencia de pacientes del grupo 3a (amplificación de MYC) y del grupo 3b (no amplificación de MYC). Aunque los MB del grupo 3 son más parecidos a los del grupo 4 que a los Shh y Wnt, los datos demográficos, clínicos y genéticos hacen pensar que los grupos 3 y 4 son entidades clínicas diferentes [6,7].

El grupo 4 de MB está formado por los MB prototipo (un 30% del total de MB): niño de unos 7 años de edad, con histología de MB clásico y con un isocromosoma 17q. Como la clasificación molecular de este grupo no está perfectamente clara, caben en él los MB que no se ajustan a las características de otros grupos. Aunque el isocromosoma 17q aparece también en MB del grupo 3 (26%), es más frecuente en MB del grupo 4 (66%) [7,30]. El 80% de las mujeres con MB del grupo 4 presentan pérdida del cromosoma X.

Se ha publicado en varios trabajos sobre MB que el grupo 4 presenta genes sobreexpresados responsables del desarrollo y diferenciación neuronal, aunque la relevancia clínica del hallazgo no ha sido demostrada todavía [6,7,26]. El pronóstico de los pacientes del grupo 4 es intermedio, similar al de los MB Shh.

Histología y grupos moleculares: Mientras la mayor parte de los investigadores de MB opinan que los marcadores moleculares van a ir adquiriendo una importancia mayor en el diagnóstico y clasificación del MB en el futuro, parece que queda todavía un campo de interés para la histopatología [1]. Los MB desmoplásicos/nodulares y casi todos los MB con extensa nodularidad y diferenciación neuronal avanzada pertenecen al grupo Shh de MB [3,31]. La histología clásica, sin embargo, aparece en los cuatro grupos de MB. Los MB anaplásicos/células grandes también aparecen en los cuatro grupos, aunque la mayoría pertenecen al grupo 3 de MB. Sin embargo, no está claro si la histología de los MB anaplásicos/células grandes les confiere mal pronóstico per se, o ligada específicamente a grupos de MB, como el grupo 3 (o más específicamente el 3a ligado a amplificación de MYC) ó el grupo 4, ambos de mal pronóstico [7].

El cilio primario es un orgánulo microtubular que protruye desde la membrana plasmática actuando como una antena que recibe señales extracelulares. Varios estudios recientes revelan el importante papel del cilio primario en biología del desarrollo y en enfermedades como el cáncer.

Los cilios primarios no son cilios motiles, sino que reciben señales físicas y químicas del exterior celular. Sólo hay un cilio primario por cada célula. En la base del cilio se encuentra el cuerpo basal, integrado por un centriolo denominado centriolo madre, unido a un centriolo hijo, anclado en la membrana plasmática. El centriolo sirve como apoyo a la estructura microtubular 9+0 que se extiende hacia el ápice del cilio.

Se han identificado cientos de proteínas que forman el cilio primario [32-40]: algunas participan en la ciliogénesis, mientras otras son activas en el tráfico de moléculas en dirección hacia el ápice o la base del cilio. La proteína de transporte intraflagelar (IFT), descrita por Rosenbaum y Whitman [41] y por Scholey [42], participa junto con el complejo motor kinesina-2 en el movimiento anterógrado de moléculas (hacia el ápice del cilio); y la misma proteína IFT participa con el complejo motor dineína-2 en el transporte retrógrado (hacia la base del cilio) de moléculas. Las mutaciones producidas en el complejo IFT causan pérdida de ensamblaje del cilio y, consecuentemente, de las funciones sensoriales del mismo [43]. Se denominan ciliopatías a las enfermedades producidas por mutaciones en genes requeridos para la ciliogénesis; entre ellas, el síndrome de Joubert, la enfermedad poliquística renal, el síndrome de Bardet-Biedl y la nefronoptosis [44]. Todas ellas conllevan una desregulación en diversas rutas de señalización del desarrollo.

Vía de señalización Shh y el cilio primario: El cilio primario participa en diversas rutas de señalización celular, tales como Shh, Wnt y PDGF [45-50], ligadas al desarrollo y a diversas enfermedades. Pero los mecanismos por los que el cilio primario regula la señalización de Shh son los mejor caracterizados. Las proteínas hedgehog son una familia de proteínas secretadas que incluyen sonic hedgehog (Shh), indian hedgehog (Ihh), y desert hedgehog (Dhh). Estos tres ligandos activan la familia de factores de transcripción Gli, que se translocan al núcleo y activan genes diana de la vía Shh. El cilio primario es un compartimento celular en el que diferentes componentes de la vía Shh, incluyendo las proteínas Gli, son transportadas dentro y fuera del cilio, dependiendo de la presencia o ausencia del ligando Shh.

En ausencia de Shh, Gli es convertida en su forma represora (Gli3R). También, en ausencia de Shh, Ptch (el receptor de Hh) en la membrana del cilio primario y Smo queda fuera del cilio [45, 53]. En presencia de Shh, los niveles de Gli incrementan en el cilio y Gli es transformada en su forma activa (Gli2A) que es transportada fuera del cilio y dentro del núcleo celular, donde activa genes diana de la vía Shh [54,57]. En presencia del ligando Shh, Ptch se retira del cilio y Smo se sitúa en el cilio, donde promueve la formación de la forma activa de Gli [45, 55, 56].

La activación anormal de la vía Shh es crítica para el desarrollo de muchos cánceres, como glioblastoma, carcinoma de células basales, MB y cáncer de mama, próstata, melanoma, pulmón y páncreas [58]. En cáncer humano, Shh está regulado positivamente mediante mutaciones en Ptch, Smo, o mediante sobreexpresión del ligando Shh. Algunos experimentos

desarrollados en modelos de cáncer en ratones muestran que el cilio primario juega un papel dual en la promoción y en la prevención de tumorigénesis a través de la regulación de la vía Shh [59,60], lo cual se debe a que el cilio enciende la vía Shh en presencia del ligando Shh (procesando las proteínas Gli en sus formas activas; G2A) y mantiene la vía Shh en "off" en ausencia del ligando Shh (procesando las proteínas Gli en sus formas represoras; G3R).

En estos modelos murinos de carcinoma de células basales y MB, se expresó una forma ectópica de Smo en ratones de tipo salvaje y en ratones modificados genéticamente que poseían cilios primarios mutados [59,60]. El resultado fue el siguiente: los ratones con Smo activo y cilios de tipo salvaje desarrollaron carcinoma de células basales y MB; mientras que los ratones con Smo activo y cilios mutados no desarrollaron tumores. Ciertamente, por tanto, la vía de señalización Shh requiere cilios en perfecto estado para la activación de proteínas Gli (G2A) por parte de Smo. Sin cilio, Smo activo no puede activar la vía Shh y no se forman tumores.

Por el contrario, cuando la vía Shh fue activada más allá del cilio, mediante expresión ectópica de la forma activada de una de las proteínas Gli (Gli2A) en ausencia de cilio primario, sí que se produjeron tumores.

Todo lo cual nos lleva a concluir que el cilio se requiere para la formación de tumores cuando la mutación originaria que cause tumorigénesis es cilio dependiente (Smo). Mientras que si la mutación se produce más allá del cilio, aun sin presencia de éste (Gli2A sobreexpresado) también se dan tumores, que podríamos denominar cilio-independientes.

Por ello se habla del carácter dual del cilio: por una parte su existencia, en ausencia del ligando Shh, hace que Ptch, situado en el cilio, frene la vía Shh a través de las formas represoras de Gli (Gli3R). Y por otra, el cilio que contenga Smo, en presencia del ligando Shh, será capaz de activar Gli (Gli2A) y producir tumores. En el primer caso (en ausencia de Shh) el cilio es supresor tumoral gracias a Ptch. En el segundo (en presencia de Shh) el cilio es oncogénico, gracias a Smo. Finalmente Gli2A per se, en ausencia de cilio, es capaz de inducir tumorigénesis. Por tanto, si hay cilio pueden darse tumores o no darse. Y si no hay cilio, igualmente, pueden darse tumores o no. Para que se den tumores debidos a activación de Shh debe haber cilio, tanto si la activación es mediante Shh sobreexpresado o mediante mutaciones de Smo. Pero podría haber activación de Shh mediante una vía no canónica que sobreexpresara las formas activas de Gli (Gli2A) y formarse tumores, incluso en ausencia de cilio.

Expresión del cilio primario en cáncer: Sólo un pequeño número de estudios han evaluado la expresión del cilio primario en células de diferentes cánceres humanos derivados de muestras de pacientes. Se ha detectado una reducción en la frecuencia de cilios en células tumorales, frente a las células normales circundantes, en carcinoma de células renales [61],

cáncer de mama [62], melanoma [57], carcinoma de células basales [52], MB [53] y cáncer de páncreas [63]. Las lesiones de neoplasia pancreática intraepitelial carecían de cilios, lo cual sugiere que puede darse una pérdida de cilios en estadios tempranos de tumorigénesis [55]. En un estudio de MB [53] la presencia de cilios se asoció a MB desmoplásico (mejor pronóstico), y la ausencia de cilios se asoció a MB anaplásico (peor pronóstico).

El grado de proliferación celular no afecta a la pérdida de cilios, según se ha demostrado en estudios de melanoma [57], carcinoma de células renales [61] y cáncer de páncreas [63], en los que la pérdida de cilios primarios se dio independientemente del nivel de expresión inmunohistoquímica del marcador de proliferación celular Ki67. Esto sugiere que la pérdida de cilios en células tumorales podría deberse a otros mecanismos, como pérdida de genes implicados en la ciliogénesis, tras mutagénesis o inestabilidad genómica [61,63,64].

Otros aspectos a tener en cuenta en la investigación sobre la implicación del cilio primario en cáncer son: aumento del número de muestras sometidas a estudio, así como tratar de agrupar las muestras en grupos histopatológicos o moleculares con el fin de ver asociaciones estadísticas entre presencia o ausencia del cilio y grupo específico de tumor. Igualmente, se debe estudiar comparativamente la expresión de cilios en las células adyacentes al tumor [65]. También es conveniente estudiar la longitud de los cilios: éstos pueden estar presentes en tumores, pero si tienen longitudes anormales, tal vez el proceso de señalización celular no funcione correctamente [51]. También es importante encontrar asociaciones entre la frecuencia de cilios y marcadores de vías de señalización relevantes, como la vía Shh, a fin de comprender si hay una relación causal entre presencia o ausencia de cilios y cáncer.

La presencia o ausencia de cilios en tumores que expresan la vía Shh proporciona una nueva herramienta para los clínicos, al poder usar drogas específicamente dirigidas contra alguno de los marcadores de la vía Shh. Por ejemplo, es de suponer que si se demuestra fehacientemente que cáncer y pérdida de cilios están asociados, el tratamiento con inhibidores de la vía Shh contra moléculas dependientes del cilio, como Smo, no será operativo, mientras que se necesitará profundizar en tratamientos específicos contra las proteínas Gli en sus formas activas (Gli2A), que pueden producirse por una vía no canónica, sin presencia de cilio.

Difusión de resultados

Publicaciones:

Cancer as a ciliopathy: the primary cilium as a new therapeutic target

Javier S. Castresana

Journal of Carcinogenesis and Mutagenesis 6: e119, 2015

Characterization of the Antiglioma Effect of the Oncolytic Adenovirus VCN-01.

Vera B, Martínez-Vélez N, Xipell E, Acanda de la Rocha A, Patiño-García A, Saez-Castresana J, Gonzalez-Huarriz M, Cascallo M, Alemany R, Alonso MM
PLoS ONE 11(1): e0147211:1-10, 2016

Laminin-adherent versus suspension-non adherent cell culture conditions for the isolation of cancer stem cells in the DAOY medulloblastoma cell line.

Javier de la Rosa, Ander Sáenz Antoñanzas, Mehdi H. Shahi, Bárbara Meléndez, Juan A. Rey, Javier S. Castresana.

Tumor Biology (admitido 29-3-2016)

Comunicaciones a Congresos Internacionales

107th Annual Meeting of the American Association for Cancer Research, New Orleans, Louisiana, April 16-20, 2016.

Isolation and characterization of cancer stem cells from the human medulloblastoma cell line DAOY: adherent vs. suspension in vitro cell cultures.

Javier de la Rosa, Ander Sáenz Antoñanzas, Xing Fan, Bárbara Meléndez, Juan A. Rey, Javier S. Castresana.

107th Annual Meeting of the American Association for Cancer Research, New Orleans, Louisiana, April 16-20, 2016

Inhibition of the Transforming Growth Factor beta pathway in human glioblastoma cell lines induces apoptosis and inhibits anoikis escape

Gabriel Gallo-Oller, Javier Dotor, Xing Fan and Javier S. Castresana

IX Jornada de Investigación en Ciencias Experimentales y de la Salud de la Universidad de Navarra

Pamplona, 17 de marzo de 2016.

Inducción de resistencia a ciclopamina en una línea celular de medulloblastoma desmoplásico: estudio celular y molecular

Javier de la Rosa, Amaia Paredes, Idoya Zazpe, Bárbara Meléndez, Juan A. Rey, Javier S. Castresana

IX Jornada de Investigación en Ciencias Experimentales y de la Salud de la Universidad de Navarra

Pamplona, 17 de marzo de 2016

Modulación farmacológica de la acetilación y metilación de histonas en líneas celulares de glioblastoma.

Alejandro Urdiciain, Jesús Aznar, Javier de la Rosa, Miguel A. Idoate, Javier S. Castresana.



IRABURU ELIZALDE, MARÍA

Título: Respuesta al estrés en el hígado fibrótico: papel de variantes de la nox no fagocíticas y de inductores fisiológicos de estrés del retículo

Presupuesto: 14.000,00 euros

Palabras Clave: fibrosis hepática; células estelares hepáticas; monocitos; Nox; UPR; señalización; homocisteína; especies reactivas de oxígeno.

Período: 2014-2017

Summary:

Hepatic fibrosis is a pathological condition characterized by an excessive accumulation of extracellular matrix (ECM) proteins in which hepatic stellate cells (HSC) play a key role. In response to acute and chronic liver damage, these liver pericytes undergo an activation process acquiring a myofibroblastic phenotype with a high ECM protein synthesis rate, specially collagen type I. In the injured liver cells are exposed to different types of stress, including oxidative and endoplasmic reticulum stress. Oxidative stress is mainly caused by the accumulation of reactive oxygen species (ROS) whereas reticulum stress is elicited due to the disfunction of this organelle, responsible for the secreted proteins folding. Both types of stress have been involved in liver fibrosis development. One of the main ROS liver sources is the NADPH oxidase (Nox), an enzymatic complex found in phagocytic and non-phagocytic forms. Among the non-phagocytic forms, Nox5 is poorly characterized. In contrast to other isoforms, it is regulated by calcium and it appears to be present in differentiating tissues and organs. The main aims of this project are to evaluate the potential role of Nox5 in liver fibrosis, elucidating the regulation of its expression, the effect of its overexpression in HSC and human monocytes and the molecular mechanisms involved. Moreover, the role of the cysteine precursor homocysteine will be evaluated in the HSC unfolded protein response (UPR) as well as its potential regulating action in the fibrogenic activity of these cells. Finally, we will also study the potential connection between the stress caused by Nox and homocysteine, analyzing the Nox5 regulation in response to homocysteine induced stress. Once established the effects on the cell biology, we will determine the molecular mechanisms involved, focusing on signaling molecules such as ROS or calcium, and several signaling pathways.

Difusión de resultados

En esta segunda anualidad se han publicado **dos artículos**:

Andueza A, García-Garzón A, Ruiz de Galarreta M, Ansorena E, Iraburu MJ, López-Zabalza MJ, Martínez-Irujo JJ. Oxidation pathways underlying the pro-oxidant effects of apigenin. *Free Radic Biol Med*. 2015;87:169-80. (IF: 5,784; Q1)

Ruiz de Galarreta M, Navarro A, Ansorena E, Garzón AG, Mòdol T, López-Zabalza MJ, Martínez-Irujo JJ, Iraburu MJ. Unfolded protein response induced by Brefeldin A increases collagen type I levels in hepatic stellate cells through an IRE1 α , p38 MAPK and Smad-dependent pathway. **Biochim Biophys Acta - Mol Cell Res**. 2016 Aug;1863(8):2115-23. (IF: 5,128; Q1)

Una asistencia a **Congreso nacional**:

Amaia Navarro Corcuera, Marina Ruiz de Galarreta Martínez, M^a Antonia García Garzón, Teresa Mòdol Betriu, María J. López Zabalza, Juan J. Martínez Irujo, María J. Iraburu, Eduardo Ansorena Artieda. EFFECT OF THE UNFOLDED PROTEIN RESPONSE IN THE PROFIBROGENIC ACTIVITY OF HEPATIC STELLATE CELLS. Presentación en poster. SEBBM, Valencia (Septiembre 2015).

Una **estancia** de investigación:

Amaia Navarro está realizando una segunda estancia de 4 meses en la Nottingham Trent University (abril-agosto 2016).



MIRANDA FERREIRO, RAFAEL

Título: Interacciones entre especies exóticas invasoras y nativas amenazadas en áreas fluviales protegidas

Presupuesto: 13.000,00 euros

Palabras Clave: Pacifastacus leniusculus, invasiones biológicas, áreas protegidas, depredación, competencia, comportamiento, conservación.

Período: 2014-2017

Summary:

Invasive alien species are the second leading cause of biodiversity loss in the world, a situation that is increased in particularly vulnerable habitats and ecosystems as inland waters. The negative impacts of these species trigger on the aquatic ecosystem are varied, and the effects on the native fauna usually have serious consequences. However, research conducted on these interactions between invasive and native species is very limited. This knowledge is essential especially in Sites of Community importance, where the study of these interactions and their mechanisms will allow to undertake appropriate management measures for the conservation of fluvial biodiversity conservation of river management measures. This project aims to further explore the population, trophic and behavioural ecology of a major invasive alien species in the Iberian Peninsula, also widely expanded throughout much of European rivers, the signal crayfish *Pacifastacus leniusculus* Dana, 1852. The aim of this project is to identify the mechanisms of interaction (e.g. predation, competence, aggression) between the signal crayfish and native freshwater species of benthic invertebrates and fishes, as well as to and evaluate the effects of these interactions (e.g. physical displacement, abundance decrease), in order to develop an knowledge and, ultimately, a tool that allows us a better management of native wildlife and its conservation.

Difusión de resultados

Publicaciones:

[1] Vedia I, Oscoz J, Rueda J, Miranda R, García-Roger EM, Baquero E, Gelder SR, 2015. An alien ectosymbiotic branchiobdellidan (Annelida: Clitellata) adopting exotic crayfish: a biological co-invasion with unpredictable consequences. *Inland Waters* 5, 89-92.

[2] Vedia I, Miranda R, Oscoz J, Baquero E, 2016. Invading the invaders: environmental conditions and relationships of an exotic branchiobdellidan with its exotic host. *Inland Waters* 6: 54-64.

[3] Vedia I, Galicia D, Baquero E, Oscoz J, Miranda R, in press. Environmental factors influencing the distribution and abundance of the introduced signal crayfish in the North of Iberian Peninsula. *Marine and Freshwater Research*.

Comunicaciones a congresos:

[4] VII Jornada de Investigación en Ciencias Experimentales y de la Salud. Pamplona, 11 de abril de 2014. Oral presentation: Vedia I, Miranda R, Oscoz J, Baquero E. Invadiendo al invasor: colonización de *Xironogiton victoriensis* en la Cuenca del Ebro y su interacción con su hospedador el cangrejo señal.

[5] V Jornadas Ibéricas de Ictiología SIBIC. 24-27 de junio de 2014. Museu Nacional de História Natural e da Ciência, Lisboa, Portugal. Oral presentation: Vedia I, Miranda R, Baquero E. Interactions between the invasive signal crayfish *Pacifastacus leniusculus* and the native fish populations in the north of the Iberian Peninsula.

[6] International Symposium on conservation of Native European Freshwater Crayfish. 23 - 25 September 2015. Olot, Girona (Spain). Oral presentation: Vedia I, Miranda R, Baquero E. Ethology of the invasive signal crayfish (*Pacifastacus leniusculus*) and its relationships with native fishes.

[7] VI Congreso Ibérico de Ictiología SIBIC. 21-24 de junio de 2016. Universidad de Murcia, España. Oral presentation: Vedia I, Miranda R, Baquero E. Competition between the introduced signal crayfish (*Pacifastacus leniusculus*) and native fishes.



VIZMANOS PÉREZ, JOSÉ LUIS

Título: Mecanismos implicados en la génesis de las neoplasias mieloproliferativas crónicas con mutaciones en CALR: desarrollo de un modelo experimental en *Caenorhabditis elegans*.

Presupuesto: 11.500,00 euros

Palabras Clave: Neoplasias mieloproliferativas, CALR, calreticulina, oncogénesis, modelo experimental en *C. elegans*, Ca²⁺ intracelular, vías de señalización

Período: 2014-2017

Summary:

The description of genetic aberrations associated with different tumours is a fundamental tool for the diagnosis, monitoring and development of new therapies specifically directed against the molecular defect. In the last ten years there has been considerable progress in the knowledge of the genetic aberrations that cause Philadelphia-negative chronic myeloproliferative neoplasms. Thus, in 2005 it was reported that most of the MPN patients showed a specific mutation in JAK2 that caused aberrant activation of the JAK-STAT signalling pathway and in December 2013 it was showed that most of the JAK2-negative patients harbour CALR mutations. This gene encodes calreticulin, a molecule involved in calcium homeostasis in the endoplasmic reticulum with a chaperone function that seems not directly involved in cellular signalling. However, in murine cell models it has been found that these CALR mutations cause activation of STAT signalling by an unknown mechanism. All the CALR mutations described to date in patients have a very curious pattern: all of them lead to an aberrant calreticulin in which the carboxyl-terminal end is substituted by another with different physicochemical and probably functional characteristics.

In this project we want to analyse the role of this aberrant calreticulin in a multicellular organism widely used in biomedical research, *Caenorhabditis elegans*. This nematode is easy to grow, transparent, and there is a huge knowledge of its biology, developmental pattern and genome. In fact, some of the most important cellular processes have been described first in this animal. Specifically for this project it has several advantages. First, there are no orthologs for the JAK proteins but it has orthologs for the STATs and

calreticulin. For this reason it seems an ideal model to explore the JAK-independent mechanisms that lead to the activation of STATs. Secondly, their transparency allows the observation of multiple defects in different tissues and organs, being capable of correlating them with other mutations already described (making it possible to infer new specific functions). Finally, this organism allows the development of a screening model for the analysis of new therapeutic tools more reliable than cellular models. For this reason, the implementation of this model could be also very useful for other areas of biomedical research at the University of Navarra.

Difusión de resultados

Publicaciones:

Eder-Azanza L, Navarro D, Aranaz P, Novo FJ, Cross NC, Vizmanos JL. Bioinformatic analyses of CALR mutations in myeloproliferative neoplasms support a role in signaling. *Leukemia* 2014 Oct;28(10):2106-2109. JCR® 2014: 10,431 (3/68, Q1 Hematology; 8/211, Q1 Oncology).

Araki M, et al. Activation of the thrombopoietin receptor by mutant calreticulin in CALR-mutant myeloproliferative neoplasms. *Blood* 2016 Mar;127(10):1307-16. Factor de impacto JCR® 2015: 11,841 (2/70, Q1, Hematology)

Marty C, et al. Calreticulin mutants in mice induce an MPL-dependent thrombocytosis with frequent progression to myelofibrosis. *Blood* 2016 Mar;127(10):1317-24. Factor de impacto JCR® 2015: 11,841 (2/70, Q1, Hematology)

Chachoua I, et al. Thrombopoietin receptor activation by myeloproliferative neoplasm associated calreticulin mutants. *Blood* 2016 Mar;127(10):1325-1335. Factor de impacto JCR® 2015: 11,841 (2/70, Q1, Hematology)

Elf S, et al. Mutant Calreticulin Requires Both Its Mutant C-terminus and the Thrombopoietin Receptor for Oncogenic Transformation. *Cancer Discov* 2016 Apr;6(4):368-81. Factor de impacto JCR® 2015: 19,783 (6/213, Q1, Oncology)

FACULTAD DE COMUNICACIÓN



GUTIÉRREZ DELGADO, RUTH

Título: Mythmaking y héroe: la creación de mitos y héroes a través de los relatos y de las narrativas mediáticas.

Presupuesto: 5.400,00 euros

Palabras Clave: Mito, héroe, narrativa, Teoría del Relato, Storytelling, Comunicación pública, cine, televisión, ficción, prensa, publicidad, vida digital

Período: 2015-2018

Summary:

This research project will focus on the notion of Myth and, more specifically, on the way that myths are represented through media narratives. From the standpoint of Poetics and Rhetoric, the study will examine how the symbolic creation of myth is articulated, as well as the narrative environments that enable the appearance of heroic characters.

The current interest in heroic narratives and Myth as portrayed in different media calls for the need to review previous studies developed in two different areas: First of all, the three main traditional visions of myth and hero, which are the allegorical-philosophical notion, the euhemeristic perspective (directly linked with the deification of social heroes) and the apologetic-Christian stance. Secondly, it is also indispensable to revise modern theories surrounding the idea of myth, propelled by semiotics, structuralism and neo-aristotelian principles.

Taking into consideration the aforementioned schools of thought, as well as the long tradition of research on myth in the fields of Poetics and representation, it seems necessary to apply these studies to the narrative content of cultural products, in order to identify the role that mass media play, as part of their duty to communicate, in the process of mythmaking.

Myths, as products of human imagination, provide people with sense and meaning, and they have the capability to become universal symbols. However, the relative youth of this specific storytelling phenomenon in media narratives –which have a clear global dimension– has made it difficult for academics to reflect on this topic. By reviewing the main visions

of Myth, established according to the academic traditions mentioned above, it would be possible to approach the manner in which films, television series, entertainment programmes, advertisements or institutional messages (channelled through cinema, television, the press and the Internet) generate mythical narratives nowadays. These narratives can be articulated in the form of heroes or referential figures, leaders, archetypes, common places, symbols, generic conventions, hierarchies of values, social movements, emotions, habits, and imaginaries of a common identity, among others. It becomes evident, then, that there is a relationship between myth, action and story. In that sense, since this relationship is present in all communicative phenomena, it is of paramount importance to examine storytelling as it is executed in media products.

This proposal to bring the study of Myth to the foreground, combining diverse traditions in the areas of Narrative theory and Public Communication, aims to achieve the three following goals:

1. To revise and define the concept of Myth and its poetic, rhetoric and logic relationship with the story. This will be done from the standpoint of the Aristotelian tradition, but establishing a dynamic dialogue with other schools of thought.
2. To advance in the design and development of a theory on mythmaking, as it is articulated in media storytelling.
3. To create an exemplary corpus that covers case studies in cinema, television, literature, the press and digital media, in order to compare these cultural products and to, ultimately, establish a wide arena of shared myths and heroes, as well as new mythical figures.

Difusión de resultados

Congresos:

Ruth Gutiérrez Delgado, "Emociones y sentimientos en la serialidad televisiva de nuestros días", II Seminario Internacional Repensar la Ficción, Pontificia Universidad de la Santa Croce, Roma, 10-11 de diciembre de 2015.

Ruth Gutiérrez Delgado, "The shaping of myth: the role of the biographer in the Sherlock case (BBC, 2010-)", TV Series in contemporary societies, Serialised Storytelling, Hanze university of Applied Sciences of Groningen, Netherlands, 18-19 de Julio, 2016.

Ruth Gutiérrez Delgado, "El mito y el héroe: dos destinos encadenados", I Jornada de trabajo MYHE: El problema del mito I: definición y recreación, Facultad de Comunicación, Universidad de Navarra, Pamplona, 23 de junio, 2016.

Ruth Gutiérrez Delgado, "Marco teórico del proyecto y el Mito, según Paul Ricoeur", Sesión del Seminario permanente MYHE, Facultad de Comunicación, universidad de Navarra, 21 de octubre, 2015.

Antonio Martínez Illán, "Don Quijote en el cine soviético", Lecciones cervantinas entre dos centenarios, Universidad de Navarra, 26-27 de noviembre, 2015.

Antonio Martínez Illán, "Representaciones del mito: la animación soviética", I Jornada de trabajo MYHE, El problema del Mito: definición y recreación, Facultad de Comunicación, Universidad de Navarra, Pamplona, 23 de junio, 2016.

Pablo Echart, "El mito del éxito en el cine de Alexander Payne", I Jornada de trabajo MYHE, El problema del Mito: definición y recreación, Facultad de Comunicación, Universidad de Navarra, Pamplona, 23 de junio, 2016.

Isadora García Avis, "Interpreting Genre in Transcultural Remakes of Scripted Television Formats: The cases of The Office and Life on Mars", 8th International Screenwriting Research Network Conference, celebrada en University College London (Londres, Reino Unido), 10-12 septiembre 2015.

Isadora García Avis, "Una propuesta metodológica para el análisis hermenéutico de los remakes transculturales en televisión". Presentada el 23 de junio de 2016 en la I Sesión de Trabajo MYHE, Facultad de Comunicación, Universidad de Navarra.

Isadora García Avis, "Una propuesta metodológica para el análisis de los remakes transculturales en televisión", I Jornada de trabajo MYHE, El problema del Mito: definición y recreación, Facultad de Comunicación, Universidad de Navarra, Pamplona, 23 de junio, 2016.

Isadora García Avis, "Sesión sobre los últimos avances de la tesis", Seminario de Departamento de Cultura y Comunicación Audiovisual, 8 de marzo de 2016.

Isadora García Avis, "Adaptación de series de televisión", Colegio Mayor Aldaz, 23 de septiembre, 2015.

Jorge Latorre, Antonio Martínez Illán, Oleksandr Pronkevich, The "Quixote" Myth and the New Eastern Europe A Hermeneutic Study Based on European Visions: Small Cinemas in Transition, 2015, edited by Janelle Blankenship, Tobias Nagl pp. 259-284, Transcript Verlag, Bielefeld, ISBN 978-3-8376-1818-1.

Artículos enviados y/o publicados:

Ruth Gutiérrez Delgado e Isadora García Avis, "Rewriting Narrative Categories in Television Remakes. 'Life on Mars' in Spain: The Case of 'La Chica de Ayer'", enviado al Journal of Media Practice.

Álvaro Pérez Álvarez y Antonio Martínez Illán, "El arte del retrato en los textos periodísticos de Manuel Chaves Nogales", en *Zer* (2016), Vol. 21, nº 40, pp. 219-236, ISSN: 1137-1102 e-ISSN: 1989-631XDOI: 10.1387/zer.15513.

Isadora García Avis, "Adapting Landscape and Place in Transcultural Remakes: The case of *Bron/Broen*, *The Bridge* and *The Tunnel*", publicado en *SERIES – International Journal of TV Serial Narratives*, Vol. 1 nº2, Winter 2015, pp. 127-138.

Capítulos de libros:

Mercedes Medina, Ruth Gutiérrez Delgado, Patricia Diego, "Dos hombres y medio: la sitcom y el paraíso de la masculinidad", en *Familia y sociedad en el siglo XXI*, eds. Ana Marta González, Pilar Arregui, Carolina Montoro, Dykinson, Madrid, 2016.

Tesis doctorales:

Isadora García Avis, "La adaptación de formatos en televisión: los remakes de series de ficción". Fecha de depósito prevista: 29 de agosto de 2016, Facultad de Comunicación, Universidad de Navarra.

Seminarios Permanentes MYHE: con Actas de las sesiones: 2 y 17 de septiembre de 2015; 21 de octubre; 18 de noviembre de 2015; 18 de enero de 2016. Se adjuntan como anexo.

FACULTAD DE DERECHO



APARISI MIRALLES, ÁNGELA

Título: La aportación del modelo de la reciprocidad a la superación de la discriminación por razón de género.

Presupuesto: 5.500,00 euros

Palabras Clave: Género, igualdad, discriminación, diferencia, reciprocidad, corresponsabilidad, conciliación, identidad.

Período: 2016-2019

Summary:

Since the late nineties of the last century , the European Union , and subsequently Member States, have adopted equality policies and, more specifically, of reconciling work and family life, framing them in order to achieve real equality opportunities for women and men. Since then, the European Union continues working in this area. However, without denying what they have got of positive in the fight against discrimination based on gender, we found that such discrimination persists. Certainly, political and legal measures are essential, but are perhaps lacking root changes, hampered by gender structures and models that do not just produce the desired results.

Against the patriarchal model of gender, which, admitting the difference, broke -and it continues to do-, equality between the sexes, historically was building a model of equality, which later, in some cases, has evolved into a egalitarianism. One problem with this model is that it is not enough to attribute to women the same rights as men, assuming that there are no differences, assimilating them in lifestyles and behavior patterns. Female difference is not formally discriminated against in the legal field, but if it exists, and it is unknown, precisely because of this ignorance is, indeed, penalized. It may happen then that legal equality, not take care of the differences and their relevance in social relations, prove ineffective.

It is well known that, in this situation, there have been various attempts to restore the difference. There have been those who have defended Equality and who have defended the Difference, as if they were incompatible issues. In the words of Victoria Camps, "adhere to the discourse of difference should not mean stop proclaim equal rights; and adhere to the

discourse of equality, should not mean a proposal for simple imitation and repetition of the masculine".

However, combine both perspectives, equality and difference, currently not integrated, it is not a simple matter. There is, indeed, a great difficulty of integrating them, explaining exactly what is the sexed difference, and which is its scope when harmonizing it with equality. In this sense, one of the primary objectives of this Project is to delve into this issue, raising the need to contribute to the foundation, both on a theoretical and a practical level, equality in difference model of sex-gender. Specifically, it is addressing the problem of reciprocity, placing ontological level, to support solidly the co-responsibility, its counterpart at the practical level. We believe that this is a very important challenge, and that is still pending in order to take steps forward in the background theme, which is the overcoming of the real and material discrimination based on gender.

II. In this context, the objectives of this Project are:

1. Contribute to the pending task, to base the model of gender equality in difference. Specifically, address the problem of reciprocity, placing ontological level, to support the co-responsibility solidly, his counterpart at the practical level.
2. Study the practical consequences of the model of equality in difference from their levels of reciprocity and responsibility in male-female relations in all areas: especially familiar.
3. From these programmatic lines, to carry out a critical and evaluative study of current regulations in
4. the European Union and Spain on the subject. Proposed guidelines.

III. Expected results

Virtuality, novelty and specificity of this Project lies in its goal of connecting an investigation incident initially on an anthropological and philosophical-legal level, with an eminently practical perspective, critical-evaluative analysis and innovative proposals in the legal field.



VELARDE QUEIPÓ DE LLANO, CARIDAD

Título: Derecho y vivienda.

Presupuesto: 5.000,00 euros

Palabras Clave: Vivienda, derechos sociales, necesidades básicas, crisis, vulnerabilidad, discapacidad, hipoteca, derecho bancario, sostenibilidad, trabajo, educación, salud, infancia, vejez, inmigración, refugiados

Período: 2016-2018

Summary:

Housing is a basic human need also the support of much human rights as it is the place of intimacy, personality development, family life; but also in the constitutional state of domicile rights conditions access to rights such as health, education or work. Moreover, decent housing today involves gathering requirements water supply and sanitation, waste management and quality of the materials used in its construction.

The law in this case refers not only to an aspiration or a claimable content but the means by which the building is managed, occupation and use of those houses which puts us primarily in the fields of civil law and administrative, besides the bank. An important part of the world the most important mechanisms are the property occupancy and rent, but this can not be taken for granted everywhere. So, in much of Latin America and Asia internal displacement of the population they have led to megalopolis that are characterized not only by the lack of infrastructure in transport but also by the accumulation of people in neighborhoods not put up the housing settlement. Calls favelas, shantytowns or slums are characterized because they are poor in the strictest sense of the term. Or construction or use rights meet formally constituted so that from its very origin are para-legal forms within the territory of a state.

The location, linking with housing (and the possible existence of a second or more houses) mark social status of its inhabitants, as well as their origin. Population displacement, both internal and external, have had a clear translation in the layout of cities and neighborhoods distribution. In some countries like Colombia paying taxes is partly indirectly (through water and telephone) greater contribution neighbors neighborhoods that are considered more affluent.

Finally, housing has been long forming an economic good. And that in various ways. In countries such as Spain in which industry and energy are relatively low, the construction is a source of wealth and job creation. It has also come to be a capital until the outbreak of the housing bubble. The latter question the *raison d'être* of the houses as revealed in recent times.

In addition to the above, the construction and maintenance of housing affects not only those who inhabit them but to all citizens. Hence it is increasing standards of both national and European regulating administrative issues relating to health, environment and safety. Dysfunctions that result from the lack of decent housing could be summarized as follows:

- a) Poverty / diseases: greater social difference is generated and poverty that causes a risk and problems in containing diseases, especially those related to water sanitation and waste.
- b) Environment: originate negative impacts to the environment, particularly contamination of soil, water (rivers, reservoirs and large dams), air, flora and surrounding fauna.
- c) Work: physical and psychological illnesses are generated and sometimes incapacity. Because of this fact, the person loses power production and consumption capacity rejection with consequent damage to the economic order of a country.
- d) Educational Exodus by the issue of transportation or loss of school performance: they are away from school, school generating exodus (if no transportation or money to use it). Examples: north and northeast of Brazil).
- e) Exclusion: housing guardian regarding privacy especially in the environment of family life. People who are in this situation, especially children, will be affected their emotional development and their social and moral identity. also related to loneliness, aggression and segregation.
- f) Proximity to crime: in places where crime lie grows and usually a parallel state conforms to the rule of law, where the law of the groups that make it up is the strongest despite being illegitimate and illegal.



SÁNCHEZ POS, Mª VICTORIA

Título: Propuestas sobre las medidas cautelares en el arbitraje interno e internacional y en el concurso de acreedores.

Presupuesto: 5.200,00 euros

Palabras Clave: Medida cautelar. Normativa aplicable. Concurso de acreedores. Arbitraje. Potestad del árbitro. Facultad del juez para acordarla. Colisión entre juez y árbitro

Período: 2015-2017

Summary:

The objective pursued in this project is the study of precautionary measures in the international and national arbitration and bankruptcy proceeding, which are two areas where the protection of private rights gives rise to many problems. Precautionary measures in these areas have led to a contradictory jurisprudence and have not yet been subject to a systematic in-depth doctrinal study.

1) Article 23 of Law 60/2003, of December 23, of Arbitration, following the criteria of the UNCITRAL Model Law (cf. art. 17) in which it has been inspired, gives arbitrators the power to adopt the precautionary measures they could deem necessary respecting the dispute, but without excluding those measures which the courts may order in support of arbitration (Article 722 LEC) . The objectives in this area and the results to be obtained by this reseach are:

- To determine the concept itself (only precautionary?), and the scope of the precautionary and provisional measures which may be ordered in arbitration, in light of both the international legislation and practice.
- To analyze thoroughly, doctrinal and jurisprudentially, both article 722 of the LEC (precautionary measures taken by the arbitrators) and article 23 of the Arbitration Act (measures taken by the arbitrators) and study the relationship between them, in particular, if it is possible for arbitrators to leave aside in a arbitration a previous measure taken by a judge.
- To delimit the respective scope of declarative authority (attributed to

arbitrators) and executive authority (attributed to judges), taking into account the legislation and practice in international arbitration.

- 2) In the bankruptcy proceeding it will be examine the two types of precautionary measures which can be raised , with special reference to those contained in article 48ter of the Bankruptcy Act. The proposed research aims, on the one hand, to clarify this provision of the Bankruptcy Act of 2003 and, on the other hand, to develop a critical analysis of it starting from the limited doctrine we have today and, especially, from the jurisprudence of the Provincial Courts (and Bankruptcy Courts). We are talking about a precautionary measure, but, as the object of the judicial resolution that this measure garantees is the full or partial coverage of the deficit, the liability -and the precautionary measure that tends to secure it -is subsidiary (for the case that the active does not totally cover the debts).

It is a precautionary measure under specific and different requirements , at least partially, by comparison with the ones generally ruled in the LEC, but , as it has been highlighted by the Provincial Courts, it lacks a sufficient regulation and it has to be integrated with the general regulation (LEC) , the same way that the precautionary measure it rules should be interpreted in connexion with to the rules governing the qualification piece of the bankruptcy proceeding (Articles 163 and s. LC) .

For the purposes specified in article 48 ter LC (to ensure the eventual judicial statement ordering to cover the deficit determined in the resolution corresponding to the qualification piece of the bankruptcy proceeding), can the judge order precautionary measures other than those provided in the rule?. Can the court to replace the preventive seizure, expressly ruled, for a less severe precautionary measure?. What if it had not been requested nor discussed in the procedure?

Difusión de resultados

Prof. Cordón Moreno:

- Ha sido ponente en el VIII Congreso Español de Derecho de la Insolvencia, organizado por Thomson Reuters en Pamplona, del 5 al 7 de mayo de 2016, con la conferencia de clausura "la ejecución de la sentencia de calificación en el concurso de acreedores".
- Ha sido ponente en el Congreso Internacional "El proceso civil, instrumento para la consecución de un nuevo panorama socioeconómico: logros alcanzados y retos pendientes", celebrado en Murcia, los días 16 y 17 de junio de 2016, presentando la ponencia "Novedades en torno a la Ley 42/2015, de reforma de la Ley de Enjuiciamiento Civil".
- Ha realizado las siguientes publicaciones en relación con el proceso arbitral:
 - o ¿son aplicables en el procedimiento arbitral las limitaciones previstas en la LEC para los procesos sumarios?

- Dos cuestiones sobre arbitraje.
- Petición de medidas cautelares a un juez español para asegurar el resultado a obtener en un arbitraje a iniciar en el extranjero.

Prof. Hualde López: ha sido ponente en el VIII Congreso Español de Derecho de la Insolvencia, organizado por Thomson Reuters en Pamplona, del 5 al 7 de mayo de 2016, con la ponencia “El ejercicio de la acción de rescisión de la constitución de garantías reales en el caso de continuación de las ejecuciones no suspendidas por la declaración de concurso o iniciadas después de esa declaración”.

Prof. Prieto García-Nieto: ha participado en el VIII Congreso Español de Derecho de la Insolvencia, organizado por Thomson Reuters en Pamplona, del 5 al 7 de mayo de 2016, como moderador de la mesa “Los concursos conexos. La conclusión del concurso”.

Prof. Sánchez Pos: ha asistido al Congreso Internacional “El Proceso civil, instrumento para la consecución de un nuevo panorama socioeconómico: logros alcanzados y retos pendientes”. Murcia, 16 y 17 de junio de 2016.

FACULTAD ECLESIAÍSTICA DE FILOSOFÍA



SÁNCHEZ CAÑIZARES, JAVIER

Título: La relación entre las ciencias y la teología en el S. XXI: una propuesta de articulación filosófica.

Presupuesto: 7.500,00 euros

Palabras Clave: ciencia, razón y fe; ciencia y religión; interdisciplinariedad; creación y origen del universo; evolución y providencia; especificidad humana; origen del hombre; espiritualidad del alma.

Período: 2015-2018

Summary:

The project "The Relationship Between Science and Theology in the 21st Century: A Proposal for Philosophical Articulation" is intended to reflect the importance of the philosophical perspective in addressing the major current issues where experimental science and theology are interwoven. According to the vision of the Research Group "Science, Reason and Faith" (CRYF), in continuity with the thought of its founder, the late Professor Mariano Artigas, philosophical reason is ultimately able to build the necessary bridges to achieve one unified image of the world, expressing the complementarity between the scientific and the religious views.

The key objectives of the project are: (i) Develop a well-defined map of the points of intersection between science and Theology along the current century; (ii) introduce the specific problems underlying the confrontation of different perspectives, listening to the criticism performed from each scientific discipline in the context of an inclusive dialogue; (iii) carrying out an attempt to respond to each of these problems according to the methodological perspective of CRYF.

The project will run over three years. Each year will be dedicated to a general topic including various subtopics for discussion, which can be addressed scientifically, theologically and philosophically. There will be a permanent cluster group of members and collaborators of CRYF. Each year, the project IP and some of the researchers of the project will be in charge of running the cluster group and will be responsible for the organization of monthly seminars on the various issues that will be discussed. The initial proposal of topics per year is:

Year 1 (Sep 2015 - August 2016): "Creation and origin of the universe" (directed by Javier Sánchez Cañizares and Rubén Herce)

Year 2 (Sep 2016 - August 2017): "The development of creation: evolution and divine providence" (directed by Javier Sánchez Cañizares, Santiago Collado, and Antonio Pardo)

Year 3 (Sep 2017 - August 2018): "Human specificity: the problem of the soul" (directed by Javier Sánchez Cañizares, Luis Echarte, and José Manuel Giménez-Amaya)

During the first and third year of the project, the third and fourth Mariano Artigas Memorial Lecture (MAML) will take place. These lectures have been developed so far with two aims: to present the figure and scientific research of professor Artigas, and to give recognition to a researcher in the field of science and religion for its work done to date. In joining the project, these two MAMLs will have a content keeping with the topic of that year.

The results of the discussions and seminars will initially be issued in the interdisciplinary journal "Scientia et Fides", published since 2013 by the Nicolaus Copernicus University in Torun (Poland) in collaboration with the CRYF. The seminars will be recorded and subsequently posted on the website of CRYF and the YouTube channel of the University of Navarra. Furthermore, the MAMLs will be published in the collection that EUNSA publisher has devoted them. Finally, as one of the main objectives of the project, we aim to develop three MOOCs on each of the topics, and a textbook on matters of science, reason and faith that can be used in the subjects taught at the University of Navarra on these issues, as well as in high schools.

Difusión de resultados:

1. Durante el curso académico 2015-16 se han llevado a cabo los siguientes seminarios CRYF:
 - 15-IX Antonio Aparicio Juan y Francisco José Soler Gil. ¿Apunta la cosmología actual a un universo autosuficiente?
 - 17-XI Francisco González de Posada. El problema básico en las relaciones entre ciencia y fe: el origen del Universo y la Creación
 - 15-XII Nathaniel F. Barrett. The Cognitive Science of Religion: History, Key Debates, and Future Prospects
 - 19-I José Ángel Lombo La racionalidad del cuerpo humano
 - 16-II Javier Armentia. El auge de las pseudociencias: del Yeti de Formigal a los milagros de los hijos e hijas de la Tierra
 - 16-III Juan Arana. La conciencia inexplicada
 - 5-IV Ewa Agnieszka Lekka-Kowalik. A new paradigm of doing science: Mode 2 Science and consequences
 - 19-IV Javier Monserrat. El gran enigma. Ateos y creyentes ante la incertidumbre del más allá

- 17-V Emili Marlés. Jesucristo y la evolución cósmica
2. El 20 de octubre tuvo lugar la tercera edición de la Lección Conmemorativa Mariano Artigas, pronunciada por el profesor Giuseppe Tanzella-Nitti con el título: "¿Se puede hablar de Dios en el contexto de la ciencia contemporánea?" (<http://www.unav.edu/evento/mariano-artigas-memorial-lecture/leccion2015>). Se ha publicado el vídeo y el correspondiente folleto.
 3. Se han publicado los fascículos 3/2 y 4/1 de la revista interdisciplinar "Scientia et Fides" (<http://apcz.pl/czasopisma/index.php/SetF>).
 4. Se ha actualizado la página web del CRYF de acuerdo con los estándares de la Universidad de Navarra (www.cryf.org).
 5. Selección de publicaciones de los participantes en el proyecto (como primeros autores)
 - a) *Publicaciones:*
 - COLLADO S., VELÁZQUEZ H. "¿A qué se llama determinismo en física?" en C. Vanney y J.F. Franck (eds.), *¿Determinismo o indeterminismo? Grandes preguntas de las ciencias a la filosofía*, Logos-Universidad Austral, Rosario 2016. ISBN 978-950-893-900-5
 - HERCE R. "Christopher Dawson on Spengler, Toynbee, Eliot and the notion of Culture", *Cultura. International journal of Philosophy of Culture and Axiology* 12 (2), 2015, 45-60
 - ECHARTE L. "After Medicine. The Cosmetic Pull of Neuroscience." In Davis JE, Gonzalez AM (ed). *To Fix or To Heal. Patient Care, Public Health, and the Limits of Biomedicine*. New York: New York University Press, 2016: 84-109
 - ECHARTE L., BERNÁCER J., LARRIVEE D., ORON J.V., GRIJALBA-UCHE M. "Self-Deception in Terminal Patients: Belief System at Stake". *Frontiers in Psychology* 2016; 7: 1-6
 - GIMÉNEZ-AMAYA J.M. "Misericordia, compasión y perdón". *Boletín MFC*, Número 113, Abril de 2016, 4-5
 - PARDO A., ECHARTE L. "La formalización del consentimiento informado en investigación y la pérdida sentimental del paciente". *Persona y Bioética* 2015; 19(2): 198-226
 - PARDO, A. "Ética médica en Obstetricia y ginecología". Publicación electrónica. https://www.academia.edu/15105214/%C3%89tica_m%C3%A9dica_en_Obstetricia_y_ginecolog%C3%ADa
 - SÁNCHEZ CAÑIZARES. J. "Entropy, Quantum Mechanics, and Information in Complex Systems: A Plea for Ontological Pluralism", *European Journal of Science and Theology* 12/1 (2016), 17-37
 - b) *Comunicaciones a congresos*
 - COLLADO S. "The Threshold of the Scientific Rationality. The impact of religious-driven world-views in scientific innovation through the history of science". Comunicación: "Ciencia y Religión a la luz del enfrentamiento del Diseño Inteligente con

- el Darwinismo". STOQ Project Workshop, Pontificia Università della Santa Croce, Rome, 19-21.XI.2015
- ECHARTE L. Adolescencia un intervalo de vulnerabilidad y posibilidad. Cuadernos de Bioética XXVI 2015/3º: 472-473. Comunicación oral presentada en "Neuroética. Yo vulnerable", X Congreso Nacional de Bioética. Pamplona, 13 y 14 de noviembre de 2015
 - HERCE R. "Evolución y creación: ¿qué nos puede aportar la controversia de auxilliis para entender su relación?", Pensar y conocer a Dios en el siglo XXI, X Jornadas de Diálogo Filosófico, 24-26 de septiembre de 2015, Salamanca
 - HERCE R. "Is Homo naledi going to challenge our presuppositions on human uniqueness?", Are We Special? Science and Theology Questioning Human Uniqueness, 16th ESSSAT Conference, April 26 - May 1, Lodz-Warsaw (Poland).
 - PARDO A. II Jornada Internacional de Ciencias de la Salud: "Bioética en la investigación". Universidad Señor de Sipán, Chiclayo (Perú), 16-17 de noviembre de 2015: 3 comunicaciones: "La formalización del consentimiento informado en investigación"; "La enseñanza de la ética en la formación de los profesionales de la salud"; "La experimentación con embriones y fetos humanos"
 - PARDO A. Jornada en el 20 aniversario de la Encíclica Evangelium Vitae. Universidad Católica de Lublin. Lublin, 27 de noviembre de 2015. Ponencia: "Reconocer el valor de la vida"
 - SÁNCHEZ CAÑIZARES J. "The Threshold of the Scientific Rationality. The impact of religious-driven world-views in scientific innovation through the history of science". Comunicación: "The Impact of Religious Worldviews on Kelvin's Physical Insights: Thermodynamics and the Age of the Earth", STOQ Project Workshop, Pontificia Università della Santa Croce, Rome, 19-21.XI.2015
 - SÁNCHEZ CAÑIZARES J. "Naturaleza humana 2.0: Web, antropotecnias, naturalización de la espiritualidad". Comunicación: ¿Es compatible el compatibilismo con la existencia de correlaciones cuánticas del tipo EPR?, Cátedra de Ciencia, Tecnología y Religión (Universidad Pontificia Comillas), Madrid, 11-13.II.2016
 - SÁNCHEZ CAÑIZARES J. "Toward a Science of Consciousness", Center for Consciousness Studies (University of Arizona). Concurrent session: "Is Compatibilism Compatible with the Existence of EPR-like Quantum Correlations?" (C3), Tucson, 25-30.IV.2014

c) Libros:

- HERCE R. "Filosofía de la Ciencia". Barañáin, Eunsa 2016
- LOMBO J.A. y GIMÉNEZ-AMAYA J.M. "Biología y racionalidad". Ediciones Universidad de Navarra, Pamplona, 2016
- PARDO A. "Para pensar la evolución". Ed. Palabra. En prensa.

FACULTAD DE EDUCACIÓN Y PSICOLOGÍA



ARELLANO TORRES, ARACELI

Título: La transición a la vida adulta de jóvenes de la comunidad gitana en Navarra. Perfil de competencias y propuestas de mejora.

Presupuesto: 7.700,00 euros

Palabras Clave: Inclusión; Comunidad Gitana; Transición a la Vida Adulta; Autodeterminación; Empoderamiento.

Período: 2016-2019

Resumen:

Roma population is a heterogeneous group that is not necessarily linked to material and cultural deprivation or social exclusion. However, due to various reasons, they are one of the most socially vulnerable groups of population. Even taking into account the progress made in recent decades, there is still a long way to achieve equality in education for Roman children. Despite inclusive education and principles as respect to interculturalism and diversity, absenteeism and school dropout of Roma students continue being a source of concern. For years, the Roma community (families and professionals) have been working to improve and reduce the disadvantage of Roma children and youth in schools; especially in transition to adulthood.

This project focuses on the educational experiences of Roman children and young people, in transition to adulthood (15-19 years), since this is a complex process for these students (who have more difficulties in the case of not having the official degree). Specifically, the main objectives are: (1) analyse the legislative and organizational context in which the education of Roman children is developed (in Navarra); (2) identify the main needs and strengths of selfdetermination of young people in transition to adulthood; (3) describe perceptions of families regarding their children self-determination and (4) contribute to improve this process of transition of Roman children.

Thus, this research supports the development of self-determination as a main goal and an important pathway that contributes to the transition of Roman students. We pretend to identify needs of Roman children in this area, taking into account the perspective of families, in order to plan actions to encourage these students, and their families, in their academic and personal guidance.



LARA ROS, SONIA

Título: Estudio de la eficacia de un sistema de enseñanza-aprendizaje de la Lengua en Primaria, que integra la enseñanza del pensamiento y el trabajo cooperativo: variables cognitivas y no-cognitivas.

Presupuesto: 6.200,00 euros

Palabras Clave: Auto-regulación del aprendizaje; perseverancia; motivación; habilidades cognitivas y no-cognitivas; soft-skills; rutinas de pensamiento; destrezas de pensamiento; aprendizaje cooperativo; mapas mentales; pensamiento visible; culturas de pensamiento.

Período: 2015-2018

Summary:

Curricular directives are set forth that highlight the importance of cooperative work, creative thinking, problem-solving, and critical thought. All this implies that the student must be an active agent that controls its own learning (Duckworth, Akerman, MacGregor, Salter y Vorhaus, 2009; Claxton et al., 2011; Whitebread, 2014; Wolters, 2010). The debate on how such teaching must be implemented is still ongoing. The incorporation of the teaching of thinking skills is being considered, such skills being embedded into different subjects, all being based on constructivist theories of learning that consider the subject of learning an active part in the creation of knowledge and comprehension (Costa, 2000; Dewey y Bento, 2009; McGuinness, 2005).

Our initial hypothesis in this project is twofold. First, the integration in the classroom of teaching-learning strategies that develop thinking, and active and cooperative learning by the student has a beneficial effect not only on cognitive-type variables (comprehension and deeper learning), but also on non-cognitive variables, such as social, emotional, motivational, self-regulation, control, autonomy, effort, cheerfulness, perseverance). Second, variables relative to the teachers (such as beliefs about teaching-learning and formation in active methodologies) and to the context (such as classroom layout, time to reflect, spaces to make work visible, regarding mistakes as proof of learning, type of teacher-student interactions, student grouping) will influence the effect that the teaching-learning system has on cognitive and non-cognitive variables of the student.

Taking as a reference the system of teaching-learning of Spanish Language in primary school, ComunicARTE, which blends the teaching of cooperative thinking and work, we want to reach a threefold objective. One, to study the effect that a system of teaching-learning of this kind has on cognitive and non-cognitive student variables has, focusing on fifth- and sixth-grade students. Two, to study the effect of the teacher and context variables have on the efficacy of the learning system ComunicARTE, regarding cognitive and non-cognitive student variables has, focusing on fifth- and sixth-grade students. Three, in view of the results in the prior two goals, we will suggest improvements in the ComunicARTE teaching-learning system. The methodological approach is quantitative and qualitative, given the importance of the context and the interrelation of the variables involved in the process of implementation of the innovation.

Difusión de resultados.

A. Producción científica: Participación en 5 congresos/conferencias internacionales con 11 contribuciones y un Simposio:

- González, A. y Muracciole, N. (2015). Developing Communicative Competence in Students in Primary School In *Project Zero Perspectives: Zeroing in on Learning*. CASIE-Harvard Graduate School of Education. 1-3 Octubre, Amsterdam, Holanda.
- Lara, S. y González-Torres, M.C. (2016, Coordinadoras). Simposio: Innovación educativa al servicio de la creación de una cultura de aula
- que desarrolle variables cognitivas y no cognitivas imprescindibles para ser competentes en el S. XXI. En *VIII Congreso Internacional de Psicología y Educación (CIPE 2016)*, 15-17 de junio, Alicante.
- Lara, S. y González-Torres, M.C. (2016). Competencias del s. XXI y variables no-cognitivas: el nuevo desiderátum educativo. En *VIII Congreso Internacional de Psicología y Educación (CIPE 2016)*, 15-17 de junio, Alicante. En *VIII Congreso Internacional de Psicología y Educación (CIPE 2016)*, 15-17 de junio, Alicante.
- González-Torres, M. Y Lara, S. (2016). Concepción disposicional de la inteligencia: la importancia de desarrollar culturas de pensamiento en el aula. En *Congreso Internacional de Psicología y Educación (CIPE 2016)*, 15-17 de junio, Alicante. En *VIII Congreso Internacional de Psicología y Educación (CIPE 2016)*, 15-17 de junio, Alicante.
- Iriarte, C. y Lara, S. (2016). Emoción y cognición: una convergencia necesaria en el ámbito escolar. En *VIII Congreso Internacional de Psicología y Educación (CIPE 2016)*, 15-17 de junio, Alicante. En *VIII Congreso Internacional de Psicología y Educación (CIPE 2016)*, 15-17 de junio, Alicante.
- Lara, S.; González, A.; Muracciole, N y Sobrino, A. (2016). Promover la autorregulación a través de la evaluación formativa con iPads.

- *En VIII Congreso Internacional de Psicología y Educación (CIPE 2016), 15-17 de junio, Alicante.*
 - *En VIII Congreso Internacional de Psicología y Educación (CIPE 2016), 15-17 de junio, Alicante.*
 - *González, A. y Muracciole, N. (2016). ComunicARTE un sistema de enseñanza-aprendizaje de la competencia comunicativa a través del iPad. En VIII Congreso Internacional de Psicología y Educación (CIPE 2016), 15-17 de junio, Alicante.*
 - *Lara, S.; González, A.; Muracciole, N y Sobrino, A. (2016). Strategies for Applying Formative Assessment with iPad in an Elementary School. In ED-MEDIA 2016. World Conference on Educational Multimedia, Hypermedia and Telecommunications. June 28-30, Vancouver, British Columbia, Canada.*
 - *Lara, S. y González-Torres, M.C. (2016). La alianza entre competencias del S. XXI y las llamadas variables no-cognitivas vista desde una visión disposicional de la inteligencia. En XVI Congreso Nacional y VII Congreso Iberoamericano de Pedagogía, 28-30 de junio, Madrid.*
 - *Iriarte, C. (2016). Competencia emocional y procesos cognitivos: predisponer hacia el aprendizaje. En XVI Congreso Nacional y VII Congreso Iberoamericano de Pedagogía, 28-30 de junio, Madrid.*
 - *Lara, S. y Ugarte, C. (2016). Análisis de las propuestas de las competencias para el s.XXI a la luz del enfoque de capacidades. En VIII Congreso Internacional de Filosofía de la Educación, 21-23 de septiembre, Valencia.*
- B. Estancias de investigación: Ana Zúñiga ha estado entre los meses entre enero y agosto de 2016 en la Facultad de Educación de St. Mary's University (UK). Esta universidad tiene prestigio en Reino Unido en la preparación de sus estudiantes del grado de Magisterio y del máster de Secundaria en este aspecto.
- C. Elaboración de los proyectos del sistema de enseñanza ComunicARTE para sexto curso y primero de la ESO.
- D. Dirección de tesis doctorales y trabajos fin de grado y trabajos fin de master.
- a. Tesis doctorales relacionadas con el proyecto:
 - Iriarte, C. y Ch. Repáraz. (Directoras). Modificabilidad cognitiva y competencia socioemocional. Efectos de una intervención mediada en jóvenes con trastorno por déficit de atención con hiperactividad. Fernando González Gatica (Defendida, febrero 2016).
 - Lara, S. y Sobrino, A. (Directores). La evaluación de las interacciones en educación infantil y su relación con el desarrollo del pensamiento y las funciones ejecutivas. Marina Cuadra (comienzo 15-16).
 - b. Dirección de Trabajos fin de Grado y de Master (disponibles en DADUN):
 - Lara, S. (Tutora). Análisis de un sistema de enseñanza-aprendizaje de Lengua y Literatura Castellana en quinto curso

de Educación Primaria ComunicARTE +10. Grado en Pedagogía. Alumna Sadra Iriarte.

- González-Torres. M. (Tutora). Competencias del S. XX y variables no cognitivas: El incremento del interés por la investigación y educación del Autocontrol. Master en Intervención Educativa y Psicológica. Alumna Teresa Muñoa.
- González-Torres. M. (Tutora). Making Learning Visible: una propuesta basada en el Proyecto Zero y en el modelo Reggio Emilia. Grado en Educación Infantil. Alumna Camila González-Artigas Vaca.
- Iriarte, C. (Tutora). Características socioemocionales y aprendizaje en alumnos con altas capacidades. Master en Intervención Educativa y Psicológica. Alumna: Patricia Olmedo Ariza.

FACULTAD DE ENFERMERÍA



CHOPERENA ARMENDÁRIZ, ANA

Título: Narrativas y práctica reflexiva: un programa para el desarrollo de competencias profesionales en enfermería.

Presupuesto: 1.300,00 euros

Palabras Clave: Nursing, Reflexive Practice, Professional Competences, Professional Practice Model, Care Model, Respect.

Período: 2016-2018

Summary:

It is generally acknowledged that a reflexive practice encourages the nurses' professional development. Reflexive attitudes and clinical self-awareness generate a highly significant practical knowledge leading to the deployment of professional competences. The production of narratives by nurses who have lived significant cases in their daily practice boosts a reflexive behavior; thus this discursive tool serves to ground new professional competences. The professional development of nurses is defined by the Professional Practice Model (PPM) of each institution, which establishes the set of components and procedures to shape care administration. Clínica Universidad de Navarra (CUN), the institution hosting this project, is currently developing its own PPM. Its core component is a specific care model ("A nursing model centered on the interpersonal relationship between the nurse and the person being cared (individuals and families)" – mRIEP), which posits the nurse-patient relationship as the nuclear part of nurse care. This model articulates a series of values which include respect. From this perspective, narratives –conceived as a device for reflexive practice– may constitute a useful tool to reinforce certain professional competences such as respect, thus contributing to improve the assistential quality of the care received by patients. In light of this, the main aim of this project is to use narratives in order to promote the development of reflexive practices among the nurses taking part in specialization programs at the Clínica Universidad de Navarra.

The present project will be carried out in four stages: the first one will include a specific training program addressed to all the student-nurses in specialization programs (enfermeras alumnas de especialidad, EAEs). This program will deal with the concept of 'reflexive practice', the Mriep model of nurse care (developed by the School of Nursing of the University of Navarra) and the competence of 'respect' within it. This training program

will also focus on several dimensions of narratives: usefulness as a tool for reflexivity; production techniques; and parameters of evaluation. The second phase will deal with the design and production of narratives following Kim's (1999) model for Critical Narrative Inquiry. In the third phase, several types of analysis and reflexive exercises will be conducted through Focus Groups. Finally, in the fourth stage the research team will carry out a comprehensive assessment of the abovementioned tasks, and the outcomes of this evaluation will be tested in personal interviews with the participants (EAEs). The interviews will also serve to track the progress done in the reflexive exercise of the selected competence (respect). As far as this team is concerned, there is no previous research linking the development of reflexivity through narratives with the development of professional competences in nursing.



SARACÍBAR RAZQUIN, Mª ISABEL

Título: El cuidado en el domicilio de la persona con enfermedad avanzada: conociendo la experiencia de la familia Narrativas y práctica reflexiva: un programa para el desarrollo de competencias profesionales en enfermería.

Presupuesto: 5.950,00 euros

Palabras Clave: Nursing, Family, Home Care, End of Life Care, Palliative Care, Qualitative Research, Narrative Research, Experience.

Período: 2016-2018

Summary:

It is estimated that more than half of the persons who die each year have previously undergone a stage of advanced and terminal illness which not only affects the patient but also his family circle. In Spain, in 2012, approximately 4,033 persons per one million inhabitants were in the terminal illness phase. While the number of individuals in this type of situation continues to rise, interest is growing regarding the places where these deaths occur. It should be pointed out that although the number of deaths in hospital settings continues to be high, an increase is observed in the deaths that take place in the home. Even though patient care at home for the terminally ill is directly related to the support provided by the social and health environment, family involvement is essential. Recognition of the work the family carries out and the challenges the family constantly faces has led this type of care to become prioritized internationally within the research on end-of-life care.

This qualitative research will apply narrative research (focus groups and narrative interviews) to address, within the framework of the nurse and family personal interrelationship, the phenomenon of family care for an adult with a terminal illness at home. The main purpose of this work is: "To know the experience of the family who cares for a terminal patient in the home, during this process of care". The specific objectives are: 1) to know the "stories" (narratives) that the families tell regarding their experiences when caring for an adult family member with a terminal illness at home; 2) to recognize how the family experience of caring for a terminally ill member at home is manifested and 3) to identify the common themes shared in all the "stories" (narratives) told by the families in charge of caring for an adult family member with terminal illness at home. These objectives will allow us to

understand what each family's experience is with respect to caring for one of its members at home at the end-of-life stage. In spite of each family's experience being unique, by means of the second and third objective, this study proposes to take things one step further, to go beyond the specific experiences and to discover the issues common to all the stories.

The knowledge acquired from this research work can help us to understand this phenomenon from the "stories" narrated by the families themselves, in terms of the type of impact that this experience has on them and what this experience signifies in their lives, their environment, and in the care of a family member. This information will help us to offer the needed support and to evaluate, diagnose and intervene in the responses that are presented. In addition, the knowledge obtained from this study can be a good foundation for taking measures or making policies of a social and health type. With this knowledge, nurses would be prepared and well-positioned, able to anticipate the responses from the families who are taking care of a family member with terminal illness in the home and also able to support them in whatever way that is needed. In addition, the information obtained from this investigation can contribute to properly focusing nursing education, contribute to the design of new nursing practice models and nursing interventions, and finally, to contribute to the development of new instruments.

FACULTAD DE FARMACIA



GONZÁLEZ PEÑAS, MARÍA ELENA

Título: Multiexposición y toxicidad combinada de micotoxinas en el hombre y animales de granjas.

Presupuesto: 12.000,00 euros

Palabras Clave: Micotoxins, feed, plasma, human milk, LC-MS/MS, combined toxicity.

Período: 2016-2019

Summary:

Micotoxins are toxic compounds produced by fungi that contaminate food and raw materials which can reach man or animals and affect their health. Taking into account data of toxicity and contamination in food and feed, maximum permitted levels have been fixed for some of them in different matrices. Moreover, the more likely situation is the co-occurrence of several mycotoxins in a matrix. This is due to the ability of a fungi to produce a variety of mycotoxins simultaneously, a given matrix could be contaminated with different fungi and because animal and human diet is made up of different products. However, the toxic effects produced for the simultaneous exposition to these compounds are not known.

In order to increase our knowledge in this field, studies regarding the simultaneous presence of mycotoxins in food and feed are needed and they should be accompanied with studies of their presence in biological fluids. These studies will give information regarding the mycotoxins concentration levels, the most frequent combinations of micotoxins found and their bioavailability through food and feed.

In order to carry out these studies, it is necessary to have validated analytical methods, with adequate sensibility and, due to the chemical variety of these compounds, using universal detectors. The liquid chromatography technique with mass detectors (LC-MS) is useful for this purpose.

On the other hand, these studies must be accompanied with combined toxicity studies using the most frequent combinations found. This data will improve the estimation of the real risk for human and animal health.

The objectives of this project address these aspects:

- to study the presence of mycotoxins in feed (for cows, sheep, pig and poultry) and animal plasma.
- to study the presence of mycotoxins in human plasma and milk.
- to study “in vitro” the combined toxicity of the most frequent combinations of mycotoxins in these matrices.

The expected results are:

- to have LC-MS/MS analytical methods for simultaneous determination of mycotoxins in feed and biological fluids
- to know the co-occurrence of mycotoxins in feed for cows, sheep, pigs and poultry
- to know the co-occurrence of mycotoxins in biological fluids from humans and animals
- to know the most frequent combinations of mycotoxins in these matrices.
- to have “in vitro” data of combined toxicity of mycotoxins



TORDERA BAVIERA, ROSA Mª

Título: Potencial terapéutico de inhibidores de HDAC5 y de Sirt2 en la depresión mayor.

Presupuesto: 15.000,00 euros

Palabras Clave: Major depression, Histone desacetylase, Sirtuin 2, HDAC5, Antidepressants

Período: 2016-2019

Summary:

Our project is a continuation of a previous project Funded by the Ministry of Economy and Competitiveness (SAF2011-27910) directed to study preliminary hypothesis that links depression and antidepressant action to chromatin remodelling. Clinical and preclinical evidences have linked major depression to failure in synaptic plasticity. Growing evidence suggests that epigenetic mechanisms play a key role in neuronal plasticity, and, therefore, mediate stable functional changes in the brain in response to environmental stimuli. Specifically, stress-mediated epigenetic changes in limbic regions, that can persist for a lifetime, could contribute to the pathogenesis of depression. Likewise, antidepressant therapy might be achieved in part via epigenetic mechanisms. Moreover, epigenetic modifications could establish the basis for the interindividual variability in vulnerability to adversity and/or response to treatment.

Indeed, experimental studies show that chronic stress and antidepressant treatment regulate histone acetylation in brain areas involved in affective disorders. Similarly, while some HDAC's regulate negatively synaptic plasticity, some unspecific inhibitors of these enzymes have shown antidepressant activity.

Briefly, we show that chronic stress upregulates histone deacetylases Hdac5 and Sirt2 in the prefrontal cortex, which, could contribute to stable stress-induced neuronal adaptations. In addition, repeated reboxetine treatment increases the phosphorylated form of Hdac5 (P-Hdac5), indicating that noradrenaline mediates cytoplasmic export of this enzyme. Moreover, Sirt2 is downregulated by all monoaminergic antidepressants (Fluoxetine, Reboxetine and Imipramine) suggesting that these effects could contribute to the well-known beneficial effects of antidepressants on brain plasticity.

We aim to study here the therapeutic potential of Hdac5 and Sirt2 as targets for major depression. Specific HDAC4/5 (MC3822, MC3823) and Sirt2 (33i, 33a) inhibitors will be used in different mouse models of depression. We aim to answer:

- (1) If Hdac5 inhibition is a good pharmacological strategy for the treatment of depression caused by low noradrenaline function.
- (2) If Sirt2 inhibition is a good pharmacological strategy for the treatment of depression caused by low noradrenaline and/or serotonin function.
- (3) If combined Hdac5 and Sirt2 inhibition accelerates antidepressant action.
- (4) If Hdac5 or Sirt2 inhibition, is a good pharmacological strategy for age-related depression or neurodegenerative illness linked to aging.
- (5) Finally the pharmacokinetic profile of the compounds or selected combinations studied previous pharmacological studies will be characterized. We aim to meet the requirements that need to be achieved before a new compound can be considered appropriate to be tested first time in humans.

The chronic mild stress (CMS), chronic social defeat stress, VGLUT1 heterozygous mice and the CMS x Samp8 (Senescence Accelerated Mouse Prone 8) will be used.

Although all these models lead to very distinct neurochemical alterations, all of them can model anhedonia, a specific symptom related to depression. In agreement with this, a specific symptom in different neuropsychiatric patients may be caused by different aberrant biologies.

This study will provide a further knowledge of different epigenetic mechanisms leading to antidepressant action, and also, will help to improve the rational prescription of existing antidepressants, known to act on biological substrates rather than on symptoms.



GARRIDO CID, Mª JESÚS

Título: Estudio de agentes inmuno-nucleares en oncología mediante plataformas preclínicas para desarrollar un modelo cinético-dinámico con carácter traslacional.

Presupuesto: 12.500,00 euros

Palabras Clave: Oncología-Inmunomodulador-liposomas dirigidos-Doxorubicina-PK/PD modelado- plataformas invitro/ in-vivo-BBB model-Biofar

Período: 2015-2018

Summary:

The immune response can be modulated by blocking some receptors such as Cytotoxic T-lymphocyte associated antigen 4 (CTLA4), programmed cell death protein 1 (PD1) and its ligand PD-L1, known also as "immune checkpoints". They represent a promising approach to activating therapeutic antitumour immunity. PD-1, a transmembrane protein expressed in T, B and NK cells and monocytes, is bound to its ligand PD-L1, upregulated in tumor cells, promoting the inhibition of antitumour T cell-mediated response, and providing the tumor proliferation. The blockage of PD1/PD-L1 by the use of specific monoclonal antibodies (mAb) leads to increase the specific-tumor T-cell response. However, the experience with anti-PD-L1 is much less than for other mAbs. Thus, the investigation of their mechanism of action, pharmacokinetics (PK) and pharmacodynamics (PD) represents a challenge for antitumor therapy providing relevant insights to establish interesting drug combinations. In that sense, some antitumor drugs like Doxorubicin (Dox) are able to induce Immunogenic Cell Death (ICD). This effect is a type of apoptosis characterized by events promoting increase CD8+ T cells in the tumor. Note that the characterization and quantification of those processes implicates in the in-vivo response such as: ligand-receptor binding, activation/ regulation of certain signalling pathways, responsible for the trafficking of endogenous molecules, can be done by mathematical models. Their parameters together with the drug PK parameters allow us to describe the relationship drug exposition/response. Thus, preclinical models (in-vitro and in-vivo) represent a useful framework to explore complex experimental designs which combined with PK/PD models provide information in detail about process/mechanism responsible for drug response. Therefore, we propose translational studies to obtain data

regarding the disease and treatments proposed here, mAb-anti-PD-L1 plus Dox, to apply to patients, optimizing drug schedules or combinations. Dox will be entrapped in different types of nanocarriers in order to decrease its site effects, and some of them will be coupled to mAb. Then, the main objective is to develop a PK/PD model able to characterize and describe the anti-PD-L1 effect and the combination Dox/anti-PDL1 using animals models bearing syngenic tumor cells.

On the other hand, the characterization of the mechanism involved in the access of the proposed treatments to tumors located in places like Central Nervous System (CNS) to achieve adequate therapeutic effect, is the objective for the subproject 2. This group has a new in-vitro model of Blood Brain Barrier (BBB) based on cell monolayers of MDCK and MDCK-MDR1 for CNS drug screening. This system permits to estimate the unbound fraction in plasma, the apparent distribution volume in brain and the partition coefficient brain/plasma. Its main advantage is that allows the estimation of relevant BBB-parameters using a single experimental system, contributing to the three R'ss policy (reduce, refine, replace) in animal experiments.

This project reflects the current drug development paradigm in which a new therapeutic strategy in oncology is proposed and where, its pharmacological optimization will be based on PK/PD models applied to drug-targeting strategies (subproject 1) and in-vitro systems for the biopharmaceutical optimization (subproject 2) ensuring the access to sites of action.

Difusión de resultados

Pósters:

“Anti-PD-L1 immunotherapy understanding its effect mechanism through biomarker” en el ***3rd immunotherapy of Cancer Conference*** celebrado el marzo (21-23) en Munich (Alemania); además, también han sido recogidos en el manuscrito titulado: ***“ Correlation between anti-PD-L1 tumor concentrations and tumor-specific and nonspecific biomarkers in a melanoma mouse model”***, enviado a finales de mayo a la revista ***Oncotarget*** situada en el Q1 del área de oncología del JCR.

“Immune checkpoint blockade in melanoma by new targeted Dox immunoliposomes “ a dos congresos internacionales dentro del campo científico diferentes, atendiendo a la temática multidisciplinar del proyecto: ***XI Spanish-Portuguese Conference on Controlled Drug Delivery: Revolutionary Approaches in Nanomedicine Development***, en enero (21-23) en Granada (España) y en el ***3rd immunotherapy of Cancer Conference***.



SANMARTÍN GRIJALBA, M^a DEL CARMEN

Título: Modulación estructural sobre antitumorales selenados inductores de apoptosis y reguladores de la vía PI3K/Akt/Mtor.

Presupuesto: 15.200,00 euros

Palabras Clave: Selenio, metilseleno, diseleniuro, apoptosis, ciclo celular, PI3K/Akt/mTOR.

Período: 2014-2017

Summary:

Numerous molecular mechanisms have been described as potential targets in antitumor therapy. In the hard pursuit of new antitumor drug research, biodirected rational design as a result of therapeutic specific target choice is nowadays compulsory. There are implicit difficulties in pharmacophore identification which justifies the interest in focusing in a target that is not excessively restrictive.

In the present project, with our experience in the field of antitumoral agents and the appliance of Medicinal Chemical Hybridization (MCH) strategy, the synthesis of three new series of molecules is proposed. Those molecules emerge from two different structural models to incorporate selenium as methylseleno and diselenide chemical entities, both with proven antitumor activity. They are linked through different nexus to carbo or heterocycles of confirmed efficacy as apoptotic agents and/or kinase activity modulators of the PI3K/Akt/mTOR pathways. The objective of this design is to achieve synergy as well as selectivity in the action in order to boost the response.

All the synthesized molecules will be evaluated as cytotoxic agents in six tumoral cell lines and in two non-tumoral cell lines in order to explore the selectivity. The most active and selective compounds of each serie will be selected to elucidate the possible mechanism of action focused in the ability to induce cell death, cell cycle blockage and the modification in protein expression that could affect the PI3K/Akt/mTOR signalling axis.

Difusión de resultados

Publicaciones:

AUTORES: Verónica Alcolea, Daniel Plano, Deepkamal N. Karelia, Juan Antonio Palop, Shantu Amin, Carmen Sanmartín, Arun K. Sharma
TÍTULO: "Novel seleno- and thio-urea derivatives with potent in vitro activities against several cancer cell lines"
REVISTA: Eur. J. Med. Chem, 2016, 113, 134-144.
CLAVE: A

AUTORES: Graciela B. Tognon, Carmen Sanmartín, Verónica Alcolea; Francine L. Cuquel, Nieves Goicoechea.
TÍTULO: "Mycorrhizal inoculation and/or selenium application affect postharvest performance of snapdragon flowers"
REVISTA: Plant Growth Regulation, 2016, 78, 389-400.
CLAVE: A

AUTORES: Beatriz Romano, Juan Antonio Palop, Carmen Sanmartín, Elena Lizarraga.
TÍTULO: "Thermal Analysis of Novel Selenocarbamates"
REVISTA: Journal of Thermal Analysis and Calorimetry 2016, 123, 1951-1962.
CLAVE: A

AUTORES: Nieves Goicoechea, Idoia Garmendia, Eliseu G. Dos Santos, Marcelle M. Bettoni, Juan Antonio Palop, Carmen Sanmartín
TÍTULO: "Selenium fertilization and mycorrhizal technology may interfere in enhancing bioactive compounds in edible tissues of lettuces"
REVISTA: Scientia Horticulturae 2015, 195, 163-172.
CLAVE: A

AUTORES: Mette Stoedter, Kostja Renko, Elena Ibáñez, Daniel Plano, Niels-Peter Becker, Janine Martitz, Juan A. Palop, Alfonso Calvo, Carmen Sanmartín, Lutz Schomburg
TÍTULO: "Strong induction of iodothyronine deiodinases by chemotherapeutic selenocompounds"
REVISTA: Metallomics 2015, 7, 347-354.
CLAVE: A

Se han presentado 6 comunicaciones a los siguientes Congresos:

En EFMC International Symposium in Medicinal Chemistry, Amberes (Bélgica) 14-16 de Septiembre de 2015. Libro de Abstract editado por ChemMedChem.

Autores: Alcolea, V; Plano, D.; Karelia, D.; Pandey, M.K.; Palop, J.A.; Amin, S.; Sanmartín C. ; Sharma, A.K.
TÍTULO: IDENTIFICATION OF A NOVEL SELENO-UREA DERIVATIVE AS A POTENTIAL MELANOMA THERAPEUTIC
Tipo de participación: Póster
Congreso: FMC 2015. Frontiers in Medicinal Chemistry
Publicación: Libro de abstracts
Lugar celebración: Amberes, Bélgica Fecha: 14 – 16 de Septiembre de 2015

Autores: Ana Carolina Ruberte, Cristina Hernández, Pablo Garnica, Nuria Díaz, Carmen Sanmartín Daniel Plano.

TÍTULO: SYNTHESIS, RADICAL SCAVENGING EFFECTS AND CYTOTOXIC ACTIVITY AGAINST PROSTATE CANCER CELLS OF NOVEL SELENOHETEROCYCLIC COMPOUNDS

Tipo de participación: Póster

Congreso: FMC 2015. Frontiers in Medicinal Chemistry

Publicación: Libro de abstracts

Lugar celebración: Amberes, Bélgica Fecha: 14 – 16 de Septiembre de 2015

Autores: Pablo Garnica, Nuria Díaz, María Font, Ignacio Encío, Daniel Plano, Carmen Sanmartín TÍTULO: NOVEL ACYLSELENOUREAS DERIVATIVES WITH POTENT IN VITRO ACTIVITIES AGAINST SEVERAL CANCER CELL LINES

Tipo de participación: Póster

Congreso: FMC 2015. Frontiers in Medicinal Chemistry

Publicación: Libro de abstracts

Lugar celebración: Amberes, Bélgica Fecha: 14 – 16 de Septiembre de 2015

Autores: Nuria Díaz, Pablo Garnica, Patricia Iribarren, Elena Lizarraga, María Font, Ignacio Encío, Daniel Plano, Carmen Sanmartín

TÍTULO: DESIGN, SYNTHESIS AND BIOLOGICAL EVALUATION OF NOVEL METHYLSELENO DERIVATIVES AS ANTIPROLIFERATIVE AND CYTOTOXIC AGENTS

Tipo de participación: Póster

Congreso: FMC 2015. Frontiers in Medicinal Chemistry

Publicación: Libro de abstracts

Lugar celebración: Amberes, Bélgica Fecha: 14 – 16 de Septiembre de 2015

Autores: Ylenia Baquedano, Clotilde Marín, Verónica Alcolea, Rocío Cañas, Esther Moreno, Socorro Espuelas, Manuel Sánchez-Moreno, Carmen Sanmartín, Daniel Plano

TÍTULO: SELENOCYANATE AND DISELENIDE DERIVATIVES AS PROMISING LEISHMANICIDAL AND ANTITRYPANOSOMAL AGENTS

Tipo de participación: Póster

Congreso: FMC 2015. Frontiers in Medicinal Chemistry

Publicación: Libro de abstracts

Lugar celebración: Amberes, Bélgica Fecha: 14 – 16 de Septiembre de 2015

Autores: Grasiela B. Tognon, Carmen Sanmartín, Verónica Alcolea, Esther Redín, Daniel Plano, Francine L. Cuquel, Nieves Goicoechea

TÍTULO: RADICAL SCAVENGING ACTIVITY, IN VITRO CYTOTOXICITY AND BIOFORTIFICATION EFFECTS OF SEVERAL SELENINIC ACIDS

Tipo de participación: Póster

Congreso: FMC 2015. Frontiers in Medicinal Chemistry

Publicación: Libro de abstracts

Lugar celebración: Amberes, Bélgica Fecha: 14 – 16 de Septiembre de 2015

FACULTAD DE FILOSOFÍA Y LETRAS



GIBSON, MARK

Título: Cognition, Learning and Intergestural Coordination: Tracking the evolutionary learning of vocal tract coordination en route from novice to expert behavior in two subject groups.

Presupuesto: 18.395,00 euros

Palabras Clave: Inter-gestural timing, speech production, dynamical systems, motor control, syllable timing, articulation

Período: 2016-2019

Summary:

This transdisciplinary and transcontinental project follows two subject groups down their paths to articulatory mastery. The project has three main parts: (1) experimentation and training, (2) materials design, and (3) assessment of progression toward adult- and/or native-like speech parameters. The subject groups chosen for this study include (1) subjects with cochlear implants (CI group) and (2) non-native (L2 group) learners of Spanish. Previously collected kinematic and electroglottographic data from native Spanish-speakers will serve as the baseline for learning (Gibson (PI), Tobin and Gafos, in preparation). The subject groups were chosen due to the nature of the physiological, cognitive and neuroanatomical constraints which shape speech-motor learning. In both subject groups, the acoustic input stream is distorted, albeit in different ways, leading to perceptible disfluencies and/or non-native like productions (e.g. foreign accented speech). And while these constraints present certain obstacles to learning, previous research shows that, with practice and/or training, native- and/or adult-like patterns of inter-gestural timing are indeed achievable (Lane, Wozniak & Perkell 1994; Catford & Pisoni 1970; Adler-Bock 2004; Adler-Bock, 2007; Gick et al. 2007; Brendel & Ziegler 2008; Albert, Sparks, & Helm 1973; Sparks & Holland 1976; Wertz, Lapointe, & Rosenbek 1984; Square, Martin & Bose 2001; Rubow, Rosenbek, Collins, Longstreth 1982; Dworkin, Abkarian, & Johns 1988; Shane & Darley 1978; Wambaugh & Martinez 2000; Reid & Lin 2006).

The combined results of previous research suggest that learners exploit a variety of alternative strategies and modalities in order to learn novel patterns of inter-articulatory and laryngo-articulatory coordination (learning in the tradition of Adams 1971; Gentile 1972; Newell 1996; Schmidt 1975; Zanone & Kelso 1992, 1997), though to date, no longitudinal study has been performed to track and document progress throughout the course of learning. The overarching objectives of this research are (1) to track the

evolutionary learning of complex articulatory coordination en route from novice to expert behavior, (2) to use the results from this research to design and diffuse a series of pedagogical materials to inform speech therapy protocols and second-language teaching of pronunciation, and (3) to create an objective statistical-based assessment tool with which to evaluate progress by learners in various groups, points (2) and (3) implying direct economical and strategical benefits for the College of Humanities and Social Sciences at the Universidad de Navarra. Results of this research are expected to have resounding impact in the domains of Motor-Control Learning, Second Language Pedagogy, Speech Therapy and Cognitive Science.

The following study is organized in three parts. The first part, described below, details the data collection and experimentation phase whereby learning is tracked around different training sessions. The second part of the study codifies the significant results from the experimentation and training phase in a series of didactic materials for public use (through publications and online resources). The third part of the study models the progression from novice to expert behavior using an assessment tool based on multidimensional scaling and similarity measures for use by educators and speech therapists.



NUBIOLA, JAIME

Título: La correspondencia del tercer viaje europeo de Charles S. Peirce (septiembre-noviembre de 1877).

Presupuesto: 6.300,00 euros

Palabras Clave: SCIENTIFIC CORRESPONDENCE, GEODESY, PRAGMATISM, ON-LINE PUBLICATION IN HUMANITIES

Período: 2016-2018

Summary:

The research project aims to advance the understanding of the American philosopher and scientist Charles S. Peirce (1839-1914) through the identification, transcription, translation into Spanish and installation in the web of his correspondence during his third stay in Europe (September-November 1877), as well as the correspondence he had with some prominent European scientists and intellectuals of his time.

The aim is not only continuing the work begun by the Grupo de Estudios Peirceanos on his correspondence of the first trip (1870-71: <http://www.unav.es/gep/PrimerViaje.html>) and his second trip (1875-76: <http://www.unav.es/gep/SegundoViaje.html>) but also aims to offer a new more cosmopolitan view of Charles S. Peirce, which is more accurate with the historical reality. Charles S. Peirce's participation in the International Conference of the International Geodesic Association in Stuttgart (27 September-2 October 1877) may be considered the culmination of his scientific work developed in the previous decade.

This project is also designed as the germ of a wider international project in which scholars of different countries may actively cooperate [the group Pragma in Italy, the Forschergruppe Bildakt-Kolleg Berlin und Verkörperung in Germany and Commens in Finland, in particular] to create an effective European co-laboratory, multidisciplinary web-based, that enhances both the reception of the thought of C. S. Peirce in the XXI century and also the introduction of new technologies for the universalization of the documentary resources hitherto confined to the archives and libraries or in inaccessible publications.



PAVÓN BENITO, JULIA

Título: Las freiras de la Orden del Hospital de San Juan de Jerusalén en la Edad Media en el reino de Navarra. Intervención arqueológica y estudio histórico-artístico del convento de Bargota.

Presupuesto: 6.451,00 euros

Palabras Clave: NUNS. HOSPITALLER WOMEN IN THE MIDDLE AGES. ORDER OF SAINT JOHN OF JERUSALEM. HISTORY, ARTISTIC HERITAGE AND ARCHAEOLOGY IN MEDIEVAL NAVARRE.

Período: 2016-2019

Summary:

This project involves the archaeological intervention and subsequent historical-artistic study of the Medieval Bargota convent (Mañeru Valley, Navarre), which belonged to the Order of the Hospitaller Knights of St. John of Jerusalem. The convent initially served as the Knights' preceptory, or military headquarters (12th to 13th century), and later became home to a community of nuns (14th to 15th century).

Scientific-academic excavation and investigation will also be used to share the project's methodology and objectives with the academic community by enabling students pursuing the Degree in History to do internships at the site. The project may also be included in the University of Navarra's social integration program (Tantaka: <http://www.unav.edu/web/vida-universitaria/eventos/solidaridad>), so that people with disabilities, the elderly and immigrants can work as tourist guides at the site after completing a training course.

The exceptional location of the archaeological site in a detached setting about two kilometres outside the town of Puente de la Reina on St. James Way will allow for an exhaustive archaeological campaign. It will also be possible to combine the material and artistic knowledge gained from the excavation with the study of documentation on the preceptory and convent from the National Historical Archive, the Royal and General Archive of Navarre and the National Library of Malta. This collection of documents was compiled, catalogued, transcribed and analysed as part of our team's research projects subsidized by the Ministry of Education, Culture and Sport

and the University of Navarra Research Plan (PIUNA) and is currently being prepared for publication.

Research into the different features of Bargota convent's historical-artistic legacy will also make it possible to study the nature and characteristics of the phenomenon of female spirituality specifically linked to the Order of the Hospitaller Knights of Jerusalem in the Kingdom of Navarre and as part of a broader analytical exercise comparing the situation on the Iberian Peninsula and in Western Europe. Communities of hospital nuns (freiras, donas) were smaller in number than their male counterparts, but brought new roles and identifying features to the order. At local and even regional level, their role complemented traditional socio-economic functions and was of vital importance within the institution's religious framework. Therefore, studying this site in Navarre in its broad institutional framework will make it possible to raise questions and find answers on a complex phenomenon that has received little attention from specialists.

Finally, recovering the ruins will certainly clear up many historical-artistic questions, but it will also transform Bargota convent by attracting visitors and helping them understand the little-known functions of the female members of the Hospitaller Order.



PÉREZ LÓPEZ, PABLO

Título: Perfiles del centro político (1976-1986)

Presupuesto: 9.300,00 euros

Palabras Clave: Spain, History, Transition, Democracy, Biography, Political centre

Período: 2016-2019

Summary:

In this project we aim to provide original knowledge about those who played a key role in the life of the political centre during the Transition to Democracy, all throughout the period in which the UCD governed Spain, and in the preceding and successive times. Our work will be based in the analysis of eleven personal archives of remarkable protagonists, several public archives, novel interviews with political actors and the review of newspaper and magazine libraries. The personal archives that we have selected will make the bulk of the research and belong to a prime minister (Leopoldo Calvo-Sotelo), eight cabinet ministers (José Pedro Pérez-Llorca, Juan Antonio García Díez, Joaquín Garrigues Walker, Antonio Fontán, Alfonso Osorio, Marcelino Oreja, José Manuel Otero Novas, Rafael Calvo Ortega), a member of parliament who promoted a regionalist split in the party (Jesús Aizpún), and the personal assistant of president Suárez (Eduardo Navarro). Taken together, these personalities represent a collection of the main families of the political centre: Independents, Christian Democrats, Liberals, "azules" (blues), Social Democrats and Regionalists.

Our primary goal is to contribute to the renewal of the history of centrism, adding new data and interpretation to the views published so far. We expect to offer a portrait, both individual and collective, of some of the men who embodied the political centre during those years, so as to obtain a deeper knowledge of the nature of the Transition to Democracy and its achievements. From the analysis of the successful –and unsuccessful– undertakings of such a historical moment of intense change, valuable conclusions will arise, of undoubted interest for the better understanding of the challenges that the Spanish society and political system are currently facing.

This project will also enable the formation of historians who will be able to adopt a biographical point of view without forgetting collective contexts,

and who will be interested in a moment of change particularly relevant in our recent history, which is nowadays the object of unprecedented attention.



PIÑERO MORAL, RICARDO

Título: Experiencia estética en la acción. Antoni Tàpies: una nueva perspectiva.

Presupuesto: 9.300,00 euros

Palabras Clave: Antoni Tàpies, Art as Experience, Action Art, Theory of Art, History of Contemporary Art, Museum University of Navarre.

Período: 2016-2019

Summary:

This project seeks to provide a new perspective on the works of Antoni Tàpies. So far, his artistic works have been interpreted within the framework of Informalism and in a context very limited to historical social circumstances in which he lived. Besides, his connection with the Catalan tradition and the symbolism of his works have been particularly highlighted.

However, we also find his works contain many elements belonging to the aesthetic current of Action art, interestingly merged with Conceptual art, both which were developed over the 20th century. The Action art, rooted in Dadaism and the theory of "art as experience", signified an important change in the way of understanding the contemporary art. The writings and artistic works of Tàpies show that his concerns are mostly placed within that aesthetic bearing, although he himself would have rejected such label. Starting with this assumption, nonetheless without undervaluing the strength of the historical, political and artistic context in which the Catalan artist lived, the principal objective of this project aims to re-read his artworks from a new perspective which has been overlooked by disciplines such as history and theory of art.

The specific goals of the present project are: firstly, to review Tàpies's writings in order to detect his relation with the above-mentioned aesthetic current through their explicit references to authors and artists, as well as to those ideas which he developed throughout his life; secondly, to spread the outcomes of the re-reading by means of taking parts in conferences and organizing work days dedicated to the artist at the University of Navarre; thirdly, to analyze and value the artworks of Tàpies housed in the Museum University of Navarra through specific studies and concrete actions so as to

make them more known and allow these works to be understood as part of a universal patrimony.

In order to achieve these objectives, periodical seminars will be organized among the members of the project, along with a workshop and an international conference, which will lead to a publication at least in three years of the project. Moreover, we will periodically disseminate the proposals and interests of the project through a website and social media.



ZABALZA SEGUIN, ANA

Título: Las elites sociales y políticas en Navarra durante la crisis del Antiguo Régimen: ¿continuidad o ruptura?

Presupuesto: 4.500,00 euros

Palabras Clave: Elites, Social reproduction, Navarra, Crisis of the Ancien Regime

Período: 2016-2019

Summary:

This project, which brings together a new interdisciplinary team focuses on a historical period, the crisis of the Ancien Regime in Navarra, which has been studied from the political, military, economic and institutional perspective. The new element is its approach: a new look from the social and cultural history, which shall fix their attention on the protagonists of the two views in debate: liberal and traditional, represented by people who lived in the time and they gave way to the particular entry of Navarra in the contemporary age. The main question is whether a new political system carries a renewal in the elites, and, if it occurs, what its draft. We try to study how the old elite adapts to new times, and this from an interdisciplinary and transversal perspective. Put the focus on the most important families, presents in both the civil world and the church, let you know what factors could influence their ideological affiliation, and if within the same family differences occur.

The research focuses therefore on Navarre elites of the late eighteenth and early nineteenth. their family history and its vital and formative experience will be studied, particularly their education. At the same time the common people will be studied, immersed in the same historical events, but carrying values and different expectations, silent majority who lived and conditioned changes.

The team intends to undertake an ambitious work on archival sources which, because of their dispersion, have not been studied so far. The same political instability and swerve of the administration have produced its dispersion among various documentary deposits.

Among the objectives, in addition to the already mentioned, this project aims to bring together scientists from different specialties: both the members

of the research team as scholars from abroad. Along with this, it aims to provide the academic community a series of publications—a book and several articles—that collect the results of three years of work. Finally, it seeks to provide Navarra society a better understanding of their past.



SOTO BRUNA, Mª JESÚS

Título: Unidad y pluralidad. Metafísica del logos en las líneas explicativas medievales de la racionalidad de la naturaleza.

Presupuesto: 2.300,00 euros

Palabras Clave: UNIDAD, PLURALIDAD, LOGOS, RACIONALIDAD, NATURALEZA.

Período: 2015-2018

Summary:

The present project is part of a wider investigation which is pending evaluation by the Ministry of Economics and Competition. Within the research plan established by the University of Navarra, this project is inserted in the Institute of Medieval Studies (Directed by Soto Bruna, IP), with the intention of promoting a central and significant line of interpretation within medieval thought.

The project described presents an innovative approach to Medieval (interdisciplinary) studies since it is centered on causality and related notions: “manifestation,” “procession,” “intelligible emanation,” “expression” and “explication”: concepts associated with Neoplatonism which has elaborated a metaphysics of the logos as the rational interpretation of an emanationist-manifestative process from the first cause as the origin of the “universitas rerum”; a question dealt with in the first metaphysics written in Spain (Avicbron-Gundisalvo) and along the lines of Eriugena to Eckhart, leaving open the question of the unity and the plurality of the causal action of the logos. This problematic has been dealt with in an original way in previous project on Logos as totality and simplicity by the research nucleus of the present project (MEC-DGICYT, TXT 99-1287; HUM2004-00983/FISO; FFI2008-02084 y FFI2011-29729).

The selection of significant lines—which turn historically, in a preceding or consequent way, around the polemics surrounding the Liber de causis—will serve for a dialogue with some contemporary expositions concerning the recovery of the classical logos, such as may be found, for example, in H.-G. Gadamer.

Anticipated objectives, and results:

1. History and lexicography: the following explanatory ways are established: a) Neoplatonic (G. of Nisa, J. E. Eriúgena, Buenaventure of B.), b) the Stoic-ciceronian tradition, W. of Auxerre, Philip the Chancellor), c) Avicennian (Avicenna and the Liber de causis primis et secundis), d) naturalist, sources on Arabic science (Herman of Carinthia), e) lexicography—emerging technologies—(lexicography brought into the Spain of the XIIIth century by D. Gundisalvo), f) systematic (Thomas Aquinas, J. Eckhart, N. of Cusa), g) medieval hermeneutics.
2. Speculation: The singular relation between the following terms will be studied: “arje,” “unity,” “plurality,” and “logos.” This is seen in the Aetas boethiana, or in the Summae of the XIIIth century, in part of Stoic-ciceronian tradition; also in the Neoplatonism of the IVth century, as well as in the Eriugenian-Cusanus way taken-up in philosophical vocabulary and in the introduction of knowledge in the XIIIth century due to the Arabic science and the Hispanic-European knowledge, which assumes a new philosophical dialogue.
3. Premediaeval edition (G. of Nisa, Eriugena); monography (ed. Brepols / FIDEM).

Difusión de resultados

Elisabeth Reinhardt

- David Albertson, *Mathematical Theologies. Nicolas of Cusa and the Legacy of Thierry of Chartres*, Oxford University Press, New York 2014, 512 p., en: “Anuario filosófico” 48/3 (2015) 567-570. Reseña.
- Ernst Christoph Suttner, *Ekklesiologische Überlegungen zur Geschichte der Kirchenspaltungen*, Echter Verlag, Würzburg 2015, 93 pp., en: “Anuario de Historia de la Iglesia” 24 (2016) 608-609. Reseña.
- Thierry of Chartres, *The commentary on the De arithmetica of Boethius*, Caiazzo, I. (ed.), Pontifical Institute of Mediaeval Studies (“Studies and Texts”, 191), Toronto, 2015, XI+262 pp., en: “Anuario Filosófico”, 49/2 (2016) 486-488. Reseña.
- Michael Estler, *Rigans montes (Ps 104,13). Die Antrittsvorlesung des Thomas von Aquin in Paris 1256*, Stuttgart: Verlag Katholisches Bibelwerk (“Stuttgarter Biblische Beiträge”, 73), 2015, 415 pp., en: *Scripta Theologica*, /2 (2016) junio 2016. Capítulo en obra colectiva: “Begegnungen mit Leo Elders”, en: J. Vijgen (ed.), «Libenter praeceptorum laudes celebrarem». *Stories and Reflections in Honor of Father Leo Elders on His Ninetieth Birthday*, un volumen de homenaje, dirigido por Jörgen Vijgen (Holanda). Junio 2016.

María Jesús Soto Bruna

Organización de Coloquios Internacionales

XI Jornadas De iustitia et iure: “Lenguajes del pensamiento medieval y renacentista” que ha coorganizado la Universidad Católica Argentina, con la Universidad de Los Andes y el Instituto de Estudios Medievales de la Universidad de Navarra, durante los días 10, 11 y 12 de agosto.

Conferencias impartidas

“Unité et bien. Boèce compris par Gundissalinus (XIIe siècle)”, en Boèce au fil du temps. La réception de son oeuvre et son influence sur les lettres européennes du Moyen Âge à nos jours, Université de Reims Champagne – Ardenne. Colloque international sous la direction scientifique de Sophie Conte, Alicia Oïffer – Bomsel & María Elena Cantarino Suñer.

Artículos y capítulos de libro

"Imago representationis creata. Liberté et union avec l'Absolu: Mystique spéculative et réflexion sur "accès à Dieu chez Nicolas de Cues", en 'Homo mysticus. Nicholas of Cusa and the Rhineland Mysticism, en: Annales de Philosophie (Roczniki Filozoficzne), LXIII (2), 2015 (Universidad Católica de Lublín), pp. 125-143. Disponible en: www.kul.pl/ap.

"El concepto de naturaleza como unidad causal en D. Gundissalinus", en J. L. Fuertes / A. P. González (eds.), De Natura. La naturaleza en la Edad Media, Volumen II. Húmus, Textos e estudios de Filosofía Medieval, 8, Lisboa 2015.

Victor Sanz

Vox naturae, vox rationis. Conocer la naturaleza, la causa y la ley en la Edad Media y la Modernidad Clásica. (G. Olms, Verlag, Hildesheim, en preparación de publicación e incluido en la Colección "Razón y normatividad" / "Reason and Normativity" / "Vernunft und Normativität", dentro de la Serie sobre razón práctica, moralidad y ley natural). Editoras: María Jesús Soto-Bruna / Laura E. Corso de Estrada (prevista publicación en octubre de 2016).

El Prof. Víctor Sanz ha colaborado en este libro con un capítulo, «La sobrenaturalización de la razón en la Cribatio Alkorani de Nicolás de Cusa» La Prof. **Soto-Bruna** ha escrito asimismo un capítulo: «Liberté rationnelle et autodétermination. Le binôme vox naturae-Vox Dei: Nicolas de Cues et Giordano Bruno». Dentro del equipo de trabajo, la Prof. Laura Corso de Estrada ha colaborado en el volumen con el capítulo: «Instinctus naturae como ratio y como naturae. Componentes del finalismo de tradición estoico y ciceroniana en la Summa de Bono de Felipe El Canciller y en el De Bono de Alberto Magno».

M. Brugarolas

1. M. Brugarolas, «Divine Simplicity and Creation of Man: Gregory of Nyssa on the distinction between the Uncreated and the Created», American Catholic Philosophical Quarterly, aceptado.
2. M. Brugarolas, «Theological remarks on Gregory of Nyssa's Christological language of 'mixture'», Studia Patristica, aceptado.

Además, en el marco de esta investigación ha participado en un seminario en la Pontificia Università della Santa Croce. Consistió en un "Patristic Seminar" organizado por G. Maspero e I. Vigorelli e impartido por los profesores Mark Edwards (Christ Church, Oxford) y Matyás Havrda (Academy of Sciences of the Czech Republic) los días 8-9 de Abril de 2016. Fue invitado a intervenir como respondent a la ponencia de M. Edwards sobre Hypostasis and Hypokeimenon in Gregory of Nyssa.

También en el contexto de esta investigación asistió a las 17th International Conference on Patristic Studies de University of Oxford, los días 10-14 de Agosto de 2015. En el transcurso de estas conferencias internacionales participó en un Workshop sobre Theology and Philosophy between Origen and Gregory of Nyssa, con una ponencia titulada: Metaphysics of the Logos and the overcoming of dualism: Notes on Gregory of Nyssa's language of 'mixture'.

Isabel León

Conferencias

“La influencia de las ideas estéticas de Boecio en San Buenaventura”, en *Boèce au fil du temps. La réception de son oeuvre et son influence sur les lettres européennes du Moyen Âge à nos jours*, Université de Reims Champagne

- Ardenne. Colloque international sous la direction scientifique de Sophie Conte, Alicia Oïffer – Bomsel & María Elena Cantarino Suñer.

Publicaciones

- Libro:

León Sanz, I. M., *El arte creador en san Buenaventura. Fundamentos para una teología de la belleza*, Eunsa, Pamplona 2016, 429 pp.

- Capítulo de libro:

León Sanz, I. M., “El universo como poema divino: la expresividad de la naturaleza en San Buenaventura”, en J. L. Fuertes – A. Poncela González (eds.), *De natura. La naturaleza en la Edad Media, Textos e estudios de Filosofía Medieval 8*, Edições Humus, Ribeirão 2015, v. II, pp. 567-575.

- Artículo:

León Sanz, I. M., “La creación como arte de la Trinidad en san Buenaventura”, en *Scripta Theologica 47/3* (2015), pp. 579-605.

- Reseña al libro: J. Ratzinger, *Obras completas II: Comprensión de la revelación y teología de la historia de San Buenaventura*, Madrid: BAC («Maion», 103), 2013
Mirela Oliva: “The Metaphysics of Language in Gadamer and Cusanus”, *Anuario Filosófico* (2016).

Agnieszka Kijewska

“Le conception de la liberté chez Boèce et sa réception dans la pensée médiévale”, en *Boèce au fil du temps. La réception de son oeuvre et son influence sur les lettres européennes du Moyen Âge à nos jours*, Universidad de Valencia. Colloque international sous la direction scientifique de Sophie Conte, Alicia Oïffer – Bomsel & María Elena Cantarino Suñer.

Alice Ramos

"Gadamer and Aquinas on Language, Being, and the Beauty of Truth"; Paris en el Symposium Thomisticum, organizado por Fran O'Rourke, los días 23-25 de junio del 2016, en le College des Irlandais.



GONZÁLEZ ENCISO, AGUSTÍN

Título: Contractor State Group. Expansión del grupo de investigación internacional.

Presupuesto: 3.700,00 euros

Palabras Clave: Contractor state, movilización de recursos, guerra, siglo XVIII, formación del Estado.

Período: 2014-2017

Summary:

The aim of the project is to set up a stable research team led from Spanish universities to serve as an international benchmark and provide a wide-ranging comparison framework for studying in depth how warfare-resource mobilisation affected state development and the underlying society.

Traditional historical research has focused on how resource mobilisation impinged on the political constitution of the states, with an apparently strict dependence on the state's economic capacity. This has gradually given way to a much more complex and thought-provoking idea, with stress placed on the efficiency obtained. This efficiency was apparently the result of the degree of collaboration between state and society in mobilising warfare resources. It was therefore not simply a problem of the state's political constitution or economic level.

On the basis of this new interpretative approach the idea now is to analyse the degree of warfareresource-raising efficiency achieved by the Spanish state during the eighteenth century. To understand the true nature and idiosyncrasies of the Spanish case it is necessary to have a real comparative framework, of countries in a similar historical context and coping with similar problems. For this reason the Spanish research team has brought in researchers who have already shown a special interest in this historical problem in other European cases, mainly Great Britain and France.

The project will be broken down into particular research projects into important aspects of the resource mobilisation problem, according to the types of resources mobilised and the methods used to supply them. This will allow us to find out the agents involved, public or private, how the markets

worked, local or international, the policy sought by the state in theory and actually applied in practice and, lastly, to assess the Spanish state's resource mobilising efficiency. To this end it is essential to liaise and compare with other European cases, enabling us to understand the true nature of the Spanish case and any new features in its way of working. In short, the ultimate aim of the project is to answer the question why the mobilisation of resources was a source of opportunities and development for some states and societies, while for others it was an endless and wearying source of problems.

Difusión de resultados

En primer lugar, hemos consolidado nuestras relaciones con el grupo internacional del Contractor State Group con nuestra presencia en los congresos de Wasenaar (Holanda) y Kyoto (Congreso Internacional de Historia Económica), lo cual se ha concretado en la publicación de un dossier monográfico sobre la guerra y los empresarios en la Europa del siglo XVIII, que se encuentra ahora en prensa en *Business History Review* (Q1).

El segundo objetivo ha sido consolidar la creación de un grupo internacional con investigadores de Latinoamérica para formar un nuevo Proyecto, para el que ahora se ha conseguido ayuda del Ministerio, orientado al estudio del Contractor State en términos imperiales: la comparación no ya de España, Francia-Gran Bretaña, sino de los tres imperios coloniales.

Asistencia a reuniones científicas

- González Enciso, Agustín: "War contracting and artillery production in Spain", en WEHC2015 XVIIth World Economic History Congress, August 3 (Mon)-7(Fri), 2015, Kyoto, Japan
- González Enciso, Agustín: "Variaciones divergentes. El cambio en las estructuras fiscales en Inglaterra, Francia y España, 1670-1730", en Comercio, ejército y finanzas en una época en transición (siglos XVII-XVIII), U.N.E.D., Madrid, 26-27 noviembre 2015.
- González Enciso, Agustín: "Spanish Eighteenth-century Contractors: from Particular Interest to Particular State Privileges", en The War Within: Finance and Morality in Europe, 1630-1815, University of Reading, 3-4 diciembre, 2015
- Torres Sánchez, Rafael: "Héroes y villanos. Ilustrados y patriotas en los suministros militares del siglo XVIII" en De ilustrados a Patriotas: Individuos al servicio del Rey (siglos XVIII-XIX), Universidad Complutense, Casa de Velázquez, 27-28 de abril 2016.
- Torres Sánchez, Rafael: "Los barcos del rey. La evolución cuantitativa de la Armada Real en el siglo XVIII", Ejército, Marina y Estado: la construcción del sistema imperial español en el siglo XVIII, Universidad Nacional Autónoma de México, 1-3 de diciembre 2015, México, DF.

- Torres Sánchez, Rafael: "Ejército y Finanzas entre los siglos XVII y XVIII", en Comercio y finanzas en una época en transición (Siglos XVII-XVIII), UNED, Madrid, 26-27 de noviembre 2015, Madrid.
- Torres Sánchez, Rafael: "Empresarios militares navarros en el siglo XVIII y construcción del Estado", en Recuperando el Norte. Empresas, capitales y proyectos atlánticos en la economía imperial hispánica, Universidad del País Vasco, 15-16 de octubre 2015, Vitoria.
- Torres Sánchez, Rafael: "The long-term consequences of the Contractor State", War and Economy. The consequences of wartime taxation, public debts and expenditure in the late medieval and early modern period, 1-7 Agosto 2015, Kyoto, Japón.

Publicaciones de libros

- González Enciso Agustín: *War, Power and the Economy. Mercantilism and State Formation in Eighteenth Century Europe*, actualmente está en prensa en Routledge (se prevé su salida para octubre 2016).
- Torres Sánchez, Rafael, *Military Entrepreneurs and the Spanish Contractor State in the Eighteenth Century*, Oxford: Oxford University Press, 2016, 320 p. ISBN: 9780198784111
- Torres Sánchez, Rafael, *Military State in Eighteenth-Century Spain*, Hampshire: Palgrave Macmillan, UK, 2015, 253 pp. ISBN: 9781137478658

Publicaciones de artículos y capítulos de libros:

González Enciso, -"Los comerciantes, el desarrollo del Estado y la comprensión del bien común en la Edad Moderna", in J. L. García Ruiz and J. M. Ortiz Villajos (eds.), *Ensayos de historia y pensamiento económicos en homenaje al Prof. Juan Hernández Andreu*, Delta, Madrid, 27-46.

González Enciso -"La supresión de los arrendamientos de impuestos en la España del siglo XVIII", en *Tiempos Modernos*, 30 (2015/1) ISSN: 1699-7778.

González Enciso - "La historiografía y los arrendatarios de impuestos en la España del siglo XVIII", en *Mélanges de la Casa de Velázquez. Nouvelle série*, 46-1, 2016 (avril), 65-75.

Torres Sánchez, Rafael, "The relief of the vassals. Absolutism and fiscal transparency in eighteenth-century Spain", en *Histoire & Mesure*, Before Fiscal Transparency, CNRS, Paris, n° XXIX, n°2, 2015, pp.189-214.

Torres Sánchez, Rafael, "El gasto público en la España del siglo XVIII", en *El gasto público en los imperios Ibéricos, siglo XVIII* Ernest Sánchez Santiró (coord.), México: Instituto Mora, 2015, ISBN: 978-607-9294-91-5, pp.23-72

Torres Sánchez, Rafael, "El miedo al déficit. La política de endeudamiento público de los Borbones en el siglo XVIII", en Carlos Álvarez-Nogal y Francisco Comín Comín, *Historia de la Deuda Pública en España (siglos XVI-XI)*, Madrid: Instituto de Estudios Fiscales, 2015, pp.111-136.

Torres Sánchez, Rafael, "La inserción de Cataluña en la Real Hacienda de la monarquía española tras el tratado de Utrecht. El caso del monopolio fiscal del tabaco" (Ponències) en Joaquim Albareda, *Els tractats d'Utrecht. Clarors i foscors de la pau. La resistència dels catalans*, Institut Universitari d'Història Jaume Vicens Vives. Universitat Pompeu Fabra, Barcelona, 2015, pp.361-372.

En prensa: monográfico 2016.- "War and Economy. Rediscovering the Eighteenth-Century Military Entrepreneur", *Business History*,

FACULTAD DE MEDICINA



AZCONA ARMENDÁRIZ, J. DIEGO

Título: Desarrollo de herramientas computacionales para evaluación de incertidumbres y adaptación de tratamientos en radioterapia estereotáctica en cáncer de pulmón.

Presupuesto: 45.800,00 euros

Palabras Clave: Adaptive radiotherapy, deformable image registration, 4D CBCT, Monte Carlo, intensity modulated radiation therapy, volumetric modulated arc therapy, flattening filter free beams, tracking, lung cancer.

Período: 2016-2019

Summary:

Respiratory motion is usual in lung tumors to be treated with radiotherapy. It hampers its delivery, increasing the uncertainty in the absorbed dose and leading to possible pulmonary, esophagic, and medular toxicity. This fact compromises the dose escalation in these tumors, which entails an increased tumor control probability.

The global objective of this project is twofold, consisting first in developing computational tools for the assessment of the global uncertainty in the absorbed dose in lung tumors treated with image-guided radiotherapy. Secondly, we will apply the developed tools to a cohort of at least ten patients, to assess the feasibility and develop a clinically practical strategy for treatment adaptation (adaptive radiotherapy).

Dose will be delivered to the patient with stereotactic body radiation therapy (SBRT), with hypofractionation, volumetric modulated arc therapy (VMAT), intensity modulated radiation therapy (IMRT), or three-dimensional conformal radiotherapy (3DCRT), using flattening filter free photon beams. Treatment planning will be performed with 4D clinical dosimetry on CT (and in specific cases also PET images with spatial and temporal correlation with the CT images, evaluating the tumor motion with its morphologic and functional information), delimiting the gross tumor volume (GTV), internal target volume (ITV), and planning target volume (PTV). The image guidance system to use for respiratory motion tracking will be 4D cone beam CT (CBCT). We will correlate the internal tumor motion with the external motion of several markers located in the patient skin, which will be tracked in real time during treatment with an optical tracking method developed by our group, and with the Sentinel/Catalyst system.

This project introduces several research novelties to achieve the proposed objectives, among which are: (1) the use and validation of deformable image registration (DIR) between sets of 4D CT images and 4D CBCT images, (2) tumor voxelization and the use of the displacement vector field (DVF) to accumulate and reconstruct the global dose tracking each voxel's trajectory, (3) the use of Monte Carlo to calculate with great accuracy the dose in each treatment fraction, on 4D CBCT images, (4) the study of the interplay effect in hypofractionated lung treatments with VMAT, and (5) the feasibility study and development of a strategy of adaptive radiotherapy in lung cancer, topic on which there is not much bibliography available up to now, The project is, thus, novel, and the expected impact of its results in the scientific national and international community is large.

After the project is concluded, we will have achieved: (1) a method with computational tools specifically developed to reconstruct the dose and assess the uncertainties in the prescribed dose delivery, and, on that base, (2) a safe, effective, and clinically practical treatment adaptation.



CARNERO GONZÁLEZ, ELENA M^a

Título: Evaluación de las variaciones en la presión intraocular en el síndrome de apnea obstructiva del sueño.

Presupuesto: 11.200,00 euros

Palabras Clave: Glaucoma, Obstructive Sleep Apnea Syndrome (OSAS), Intraocular pressure (IOP), Patient monitorization during 24 hours, Sensimed triggerfish, Prevention.

Período: 2016-2019

Summary:

Open angle glaucoma is a chronic disease that results in a degeneration of optic nerve affecting the retina fibers, this could induce long-term patient blindness. The actual treatment consists in reduce intraocular pressure (IOP), although there are other risk factors under investigation and could be treated in order to slow the progression of the disease. There is an extensive literature that studies the relationship between obstructive sleep apnea syndrome (OSAS) and the appearance or progression of glaucoma, although initial studies showed some discrepancies, today it seems clear the presence of OSAS as a factor development risk glaucoma¹⁻⁷. Factors associated with OSAS might contribute to the development of glaucoma however, the only controllable factor so far is the IOP. Several studies have suggested that patients with moderate or severe OSAS have higher levels of IOP than healthy controls^{5,7,8}. In addition, there are evidences that IOP increases at night when compared with the measures taken during daytime⁹⁻¹¹. In fact, it likely that rises in the IOP during the night might pass unnoticed in daytime measurements made by doctors¹². Recent studies have established the importance not only of the mean IOP importance but also the IOP peaks in the visual field deterioration in glaucoma patients¹³. All these data recommend a deeper study of the IOP, their average levels, peaks and fluctuations in order to evaluate the relationship between IOP and OSAS and its role in the onset of glaucoma.

Other factors studied that occur during night time and may be associated with the progression of glaucoma are changes in head position - body and blood pressure. Regarding the position of the head several authors have found that the mean IOP is lower when the head is slightly elevated at a 30° angle compared with the supine position ¹⁴ . On the other hand, supine position showed the lower IOP level compared with lateral decubitus and prone positions¹⁵. About blood pressure, there is a physiological decrease in

blood pressure during the night that may be higher in the case of patients with glaucoma, this would result in a decrease in perfusion pressure eye, increasing IOP and the risk of disease progression.

Recently, Sensimed AG, (Lausanne, Switzerland) has developed a system, Sensimed Triggerfish, consisting of a contact lens connected by antenna to a recorder able to collect changes in IOP continuously during 24 hours in an outpatient setting. The main advantage of this system is that it can be used overnight and enables the IOP measurement (three hundred data points are acquired over a period of 30 seconds measurement repeatedly every 5 minutes) without waking up the patient. Previous studies on the evaluation of IOP during sleep time with traditional tonometer required the patient cooperation and the measurements are considerably less. Therefore, this is the only real and serious possibility of studying how OSA can affect IOP during sleep time and continuously.

The objective of this project is to analyze what factors may influence the IOP during sleep in OSAS patients compared to patients without OSA. To perform the analysis, we will register multiple biological parameters (Sleep Study Unit) and IOP to be recorded by a disposable contact lens Sensimed. This project will be developed by the Department of Ophthalmology (Clinic University of Navarra) and the Unit of Sleep Laboratory (Department of Neurophysiology, Clinic University of Navarra).



DE ANDREA, CARLOS EDUARDO

Título: A non-invasive liquid biopsy approach to evaluate the DNA methylation status in patients with NSCLC

Presupuesto: 20.000,00 euros

Palabras Clave: Non-small-cell lung cancers, squamous cell carcinoma, SHOX2, TMPRSS4, liquid biopsy, circulating tumour DNA, digital PCR, Next-generation parallel sequencing, diagnosis, prognosis..

Período: 2016-2019

Summary:

Non-small-cell lung cancers (NSCLCs), the most common type of lung cancers, are known to have diverse histopathological features. The most two common NSCLC pathological phenotypes are adenocarcinoma (ADC; ~50%) and squamous cell carcinoma (SCC; ~40%). ADCs often have glandular histology and SCCs are characterized by squamous differentiation. Epigenetic silencing of genes through promoter methylation of cytosines affects the expression of several genes during initiation and development of lung cancer. Aberrant patterns of DNA methylation of certain genes are currently used as a prognostic biomarker, as well as a diagnostic marker in lung cancer. Aberrant SHOX2 (Short stature homeobox 2) DNA hypermethylation is associated with an adverse overall survival and the DNA hypermethylation levels significantly correlate with a worse outcome in lung cancer. In addition, aberrant SHOX2 DNA methylation has been proposed as a diagnostic tool able to differentiate lung cancer tissue from normal lung tissue. Recently, aberrant TMPRSS4 (transmembrane protease, serine 4) DNA methylation has also been proposed as (i) a diagnostic tool able to differentiate ADC and SCC lung cancer subtypes from normal lung tissue, and (ii) a prognostic biomarker in SCC. The aim of this project is (i) to development of a very sensitive and specific SHOX2 and TMPRSS4 promoter DNA methylation digital PCR assay, and (ii) to investigate the genetic profile of SCC lung tumours harbouring TMPRSS4 promoter DNA hypomethylation. The DNA methylation levels of SHOX2 and TMPRSS4 promoter, alone or in combination, could be used as a diagnostic marker able to differentiate ADC and SCC lung cancer subtypes from normal lung tissue. In addition, the screening of TMPRSS4 promoter DNA methylation in the circulation could be a non-invasive approach to monitoring treatment response in NSCLC patients with squamous histology and to predict poor prognosis in patients with lung SCC at early stages. Currently, there are no approved targeted therapies specifically for squamous cell lung cancer.

SCC is characterized by complex genomic alterations with recurrent mutations in several genes. The association between aberrant *TMPRSS4* promoter methylation and the most common recurring mutations in squamous NSCLC is so far unknown and could thereby form the rationales for novel therapeutic strategies.



DEL POZO, JOSÉ LUIS

Título: Evaluación de diversas formulaciones combinadas de ivermectina en dosis única para su potencial uso en el bloqueo de la transmisión de la malaria.

Presupuesto: 11.000,00 euros

Palabras Clave: Malaria, Anopheles, ivermectina, endectocidas, liberación prolongada, P-glicoproteína, citocromo p4503A4, antifúngicos, ketoconazol, itraconazol, posaconazol, fluconazol.

Período: 2015-2018

Summary:

Malaria continues to be a public health problem in the developing world. In 2013 it caused 198 million cases and 584.000 deaths worldwide, most of these in children under five living in Sub-Saharan Africa.

The most effective malaria control interventions are those to control the mosquito vector. Some recent challenges to vector control are: 1) the appearance of mosquitoes resistant to the insecticide used to impregnate nets (LLITNs) or in Indoor Residual Spraying (IRS), 2) the behavioural adaptation of mosquitoes to the selective pressure of LLITNs and IRS, this has shifted transmission outdoors, where core interventions are not effective and 3) in the areas of high transmission it has been deemed impossible to interrupt the cycle without innovative vector control tools.

Ivermectin is an antiparasitic drug with an excellent safety profile. It is commonly used for the control of Onchocerciasis and some intestinal helminths. Mosquitoes feeding on an ivermectin-treated person for the first 72 hours, die quickly after feeding. This makes ivermectin an endectocide and a potential and very attractive malaria control tool.

The half-life of ivermectin is short. It is metabolized by the cytochrome P4503A4 and excreted by the P-glycoprotein. Inhibiting the activity of these two enzymes using antifungal azoles such as ketoconazole, is a potential strategy to prolong the mosquitocidal life of ivermectin.

The objective of the first phase of this project is to prolong ivermectin's mosquitocidal life in pigs by co-administering it with ketoconazole or other antifungal azoles such as posaconazole, itraconazole or fluconazole.

The second phase of the project consists in elaborating, categorizing and in vivo testing of bio-adhesive nanoparticles of ivermectin, aiming at prolonging the effect on mosquitoes. The third phase seeks to combine the result of the previous steps by co-encapsulating ivermectin and antifungal azoles in nanoparticles to maximize the PK effect.

At the end of the three year project we expect to prove three concepts:

1. Co-administration of ivermectin with antifungal azoles leads to a longer mosquitocidal concentrations of ivermectin.
2. A formulation of ivermectin in nanoparticles significantly increases the duration of ivermectin mosquitocidal effect.
3. Combining antifungal azoles with ivermectin in nanoparticles will greatly increase the duration of the mosquitocidal effect.

Difusión de resultados

Los resultados del piloto presentados en 2015 en el congreso Americano de Medicina Tropical han sido sujeto de un artículo en The New York Times: http://www.nytimes.com/2015/11/03/health/to-prevent-malaria-in-humans-scientists-try-protecting-pigs.html?_r=0

Se ha enviado un abstract con los resultados farmacocinéticos al congreso Americano de Medicina Tropical 2016, se espera respuesta en Agosto 2016.



ESPAÑA ALONSO, AGUSTÍN

Título: Papel de los ligando de los receptores HER en la acantólisis del pénfigo vulgar en un modelo murino.

Presupuesto: 17.000,00 euros

Palabras Clave: Acantólisis – Inmunoglobulina G – Modelo murino - Pénfigo vulgar.

Período: 2015-2018

Summary:

Introduction. Pemphigus vulgaris is an autoimmune bullous skin disorder, mediated by IgG autoantibodies against desmogleins, cadherin proteins localized in epidermal desmosomes (acantholysis). Patients affected with PV develop erosions and blisters on cutaneous Surface and mucosa. Activation of HER receptor isoforms by their ligands ((TGF-__transforming growth factor), EGF (epidermal growth factor) and BTC (betacellulin)), some intracellular signaling pathways (phosphoinositide pathway), and several kinases (mTOR, FAK, Src) have been implicated in PV pathogenesis. Nevertheless, neither the mechanism regulating the expression of HER ligands is known, nor the hypothetical cross-talking between both these ligands and kinases during PV acantholysis.

Objectives. The main objective will be to determine the role of ADAM10 and ADAM17 in the induction of PV lesions in a mouse model. Secondary objectives: to know the timing of epidermal expression for HER1-3 isoforms, HER ligands (TGF-_, EGF, BTC), and ADAM10 and ADAM17 after injecting mice with PV IgG; to establish the epidermal expression for HER ligands (TGF-_, EGF, BTC) and ADAM10 and ADAM17 in mice pretreated with inhibitor for several molecules (mTOR, panHER, Src, nNOS and FAK) before PV IgG administration; and finally, to know the intensity of acantholysis in epidermis of mice (by clinical observation and histological and immunofluorescence studies) when animals are pretreated with ADAM10 and ADAM17 inhibitors before PV IgG injections.

Materials and Methods. A mouse model of passive IgG transferring, similar to that used in previous Projects of our group, will be used. Three cutaneous-mucosal PV sera and serum sample of a normal healthy person will be included as control. We propose to study in mice skin the expression of HER isoforms (HER1-3), their ligands (EGF, TGF-_, BTC), some enzymes (nNOS) and

several intracellular kinases (mTOR, Src, FAK) by immunohistochemistry. Additionally, inhibitors of these molecules used in our previous Projects will be included as well. Image analysis of all immunohistochemical findings will be performed using Matlab Software.

Results. Based on previous findings obtained by our group and others, we hope to find a relevant role of both ADAM10 and ADAM17 in the production of those HER ligands previously reported taking part in PV acantholysis. In addition, as observed in other inflammatory disorders, we expect to find a link between those activated intracellular kinases taking part in PV lesions, and the production of HER ligands synthesized during PV acantholysis. Therefore, all these findings would allow us to use a new and more specific management of PV, thus preventing in this group of patients an elevated number of side effects due to corticosteroids and immunosuppressive drugs administered for a long period of time. As already published by our group, we expect to find a relevant role of both ADAM10 and ADAM17 in the production of those HER ligands implicated in PV acantholysis.



MARTÍNEZ DE TEJADA, GUILLERMO

Título: Péptidos antimicrobianos para el control de biofilms asociados a implantes médicos.

Presupuesto: 15.000,00 euros

Palabras Clave: Biofilm, Biocapa, antibiótico, resistencia antibiótica, péptido antimicrobiano, implante médico, Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus, Candida albicans.

Período: 2015-2018

Summary:

Biofilms are complex aggregates composed of microorganisms that are embedded in an extracellular matrix containing exopolysaccharide, proteins and nucleic acids. These structures allow microbial cells to adhere to both biotic and abiotic surfaces. It is estimated that up to 65% of bacterial infections are associated with the presence of biofilms (Lewis, 2001). In addition, biofilms are extremely difficult to eradicate with the currently available antibiotics, highlighting the importance of developing effective anti-biofilm therapies.

The antibiotic resistance of biofilm-producing bacteria has a multifactorial origin and has been attributed to factors such as the permeability barrier posed by the exopolysaccharide, the microenvironment within the biofilm, the physiological heterogeneity of the bacterial population and the emergence of "persistent" cells.

Due to their properties, antimicrobial peptides are well suited to counteract the mechanisms of resistance of biofilms. Thus, these compounds are active against bacterial cells at different stages of growth. In addition, they are rapidly bactericidal, have a wide spectrum of activity, and combined with antibiotics, can form synergistic combinations against multiresistant microorganisms. Finally, resistance to antimicrobial peptides arises at much less frequency than that to conventional antibiotics. Because of all this, our hypothesis is that antimicrobial peptides could form the basis of efficient antibiofilm treatments.

We already have a peptide library containing 240 compounds that were derived from human lactoferricin. In preliminary studies, several of these compounds displayed a potent antimicrobial activity against Gram-positive and Gram-negative planktonic bacteria as well as a high permeabilizing activity on *Pseudomonas aeruginosa* and efficiently protected animals against a lethal septic shock. Furthermore, when used in vitro at ten times their minimum inhibitory concentration, these compounds reduced 10,000 times the viability of mature biofilms of *P. aeruginosa* within 1 h.

In the present study, we will determine the activity of antimicrobial peptides on microorganisms producing biofilms of high clinical relevance such as the Gram-negative *P. aeruginosa* and *Escherichia coli*, the Gram-positive *Staphylococcus aureus* and the yeast *Candida albicans*. We will perform structure-activity relationship analysis to determine the structural basis of the different activities evaluated (the peptide bactericidal activity both on planktonic and biofilm cells, as well as the peptide ability to remove and/or inhibit biofilm). These studies will allow us to predict and design an improved generation of peptides (objective 1). After selecting the most promising compounds, we will investigate two strategies to control biofilms. First, we will immobilize the peptides on polymer surfaces (biomaterials) and assess their ability to inhibit biofilm formation (objective 2). Secondly, we will evaluate the use of the peptides (alone or in combination with antibiotics) as anti-biofilm agents on mature biofilms (objective 3). Furthermore, we will conduct studies on the lead compounds to determine their toxicity in eukaryotic cells and their mechanism of action. Finally, the in vivo effectiveness of the two strategies (therapeutic and prophylactic) will be evaluated in a murine model of infection by biofilm producing bacteria using medical devices surgically implanted in the animals (objective 4).

Difusión de resultados

1. Publicaciones

Sánchez-Gómez, S y Martínez de Tejada, G.. 2016. Antimicrobial peptides as anti-biofilm agents in medical implants. *Current Topics in Medicinal Chemistry*. *In Press*. Índice de impacto: 3,6; Número 12 de 59 revistas en el área de Química Medicinal (1er cuartil; Q1) <http://benthamscience.com/journals/current-topics-in-medicinal-chemistry/upcoming-articles/#top>

2. Congresos

- Ferrer, R. y Martínez de Tejada, G. 2015. Synergistic three component combinations (Peptide, Antibiotic, Enzymatic Inhibitor) against biofilms or planktonic *Pseudomonas aeruginosa*. Comunicación oral al XXV Congreso Nacional de la Sociedad Española de Microbiología. Logroño, 7-10 de Julio de 2015.
- Bárcena-Varela, S., Gutiérrez-San José, E., Ferrer-Espada, R., Brandenburg, K., Heinbockel, L., Martínez de Tejada, G. 2016. Fighting antibiotic resistance: novel antimicrobial and anti-sepsis peptides. EMBO Spetses Summer Course. Spetses (Grecia) 24 agosto 2016.



VIVAS PÉREZ, ISABEL

Título: Electroporación irreversible con adyuvantes inmunológicos para el tratamiento percutáneo de tumores sólidos.

Presupuesto: 10.000,00 euros

Palabras Clave: Electroporación irreversible, adyuvante inmunológico, PolyI:C, cáncer, tratamiento percutáneo, tumor sólido.

Período: 2015-2017

Summary:

In cancer treatments, there are a group of techniques based on the intratumoral application of electric fields through the use of electrodes. Irreversible electroporation is a technique of soft tissue ablation using ultra short but very intense electric fields to create permanent nanopores to the cell membrane and therefore lethal for the tumoral cell. However, this technique appears to induce a non immunogenic death by apoptosis so that it does not promote inflammation to stimulate activation of an antitumor response. Thus, the presence of residual tumor cells can continue the tumor process, reducing the therapeutic effect of this technique. We believe it is possible to increase the therapeutic efficacy of electroporation by intralesional injection of an immunogenic adjuvant as Poly IC, a TLR3 ligand, prior to the irreversible electroporation procedure. This will allow the tumor cell be reloaded within Poly IC molecules, which will serve as a potent adjuvant when they are phagocytosed by dendritic cells entering the electroporated tumor. In this project we aim to obtain the proof of concept in a rabbit tumor model.

The results of this project will permit the development of new therapeutic strategies based on the combination of a physical technique such as electroporation, with an immune adjuvant, to induce a systemic response to protect patients from residual tumor growth and secondary metastasis.



BARRIO BARRIO, JESÚS

Título: Estudio multicéntrico de factores genéticos implicados en la hipermetropía infantil.

Presupuesto: 12.000,00 euros

Palabras Clave: Hipermetropía, genética, infancia, polimorfismos.

Periodo: 2014-2017

Summary:

Refractive errors are the leading cause of treatable visual loss and blindness affecting two billion people worldwide. The prevalence of these conditions is increasing worldwide, being in the adult Western population 10% for hyperopia and around 25% for myopia. Hyperopia has a higher prevalence in children affecting up to 20% of children in the Western population. Hyperopia is also the main cause of amblyopia and strabismus in the pediatric population.

Studies that have investigated the refractive errors have clearly demonstrated a genetic involvement in their etiology. Refractive errors are transmitted as polygenic and multifactorial inheritance. Heritability studies have quantified the genetic component of the refractive errors indicating that between 50 and 90% of the phenotypic concordance is explained by genetic effects. Despite this, very little is known about the specific genetic factors associated with refractive errors. This is especially true for hyperopia for which no genetic association has been found until 2010, when its association with some of the HGF gene polymorphisms in an Australian adult population was described.

This project that is now being presented as a multicenter study, is the continuation of a previous project. The former project was designed to validate the polymorphisms associated with hyperopia, described in an adult Australian sample, in a Spanish pediatric sample. The goals of this multicenter project is to implement, in a sample of 600 pediatric patients and 600 hyperopic emmetropic controls: 1) A genotype analysis of the described polymorphisms associated with hyperopia, 2) A whole exome sequencing in a group of patients with extreme phenotypes and 3) the subsequent validation of the identified genetic variants in the multicenter sample.

Therefore, the aim of our project is to identify the greatest possible number of genetic factors involved in the hyperopia phenotypic trait in children. The development of an effective, non-invasive, early diagnosis test of genetic susceptibility to hyperopia to be applied to the population at risk, would be a major step forward to prevent the associated morbidity of this refractive error. In addition, the increasing knowledge of the genetic basis of the disease would progress towards designing an early genetic personalized treatment, from which hyperopic patients at risk of developing severe complications with visual implications on their health and quality of life would benefit.



MENGUAL POZA, ELISA

Título: Transmisión GABAérgica desde los ganglios basales a los núcleos pedunculopontino y laterodorsal: dianas celulares de la proyección palidotegmental y receptores GABAérgicos implicados en el animal control.

Presupuesto: 8.500,00 euros

Palabras Clave: enfermedad de Parkinson, trastornos de la marcha, receptores GABA-A, GABA-B, hibridación in situ, transportador vesicular de glutamato, GAD67, GAD65, acetilcolina, trazadores, inmunofluorescencia.

Período: 2014-2017

Resumen:

Los ganglios basales son una serie de estructuras subcorticales que juegan un papel fundamental en el control del comportamiento dirigido a un objetivo, y en particular, del movimiento voluntario, y sus alteraciones producen trastornos del movimiento como la enfermedad de Parkinson. Los núcleos tegmentales pedunculopontino (PPTg) y laterodorsal (LDTg) son dos estructuras troncoencefálicas asociadas entre sí, que están anatómicamente y funcionalmente relacionadas con los ganglios basales, ya que reciben las proyecciones que desde los núcleos de salida –núcleo entopeduncular (EP), pálido ventral (VP) y sustancia negra- se dirigen al tronco del encéfalo. Es más, las alteraciones de los ganglios basales que tienen lugar en la enfermedad de Parkinson afectan también específicamente a PPTg.

PPTg y LDTg están formados por una población colinérgica característica con la que coexisten neuronas glutamatérgicas y GABAérgicas. A pesar de los múltiples estudios anatómicos y electrofisiológicos llevados a cabo en relación con la proyección palidotegmental desde EP y VP, aún se desconoce sobre qué población neuroquímica terminan estas fibras. Actualmente es de vital importancia conocer con detalle cómo se organizan los circuitos de salida de los ganglios basales en PPTg, dado que este núcleo está siendo utilizado como diana terapéutica en pacientes con enfermedad de Parkinson sin conocer los mecanismos de esta intervención.

El primer objetivo de este proyecto es, por tanto, determinar de modo conclusivo el fenotipo de las dianas celulares de la proyección palidotegmental. Para ello realizaremos inyecciones de un trazador axonal anterógrado en EP y VP y mediante técnicas de triple marcaje fluorescente

que identifiquen inequívocamente las neuronas colinérgicas, glutamatérgicas y GABAérgicas, analizaremos los posible contactos de las fibras palidotegmentales con cada una de estas tres poblaciones de PPTg y LDTg.

Las salidas de los ganglios basales desde EP y VP es GABAérgica, y está mediada fundamentalmente por los receptores GABA-A y GABA-B. A pesar de que múltiples estudios farmacológicos y de conducta han puesto de manifiesto la presencia de ambos receptores en PPTg y LDTg, su localización celular precisa no ha sido abordada hasta el momento.

Determinar dicha localización es crucial para entender cómo se realiza la transmisión GABAérgica palidotegmental a nivel celular en situación normal y sus posibles alteraciones, y permitirá clarificar la acción de agonistas y antagonistas GABAérgicos en dichos núcleos. Datos farmacológicos previos sugieren que ambos tipos de receptores estarán presentes en PPTg y LDTg y que ambos receptores se localizarán probablemente en más de un fenotipo celular tanto en PPTg como en LDTg. El segundo objetivo de nuestro proyecto es por tanto determinar los sitios celulares específicos de acción de la proyección GABAérgica palidotegmental en PPTg y LDTg, es decir, cuál o cuáles de las tres subpoblaciones neuroquímicamente definidas expresa alguno de los dos receptores mencionados. Para ello realizaremos un triple marcaje inmunofluorescente para detectar la colocalización de los receptores GABA-A o GABA-B con neuronas colinérgicas, glutamatérgicas y GABAérgicas. Los resultados de este trabajo de investigación contribuirán a entender los circuitos celulares que intervienen en funciones tan diversas como el equilibrio y la marcha, el sueño paradójico o el aprendizaje, y su posible modulación farmacológica con fines terapéuticos.

Difusión de resultados:

Comunicación presentada en el congreso *Society for Neuroscience 2015*:
- Luquin E, Paternain B, Mengual E. *Distribution of GABA-A receptor alpha 1 subunit- and GABA-B receptor R2 subunit- immunoreactivities in the pedunculo pontine and laterodorsal tegmental nuclei in the rat.* (17-21 octubre, 2015 - Chicago (IL,USA))



MERINO RONCAL, JUANA M^a

Título: Caracterización de los mecanismos de heterogeneidad clonal y quimiorresistencia primaria en Leucemia Mieloblástica Aguda: una aproximación integradora fenotípico-molecular basada en estudios de Enfermedad Mínima Residual.

Presupuesto: 15.000,00 euros

Palabras Clave: leucemia mieloblástica aguda; enfermedad mínima residual; citometría de flujo multidimensional; ultrasecuenciación; heterogeneidad clonal.

Período: 2014-2017

Summary:

The Acute Myeloid Leukemia (AML) is the most common acute leukemia among non-pediatric patients. Despite decades of continuous research both at the clinical and biological levels, AML remains one of the most aggressive hematological neoplasms: more than half of the patients achieves complete remission (60%-80%), but the vast majority ultimately relapses, and overall survival at 5 years stands typically below 50% of AML patients. Accordingly, prolongation of patients survival has been scarce, with the exception of specific subgroups such as transplant-eligible patients or those with favorable cytogenetics.

In the current research project we will take full advantage of recent technological innovation at the immunophenotypic and molecular level to further characterize the mechanisms of clonal heterogeneity/selection and chemoresistance in AML. The advent of multidimensional polychromatic flow cytometry (≥ 8 -colors) and new software tools allow the simultaneous measurement of more than 30 antigens at the single-cell level. This ability, combined with principal component analysis (PCA) of phenotypic patterns of hematopoietic maturation would allow to: i) characterize the subclonal phenotypic heterogeneity of AML; ii) correlate the PCA phenotypic classification of AML with the cytogenetic classification; iii) standardize and increase the sensitivity of multidimensional flow cytometry to monitor minimal residual disease (MRD) levels; and iv) sorting of distinct (maturation-related) phenotypic subclones at diagnosis to compare their molecular features with those of MRD blasts that persist after chemotherapy.

Our objective is to unravel the molecular profile of those blasts with truly primary chemoresistance (MRD cells), comparing it against patient-paired diagnostic subclones in a series of newly-diagnosed and uniformly treated 372 AML patients. Additionally, we aim to generate the data that could potentially allow the standardization of flow cytometry for the differential diagnosis and MRD monitoring of AML.

Overall, this project represents one of the most comprehensive and large biological studies ever performed in a series of elderly AML patients, keeping in mind that this specific subgroup represents the largest among AML patients, the one with the poorest prognosis, and where the identification of novel therapeutic targets is an unmet medical need.



RIVEROL FERNÁNDEZ, MARIO

Título: Evaluación de una intervención para mejorar la convivencia con la enfermedad de parkinson de pacientes y familiares.

Presupuesto: 4.800,00 euros

Palabras Clave: DEPENDENCIA, AFRONTAMIENTO, CALIDAD DE VIDA, ADAPTACIÓN PSICOSOCIAL, ENFERMEDAD DE PARKINSON.

Periodo: 2014-2017

Summary:

The aim of this project is to improve the quality of life of Parkinson (PD) patients and their family/carers through an intervention which will focus on improving coping skills and promoting the psychosocial adjustment to the illness.

This project, which is also integrated in the Research programme, ReNACE, has a quasiexperimental design with a control group, pre-test and post-test and repeated measures. The project will be developed in the health centre San Juan of the Navarra Public Health Services (SNS-Osasunbidea) (intervention centre), in the outpatient consultation of the Department of Neurology and the Unit of Movement Disorders of the Clinica Universidad de Navarra (control centre). Furthermore, a baseline data collection, involving focus groups in a centre not involved in the quasiexperiment (Parkinson Association of Navarra), will take place to avoid contamination of data between participants involved in the intervention.

The intervention will involve a psychoeducative programme to promote the development of positive coping skills which could lead to a better psychosocial adjustment to PD and consequently, to better quality of life. The control group will receive a general education programme about PD and available resources. The following data collection will take place pre and post intervention: 3 baseline focus groups (6-8 health professionals, 6-8 patients with PD patients and 6-8 family/carers), and 2 post intervention focus groups (6-8 PD patients and 6-8 family/carers), and a sociodemographic form (only baseline). Also different measures with validated scales will take place before the intervention (T0), immediately after the intervention (T1) and 6 months after the intervention (T2) in the two centres involved in the quasiexperiment with the following scales: Brief COPE Scale, Psychosocial Adjustment to Illness Scale (PAIS-SR) with patients and

family/carers, the PDQ-39 and the Scale Hoehn y Yahr with patients, and the Scale of Quality of Life of Caregivers (SQLC). Intention to treat analysis will be performed.

Consecutive cases sampling will take place to recruit PD patients and family/carers in the two centres involved in the quasiexperiment. An ideal sample size has been calculated to ensure statistical power of 80%. At least 52 patients and 53 family/carers should participate in each centre. Purposive sampling will be applied to recruit participants for the focus groups.

Results in this project will constitute the beginning of future multidisciplinary interventions which will improve PD patients and family/carers quality of life through the promotion of coping skills and psychosocial adjustment to illness in Spain.

Difusión de resultados

Comunicaciones a congresos

Autores: Navarta-Sanchez, V; Caparrós, N; Ursua, ME; Diaz de Cerio, S; Riverol, M; Portillo, MC. Título: The role of coping skills in the psychosocial adaptation to Parkinson's disease in patients and family carers: The qualitative perspective in a mixed-methods study. Tipo de participación: concurrent presentation. Congreso: International Nursing Research Conference. Royal College of Nursing. Lugar de celebración: Edimburgo. Fecha: 6, 7 y 8 de abril de 2016.

Autores: Anaut Bravo, S, Caparrós Civera, N, Portillo Vega, MC. Título: Respuestas socio-sanitarias a personas afectadas por la enfermedad de parkinson y sus cuidadores principales. Tendencias a corto y medio plazo. Tipo de participación: comunicación. Congreso: XVIII Congreso de la Sociedad Navarra de Geriátría y Gerontología. Lugar de celebración: Pamplona. Fecha: 5-7 de mayo de 2016.

Artículos

Navarta-Sánchez MV, Senosiain García JM, Riverol M, Ursúa Sesma ME, Díaz de Cerio Ayesa S, Anaut Bravo S, Caparrós Civera N, Portillo MC. Factors influencing psychosocial adjustment and quality of life in Parkinson patients and informal caregivers. Qual Life Res. 2016 (publicado online)

Caparrós Civera, N., Anaut-Bravo, S., Portillo Vega, MC. Ressources sanitaires et sociaux pour des personnes avec Parkinson: tendances et propositions en Navarre (Espagne). Revue Française de service social, 2016. (aceptado en prensa).

M.V. Navarta-Sánchez, N. Caparrós, M.E. Ursúa Sesma, S. Díaz de Cerio Ayesa, M. Riverol, M. Portillo. Estrategias psicosociales para fortalecer el

afrontamiento de la Enfermedad de Parkinson: perspectiva de pacientes, familiares y profesionales sociosanitarios. Atención primaria, 2016 (aceptado en prensa).



VITAS PEMÁN, ANA ISABEL

Título: Caracterización fenotípica y filogenética productores de betalactamasas de espectro extendido aisladas en Navarra.

Presupuesto: 8.600,00 euros

Palabras Clave: Enterobacterias, BLEE, Beta-lactamasa, genes bla, secuencias de inserción, transposones, filogenia, MLST, PCR.

Período: 2014-2017

Summary:

In last years there has been an increase of Enterobacteriaceae strains resistant to β -lactam antibiotics and in particular those that producing Extended-Spectrum β -lactamases (ESBL). The increasing of antimicrobial resistance is a serious public health problem, mainly in the case of ESBL-producing Enterobacteriaceae (ESBL-E) for its high presence and dispersion in different environments.

This fact has been confirmed by our research group, in previous studies resistant strains were isolated from aquatic environments (effluent treatment plants and rivers), from primary animal production sector (farms and feed) and from various groups food, with prevalences ranging from 19% (feed) and almost 70% (fresh meat and farms). These data reflect the wide mobility of these microorganisms and the human exposure to many sources of contamination.

With these results, we can see that it is very necessary to continue the study that we started, in order to perform phylogenetic comparisons of genetic markers of the bacteria that we isolated.

Therefore, in this project we propose to complete the spread of E-ESBLs map in Navarra, including new ecological niches (healthy carriers, food groups at risk and waste water). The aim of this project is to study the phenotypic and genetic markers for all isolates (we have a collection of over 700 strains). In addition, we will study by phylogeny and Multi-Locus Sequence Typing (MLST) all strains of E. coli (predominant species in all ecological niches), in order to establish clonal groups to help us to understand routes dispersion of these microorganisms.

The information obtained in this project will allow us to determine the main reservoirs of resistance and to track the spread of these resistant bacteria.

This knowledge is essential to implement preventive measures and interventions in order to reduce human exposure to this hazard through the ingestion of food and water.

Difusión de resultados

Publicaciones:

- Ojer-Usoz, E., González, D. and Vitas, A.I. Phylogenetic Study of Extended-Spectrum β -Lactamase-Producing E. coli: food, human and environmental approach. Applied and Environmental Microbiology (enviado mayo 2016)
- González D, Leiva J. and Vitas AI. Prevalence and Characterization of Extended-Spectrum β -lactamase-Producing Enterobacteriaceae from healthy people in Navarra (Spain). En redacción para ser enviado a Antimicrobial Agents and Chemotherapy.

Congresos:

- XX Congreso Nacional Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC). Barcelona, 26-28 mayo de 2016.
Autores: Vitas AI., González D., Zúñiga T., Gallagher E., Rúa M. y Leiva J.
Tipo de presentación: Póster
Título: Prevalencia y caracterización fenotípica de enterobacterias productoras de β -lactamasas en portadores sanos de la comunidad
- XX Congreso Nacional Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC). Barcelona, 26-28 mayo de 2016.
Autores: Castejón S., Rúa M., Armendáriz L., Losa C., Del Pozo JL., Rubio M., Fernández-Alonso M., Reina G., Vitas AI., González D. y Leiva J.
Tipo de presentación: Póster
Título: Portadores fecales de Enterobacterias productoras de betalactamasas de espectro extendido aisladas en coprocultivos de rutina en un hospital terciario.

FACULTAD DE TEOLOGÍA



ALONSO GARCÍA, JUAN

Título: Conciencia y verdad en el John Henry Newman anglicano (1825-1845).

Presupuesto: 4.100,00 euros

Palabras Clave: John Henry Newman, conciencia, verdad, conversión, subjetivismo, objetividad, relativismo, fe, experiencia, anglicanismo, catolicismo.

Período: 2015-2018

Summary:

The project aims to explore how John Henry Newman (1801-1890) understands the relationship between conscience and truth in his works of the Anglican period. We choose the biographical time frame between the start of his activity as an Anglican deacon in 1825 until his conversión to Catholicism in 1845, because in that period Newman lived a long and rich experience of seeking the truth.

This experience went through several phases. First, the important biographical events of his youth (his "first conversion" in 1816, the dispute with his brother Charles etc.) which influence later his understanding of consciousness and his way to reflect on it. Second, the examination of the doctrinal and practical state of the Anglicanism, as expressed in his sermons. Third, the search for the sources of such doctrinal body, through the research on the Arians of the Fourth Century. Fourth, the awareness of a personal mission to search and spread the truth that Newman experienced in his trip to Sicily (1833), which later gave rise to the remarkable "Oxford Movement." And fifth, on his personal conversion to Catholicism.

This study seeks to center on how Newman was becoming aware of the truth of Catholic doctrine, that is, how he was discovering subjectively and personally the objective force of the truth in and through his own conscience.

Newman has been called "Doctor of conscience", even more so since his beatification presided by Pope Benedict XVI in 2010. Newman's thought about conscience is linked to a long tradition starting from Socrates and Augustine, is exemplified remarkably by figures such as Thomas More, and produced abundant fruits in the Twentieth Century, both in Philosophy (in

the movement of phenomenology) and theology (eg, for Benedict XVI, Newman is one of his greatest inspirators).

The hypothesis of this research project is the possibility to find the truth from the subjectivity without falling into subjectivism or relativism. And, therefore, the main objective of the project is to elucidate and describe -from the living experience of Newman and from his works- how and in which conditions (subjective and objective) this process takes place, both in a broad sense and in relation to Christianity. The relevance of this research is justified, first, by the doctrinal and cultural importance which nowadays is given to personal conscience, often confusingly and ambiguously used to justify a subjectivist and relativist stance. Secondly, the steady growth of interest in the person and the thought of Newman, both in the Anglo-Saxon world and outside of it, as evidenced by the activities of Newman associations in various countries and the constant publication of papers on his person and work, also give grounds for this research.

The methodology consists in analyzing the texts concerning the Newman's experiential stages mentioned above, where his personal testimonies and thematic writings are combined. These texts are mainly: University Sermons, Parochial and Plain Sermons, Ariens of the Fourth Century, Tracts for the Times and a selection of his letters.

The expected results are:

- Translation to Spanish and editing of the following Newman's works: the eighth volume (the only volume that has not been translated to Spanish) of Parochial and Plain Sermons; Ariens of the Fourth Century; and a selection of Tracts for the Times.
- Publication of a monograph entitled I have not sinned against the light about J.H. Newman's experience during his Mediterranean voyage and his disease in Sicily (1833), based on his letters and memorial My Illness in Sicily.
- Publication of 6 articles in academic journals.
- Three research stays at The National Institute for Newman Studies (Pittsburgh, PA).
- Attendance at various national and international conferences.
- Organization of an international one-day conference at the University of Navarra, in collaboration with The National Institute for Newman Studies (Pittsburgh, PA).
- Establishment of contacts and relationships with members of the Newman Association of America and the Association Française des Amis de Newman.

Difusión de resultados

Los avances alcanzados en el primer año de trabajo de este equipo de investigación son los siguientes:

- 1) Traducción y publicación del volumen 8 de los Sermones Parroquiales de John Henry Newman (Editorial Encuentro, Madrid 2015).
- 2) Publicación de varios artículos sobre Newman:

- J. Alonso, "Sensus fidelium y conciencia. Un acercamiento desde el pensamiento de John Henry Newman", en J. L. Cabria Ortega y R. De Luis Carballada (eds.), Testimonio y sacramentalidad. Homenaje al Profesor Salvador Pié-Ninot, San Esteban, Salamanca 2015, 333-354.
- J. Alonso, "Testimonio personal y evangelización según John Henry Newman", en Revista Española de Teología 75 (2015) 469-480.
- S. Sánchez-Migallón Granados, "John Henry Newman", en F. Fernández Labastida – J. A. Mercado (editores), Philosophica: Enciclopedia filosófica online, URL:<http://www.philosophica.info/archivo/2016/voces/newman/Newman.html>

LÍNEAS ESPECIALES



SIGLO DE ORO

**ARELLANO AYUSO, IGNACIO
JESÚS**

Título: SIGLO DE ORO.
Presupuesto: 346.000,00 euros

Productividad científica

El grupo consta de 12 doctores, de los que 4 son investigadores a tiempo completo, 1 Catedrático, 4 Titulares, 3 Agregados. Además tienen un administrativo. Han tenido 3 becarios de ADA.

Los resultados de la investigación del grupo se han difundido a través de 31 artículos, de los que 23 están indexados. Además han producido 4 libros (2 de ellos de carácter internacional), 25 capítulos de libros (15 de carácter internacional) y 2 obras completas. Por otro lado han organizado 21 congresos y han participado en 70 congresos (incluyendo ponencias invitadas y plenarias).

Han defendido 5 tesis doctorales, 2 de ellas internacionales.

Tasa de actividad

Tasa actividad de artículos indexados 1,91 ítems

Tasa actividad total de ítems 5,2



PENSAMIENTO CLÁSICO

ZORROZA, IDOYA

Título: PENSAMIENTO CLÁSICO

Presupuesto: 64.050,00 euros

Productividad científica:

Equipo formado por un total de 21doctores (52% de universidades extranjeras) y 9 becarios, de los que 4 han estado financiados por ADA.

Han difundido los resultados de su investigación a través de 25 artículos en revistas, de las que 13 son indexadas. Además han publicado 16 libros (1 de ellos internacional) y 34 capítulos de libros (18 de ellos internacionales).

Se han organizado 4 congresos y se han presentado 41 comunicaciones a congresos.

Durante el curso se han defendido 7 tesis, una de ellas internacional.

Se ha tenido1 proyecto con financiación externa (nacional).

Tasa de actividad

Tasa de actividad de artículos en revistas indexadas 0.61

Tasa de actividad de total de ítems producidos 4,52