MEDICAMENTOS INNOVADORES
Plataforma Tecnológica Española

farmaindustria

Acción experimental para el fomento de la cooperación entre compañías farmacéuticas y empresas y grupos de investigación en el ámbito de la biotecnología

XIV Encuentro de Cooperación Farma-Biotech

Martes, 17 de noviembre de 2015

La jornada tiene por objeto estimular la cooperación entre compañías farmacéuticas nacionales e internacionales, empresas españolas de biotecnología y grupos de investigación, en torno al desarrollo de nuevos medicamentos innovadores.

La iniciativa diseñada por FARMAINDUSTRIA se propone a través de esta jornada que empresas españolas y grupos de investigación de centros especializados, previamente seleccionados, expongan, ante las compañías farmacéuticas interesadas, productos en desarrollo con el potencial suficiente (innovador, eficaz, protegido) que pueda representar una oportunidad de cooperación para ser explorada por ambas partes.

Tras un cuidadoso estudio de necesidades expresadas por las compañías farmacéuticas y del estado de desarrollo de las investigaciones en curso en las empresas biotecnológicas y los grupos de investigación, se han seleccionado ocho propuestas para que realicen su presentación en la jornada del martes día 17 de noviembre en Madrid.

Por parte del sector farmacéutico asistirán directivos de I+D y Desarrollo de Negocio de las compañías que han expresado su interés en participar. El grado de información manejado durante la jornada se clasifica como "no confidencial" por lo que no se requiere ningún acuerdo previo al respecto.

La jornada se configura por lo tanto como un foro individualizado no abierto a terceras partes, y en donde se desea generar un clima de interacción suficiente que permita identificar el valor añadido derivado del intercambio de información entre demanda y oferta, con suficiente contenido diferencial e innovador en el ámbito de las nuevas terapias y los medicamentos avanzados.

Para cualquier duda o aclaración sobre esta jornada por favor contactar con:

Amelia Martín Uranga

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Agenda

La organización de la jornada pretende dar énfasis tanto a las presentaciones como a la interacción personal entre los asistentes, de acuerdo con la siguiente agenda:

08:45 09:15	Recepción, contactos informales, café	Estado de Desarrollo	Ponente
09:15 09:30	Bienvenida y presentación de la jornada		Farmaindustria
09:30 10:00	*CM-363 y CM-728, quinonas de origen natural para el tratamiento de cáncer de mama triple negativo*	Preclínica no regulatoria	***B. Nicolás Díaz Chico*** CEAMED, S.A.
10:00 10:30	*Plataforma para el diseño y desarrollo de vacunas universales*	Preclínica no regulatoria	***Germán Bou Arévalo*** Hospital U. A Coruña
10:30 11:00	*Inmunoterapia para enfermedades autoinmunes*	Preclínica no regulatoria	***Marta Vives-Pi*** IGTP
11:00 11:30	*CM-352: Nueva molécula potente y segura para la prevención y tratamiento de la hemorragia*	Optimización candidato	***Julen Oyarzabal*** CIMA
11:30 12:00	Café, refrescos, contactos directos		
12:00 12:30	*Protector, en administración intravenosa, contra la cardiopatía isquémica*	Preclínica no regulatoria	***Lina Badimon*** ICCC
12:30 13:00	*Inhibidor de la adrenomedulina como prevención y/o tratamiento de la osteoporosis*	Preclínica no regulatoria	***Alfredo Martínez*** CIBIR
13:00 13:30	*Activadores de AMPK para el tratamiento de la diabetes tipo 2 y otras enfermedades relacionadas*	Optimización candidato	***Pascual Sanz*** CSIC-CIBERER
13:30 14:00	*Reposicionamiento de Doxorubicin para el tratamiento de la esteatohepatitis y otras enfermedades hepáticas*	Pruebas de eficacia y toxic.	***Rubén Nogueiras*** USC
14:00- en adelante	Aperitivos y refrescos. Contactos directos		

Todas las presentaciones se harán en español, si bien la documentación escrita se dispondrá en inglés para facilidad de circulación interna entre los órganos de las compañías internacionales

Lugar de celebración: **Sede de Farmaindustria en Madrid. Calle María de Molina nº 54. 7ª planta**
Fecha: **Martes día 17 de noviembre de 2015**

La plataforma tecnológica Española Medicamentos Innovadores, cuenta con apoyo financiero del Ministerio de Economía y Competitividad (PTR-2014-0337)

PRESENTACIONES QUE TENDRÁN LUGAR EN ESTA JORNADA

CEAMED, S.A.

PROFILE

CEAMED SA is a private company created in 2006 whose primary focus is the identification and development of new medications for cancers with poor prognoses. In particular, those cancers in which Signal Transducers and Activator of Transcription (Stats) play a critical role for either resistance to current treatments or increase the likelihood of recurrence or metastasis. CEAMED also provide a compound/extract screening service against a variety of human cancer cell lines, and perform quality control analysis for the aloe vera industries (ISO 9001:2008).

SPEAKER

B. Nicolás Díaz Chico, Founder, President and CEO, Professor of Human Physiology, Medical School, Las Palmas, Spain (ULPGC), Founder and Vice-President of the Canary Island Cancer Research Institute (ICIC), Former President of the Spanish Association for Cancer Research (ASEICA), Former R&D Vice-Rector, University of Las Palmas (ULPGC), Spain, Former CEO of Technology Institute of Canaries (ITC SA)

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PRODUCT

CM-363 & CM-728, fused natural quinones for treatment of triple negative breast cancer

MECHANISM OF ACTION

Many cancers have poor prognosis due to higher levels of "stemness" or activation of signaling cascades. Stats are activated by growth factor, hormones and cytokines, and are involved in cell survival and drug resistance. Stat3 and Stat5 are overexpressed in many different tumors, and are considered as key targets in cancer treatment. In particular, evidence suggests that inhibition of STAT3 can reduce stem cell load and metastasis in breast cancer. CM-363 acts as an inhibitor of Stat5 activation in CML and breast cancer cell lines, while CM-728 has been demonstrated to be an inhibitor of Stat3 in a TNBC cell line.

TARGET INDICATIONS

Oncology. Treatment of triple negative breast cancer (TNBC). Treatment of Imatinib-resistant chronic myelogenous leukemia (CML). Treatment of other solid tumors overexpressing Stat3.

CURRENT STATUS

- With respect to CM-363 we have demonstrated that it can significantly reduce the growth of tumors produced by a human CML cell line implanted in mice. We have also demonstrated that it can reduce the viability of a CML cell line which has become resistant to Imatinib overtime (an effect seen in patients), and also to one which contains a mutation found in human that also leads to Imatinib resistance.

- With respect to CM-728 we have demonstrated that when given orally it can significantly reduce orthotopic xenografts induced by an aggressive TNBC cell line. We have also demonstrated that a combination of CM-728 and Docetaxel is more effective than either treatment alone.
- CM-728 inhibits microsphere formation by MDA-MB-231 cells, and rapidly reduces the protein levels of activated STAT3 and the oncogenes c-Myc and PIM1, which are key targets for stemness.

INNOVATIVE ASPECTS

- Compounds here presented were designed, synthetized and characterized by CEAMED by fusing natural quinones bearing antitumoral properties, with diverse chemical structures to obtain effective antitumoral drugs.
- Two of them, CM-728 and CM-363 have been successfully proved in vivo: CM-728 (5-10 mg/kg, oral) significantly decreases xenograft growth produced by MDA-MB-231, an aggressive triple negative breast cancer (TNBC) cell line, in nude mouse. CM-728 also synergizes with Docetaxel in vivo. CM-363 (10 mg/kg, IP) significantly reduced the growth of xenografts produced by human K562 chronic myelogenous leukemia (CML) cells, and synergizes with Imatinib.
- CM-728 is able to prevent the growth of TNBC, pancreas, lung cancer and other solid tumors at nanomolar concentrations. Docetaxel and Adriamycin, which are used for treatment of these types of tumors, can only slow their growth.
- CM-728 rapidly and effectively inhibits the activation of Stat3, which in should reduce stem cell load, tumorigenic potential and metastasis, which are the leading causes for the poor prognosis in these cancers.
- CM-363 is active in two different types of Imatinib resistant CML cells and synergizes with Imatinib.

IPR

European (EP 2690094) and world patent applications (WO2014/016314) that include CM-363 have been published (priority dates: 24-07-2012). An application including compound CM-728 is ready for filing.

PARTNERING OPPORTUNITIES

CEAMED is open to an agreement with a pharmaceutical company to develop our lead compounds, to complete their preclinical regulatory development and beyond. CEAMED prefers a long term association, but will also consider signing a joint venture agreement.

University Hospital A Coruña

PROFILE

The main topics of the research group work are related to the development of new techniques for rapid diagnosis of infectious diseases and mainly the study of antimicrobial resistance, from a basic and clinical point of view. Recently the development of vaccines against multidrug resistant pathogens. The group of Dr. Bou is made up of 19 researchers (3 senior, 8 post-doc, 8 predoc students) a laboratory technician and administrative personnel.

SPEAKER

German Bou Arévalo. Head of Microbiology Department (University Hospital A Coruña). Director of the Area of Microbiology and Infectious Diseases at Biomedical Research Institute at La Coruña (INIBIC). Associate Professor of Medical Microbiology at University of Santiago de Compostela. Author or co-author of more than 160 international peer-review manuscripts, including Clin Microb Reviews, J Clin Invest, PNAS, Clin Infect Dis, Antimicrob Agents Chemother, Nature, J Antimicrob Chemother, J Clin Microb, Annals Intern Med, etc. In addition Dr. Bou has authored or co-authored 5 patents (1 national, 4 international). He already has an H index of 41 and is a member of the Editorial Board of the Journal of Clinical Microbiology (2015-2017).

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PRODUCT

Platform for design and development of universal bacterial vaccines, based on an innovative biotechnological approach

MECHANISM OF ACTION

Alternatives to antibiotics are urgently needed to combat multidrug resistance in bacteria. Vaccine development is a priority to overcome this global health problem.

Auxotrophs microorganisms are generated by eliminating essential genes for bacterial growth. This generate a molecular switch that allows to control and modulate externally the bacterial replication. It has been removed the ability to synthesize bacterial D-Glutamate, a key component of the bacterial cell, thus bacterial death happens in a short time after injection into the host (no D-Glutamate is present). Prior to self-destruction the host is capable of generating a protective immune response towards either related and genetically unrelated bacterial strains.

D-glutamate synthesis is an universal key step in cell wall bacterial formation. Here we present a strategic platform for generating effective bacterial whole-cell vaccines auxotrophic for D-Glutamate. This strategy was successfully applied to generate Dglutamate auxotrophic vaccines in three major multi drug resistant pathogens: Acinetobacter baumannii, Pseudomonas aeruginosa and Staphylococcus aureus.

These bacterial vaccine-strains showed virulence attenuation and self-limited growth in vivo. Immunization with these auxotrophic vaccines elicited crossreactive antibodies and cytokine secretion. These responses correlated with mice protection against acute lethal infection with genetically unrelated multidrug resistant, virulent and high-risk clones: A. baumannii, P. aeruginosa, and community-acquired methicillin-resistant S. aureus. This innovative and universal approach overcomes the classical difficulties in obtaining virulence attenuation and represents a hallmarked progress in vaccine development.

TARGET INDICATIONS

Infectious Diseases. Human and animal health. Multiple final products depending on final indications. With our platform is virtually possible to design vaccines for most of human bacterial pathogens in their various clinical indications. Therefore, each clinical indication is a different final commercial product and therefore a different business. We have now an initial product with great potential but requires since now (preclinical phase) cooperation with pharmaceutical companies of the sector to focus the final products.

CURRENT STATUS

- Preclinical phase with the 3 pathogens. They (three pathogens) have been proven useful in the model of severe infection/sepsis both in terms of efficacy and safety.
- Adequate immune response and high mice protection in sepsis models with mice challenged with a set of diverse strains (multidrug resistant and highly virulent strains, or international high risk clones such as USA300). Auxotrophic vaccine strains are unable to grow beyond the control of the laboratory as well as to reverse to the wild-type phenotype in the absence of D-Glu.
- Pseudomonas aeruginosa safety study with regulatory validity has been demonstrated by a certified external company. With this pathogen we are in industrial phase of development.

INNOVATIVE ASPECTS

- To date there is no vaccine on the market against the three pathogens that we describe here, or even expected short term. Therefore it would be a commercial product with little competition.
- Besides, its universality (elimination of D-Glu synthesis) makes it simple in design and execution for their applicability to many other pathogens. A unique and universal way to attenuate bacteria is described in our proposal, which greatly simplified the manner how bacterial vaccines are produced.
- Traditional strategies for bacterial vaccines development included attenuation or inactivation. Auxotrophic vaccines (our proposal) combine the advantages of attenuated and inactivated vaccines without displaying its disadvantages.
- In summary, we describe other biotechnological approach to make bacterial vaccines.

IPR

The vaccine platform of D-glutamate auxotrophs is currently under protection by PCT/EP2014/071296, currently in force. On April 2016 we shall enter the national/regional phase. Furthermore, in most countries, we shall in addition to the submission of the documents needed to correctly enter the national/regional phase, further submit additional experiments and an expert declaration that illustrates the generality of the technical effect, in particular of the medical effect.

PARTNERING OPPORTUNITIES

Co-development agreement with an industrial partner. We dont want to sell the patent nor fee for services. We would like to negotiate with a Pharma a workplan for mutual benefit. To design a working path with milestones and deliverables. Investments according to the delivery of deliverables.

Germans Trias i Pujol Research Institute

PROFILE

Research at the Immunology of Diabetes group is focused on the study of the ethiopathogenesis of autoimmune diseases, specifically of type 1 diabetes, the loss of peripheral tolerance and the development of innovative immunotherapies. The main goals are to understand immunological mechanisms of destruction in autoimmunity and to define potential antigen-specific strategies for therapeutic immunointervention in human type 1 diabetes.

SPEAKER

Dr Marta Vives-Pi has been working for 15 years as Biomedical Researcher and group leader at the Germans Trias i Pujol Research Institute. Her research is focused on the study of autoimmunity and immunology of type 1 diabetes. She is also Associate Professor of Immunology at the Universitat Autònoma de Barcelona since 2000.

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PRODUCT

Liposome-based immunotherapy for autoimmune diseases

MECHANISM OF ACTION

The antigen-specific liposomes arrest autoimmunity through the re-establishment of tolerance, driven by phosphatidylserine. The mechanisms of action are through the generation of tolerogenic dendritic cells and the impairment of autoreactive T cell proliferation as well as the expansion of immunomodulatory antigen-specific T cells.

Tolerance reestablishment was assessed in non obese diabetic (NOD) mice, the gold standard experimental model of type 1 diabetes to simulate human disease. Liposome treatment in NOD mice confirmed the reduction of autoimmunity and the prevention of the disease.

TARGET INDICATIONS

The technology uses autoantigen-encapsulating liposomes to prevent or treat type 1 diabetes. The validation of the liposomes' mechanism of action supports the technology's potential to be applied in other autoimmune diseases, pointing to Psoriasis, Multiple Sclerosis or Celiac Disease, among others.

CURRENT STATUS

- The invention is based on a previous strategy of the group, consisting on a cell immunotherapy based on autologous dendritic cells loaded with apoptotic β-cells for the treatment of autoimmunity in experimental diabetes.
- To overcome the difficulties of sourcing apoptotic β-cells, a synthetic therapy based on liposomes rich in phosphatidylserine loaded with insulin peptides has been developed.
- The researchers demonstrated that liposomes are effectively engulfed by dendritic cells, thus inducing tolerance to the antigen and down modulating the autoimmune cascade.

- This process is able to decrease the incidence and delay the onset of experimental type 1 diabetes.
- Apoptotic mimicry provided by liposomes can offer a solution to the complexity of cell-based therapies.

INNOVATIVE ASPECTS

- The technology is a new autoantigen-specific immunotherapy based on the encapsulating of autoantigens, associated with the autoimmune disease to be treated, in liposomes.
- These nanoparticles comprise phosphatidylserine in their membrane to simulate apoptotic cells recognition by antigen presenting cells. The technology design has been chosen to induce of antigen-specific tolerance and down-modulate the autoimmune cascade thus restoring tolerance to self in autoimmune diseases.
- Currently, some immunotherapies are in development. The added benefit of liposome approach is the delivery of autoantigens along with phosphatidylserine, a combination that induces a stable and longterm specific tolerance reestablishment.
- Liposomes have the advantages of being easy to prepare, customize and administer, and of constituting a low-cost strategy compared to other current immunotherapies.
- Moreover, liposomes protect encapsulated antigens from degradation by proteases in the plasma. Lipid-based nanotechnology is an innovative area of great scientific interest that includes liposomes, which are currently used clinically as vehicles for anticancer drugs and vaccines.

IPR

International Application PCT

PARTNERING OPPORTUNITIES

We are looking for partnership to achieve final development including licensing out the technology.

Center for Applied Medical Research (CIMA)

PROFILE

cima
CENTER FOR APPLIED MEDICAL RESEARCH
UNIVERSITY OF NAVARRA

The Center for Applied Medical Research (CIMA) is a biomedical research institution of the University of Navarra, based in Pamplona, Spain. CIMA performs high quality scientific work with a strong translational focus. Our research group is interested in the identification and validation, in-vitro and in-vivo, of new mechanisms of action involved in the fibrinolytic process as well as in the discovery of therapeutic agents that modulate this process.

SPEAKER

Dr. Julen Oyarzabal got his PhD in Pharmaceutical Chemistry. After finishing his PhD in 1998, he moved to the University of California, San Francisco; and later, he joined the University of Southampton. In November 2001 he started working at Johnson & Johnson Pharma R&D in Toledo (Spain), and in 2006 he joined Spanish National Cancer Research Centre (CNIO) where he set up and led the Computational Medicinal Chemistry Section. Dr. Oyarzábal joined CIMA in 2010 and he is co-inventor of 18 published patents.

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PRODUCT

A new, potent and safe, molecule for the prevention and treatment of haemorrhage: CM-352

MECHANISM OF ACTION

Novel MoA has been identified and validated. Target identification from array analyses (Affymetrix) using human cells: MMP3 & MMP10. Initial validation was done with MMP10 knock-out mice that showed the desired biological response and with MMP10 hMAb that showed the expected in-vitro functional response.

TARGET INDICATIONS

Prophylaxis and acute treatment of bleeding in major surgery. Trauma and first-aid. Intracerebral Haemorrhage (ICH).

Aprotinin withdrawal has generated demand and opportunity for new antifibrinolytics that could significantly reduce the blood transfusions in major surgery.

On the other hand, ICH (15% of all strokes) is associated with high mortality (40%) and there is no proven medical or surgical treatment

CURRENT STATUS

Optimized lead compound (pre-clinical candidate), CM-352, was tested in-vivo in 3 different bleeding models:

- Tail Bleeding: CM-352 was significantly more effective ($p<0.001$) that current standard of care (SoC) at 30,000 times lower dose
- Hepatectomy: CM-352 significantly reduced blood loss ($p<0.05$) during major surgery, while current SoC had no effect.
- Intracerebral haemorrhage. CM-352 significantly reduced lesion volume ($p<0.001$) and led to neurological recovery ($p<0.01$)

INNOVATIVE ASPECTS

- Novel proprietary chemical series (2 patents filed, different Markush formulas)
- Multifactorial optimization process, from initial proprietary hits to an optimized lead compound: CM-352 as a pre-clinical candidate,
  - Hitting two key targets at low nM range (IC50<20nM).
  - In-vitro efficacy in functional assay (using human whole blood): delay in lysis time; EC50LT is <1nM
  - Optimal solubility, P450s profiling, hERG and plasma protein binding (unbound fraction).
  - Optimal therapeutic window, efficacy vs toxicity, >4 log units
  - No cardiovascular (patch clamp) or Ames issue
  - Anatomopathological analyses (lung, brain, kidney and liver) did not show any alteration
  - Optimal pharmacokinetics (short half-life)

IPR

Two patent applications for novel proprietary compounds were filed. One patent application for drug repositioning (known MMP inhibitors in acute scenario) was filed.

PARTNERING OPPORTUNITIES

CIMA is open to various types of partnerships with academia and biopharmaceutical companies in order to facilitate the advancement of the research, with the ultimate goal of improving patient quality of life. By joining capabilities and resources, this win-win cooperation facilitates the advancement in the different research stages, from target validation to lead optimization or early candidate development.

Institut Català de Ciències Cardiovasculars (ICCC)

PROFILE

Institut Català de Ciències Cardiovasculars

The ICCC-group focuses its research in the cardiovascular disease area by generating basic and applied research knowledge to be further applied in diagnostic and therapeutic development with the general objective of improving health care. A priority area of the ICCC-Research Group is the identification of new therapeutic targets and biomarkers and the design of interventions aimed to provide cardiovascular protection, and pre-clinical and clinical research into prognostic and diagnostic markers of disease.

SPEAKER

Prof. Lina Badimon is the Director of the Cardiovascular Research Center in Barcelona (CSIC-ICCC), Lecturer Adjunct Associate Professor of Medicine - Cardiology - at Mount Sinai School of Medicine, New York and Visiting Professorship of the Manchester Metropolitan University. Prof. Badimon is also coordinator of the research group on "Molecular Pathology and Therapeutics of Ischemic and Atherothrombotic Diseases" at the Biomedical Research institute Sant Pau (IIB Sant Pau)-Hospital de la Santa Creu i Sant Pau since 2009 and currently she is Vice-President-elect of the Spanish Society of Cardiology (2012-2016), and Chairman of the Council on Basic Cardiovascular Science (2014-2016) and Vice-Chair of the Working Group on Coronary Pathophysiology and Microcirculation (2014-2016) of the European Society of Cardiology. She has published over 400 articles (Times Cited 19.476; h-index 62) and more of 200 reviews and book chapters.

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PRODUCT

Intravenous administration of a modified HMG-CoA reductase inhibitor-like to protect against ischemic heart disease (CARDIOSHIELD)

MECHANISM OF ACTION

Beyond improving lipid profiles through chronic blockade of liver LDL-cholesterol synthesis, the inhibition of HMG-CoA has additional acute targets with direct effects on the synthesis of isoprenoid intermediates which are involved in post-translational modifications of a variety of proteins that modulate cell survival, inflammation, cytoskeleton organization and nitric oxide synthesis.

We have shown that these mechanisms of action when timely exploited can prevent myocardial cell death to occur thereby limiting the size of infarction.

TARGET INDICATIONS

This drug has been designed to be intravenously infused in the setting of acute myocardial infarction with the aim of protecting the heart against myocardial ischemic damage and further revascularization of the occluded coronary artery.

Accordingly, it may also provide protection in those clinical settings in which ischemia/reperfusion damage occurs (by-pass surgery, organ transplant, endarterectomy, general surgery, etc).

CURRENT STATUS

- We have reported in a pig model of closed-chest coronary balloon occlusion/reperfusion that just one intravenous administration of HRIL before the restoration of the coronary flow (at the onset of reperfusion) induces heart protection by attenuating tissue and functional determinants of reperfusion injury (oxidative stress, mitochondrial dysfunction, apoptosis, inflammation) thus limiting reperfusion-related myocardial damage.
- n addition, we have also demonstrated in a mice model of myocardial infarction that early administration of one dose of HRIL at the onset of ischemia protects the myocardium against ischemia-related deleterious effects.
- Both protective effects are associated with the myocardial inhibition of the small GTPase RhoA.
- Finally, supporting our observations and HRIL-mechanism of action, we have demonstrated that administration of a selective RhoA inhibitor laboratory chemical (CCG-1423) during ischemia reduces the size of infarction.

INNOVATIVE ASPECTS

- Prevalence of ischemic heart disease imposes a tremendous European human, social and economic cost. Currently, there is no drug available for clinical use capable of reducing cardiac damage in the setting of ischemic heart disease.
- In fact, research efforts are currently focused in the search of therapeutic strategies able to limit cardiac damage in the setting of reperfusion injury (myocardial infarction and further revascularization-induced injury). The latest attempt was presented in the recent ESC-2015-London meeting with unsuccessful results.
- The cardioprotective approach we are proposing has robustly shown in two animal models, one of them a large animal model with human-resemblance, to markedly reduce infarct size and significantly improve cardiac contractility without the presence of concomitant side-effects.
- We have developed an innovative therapeutic approach that responds to an unmet need to counteract myocardial damage in high-risk patients (myocardial infarction patients).
- The novelty focuses on modifying HMG-CoA reductase inhibitor (HRIL) for a novel therapeutic use in order to be intravenously delivered at the onset of ischemia or prior mechanical reperfusion.
- Due to the wide applicability of HMG-CoA-RI and acceptable safety profile, this is an exciting and promising therapeutic option extensible to all procedures that curse with spontaneous or induced (surgery/catheterisms, etc) organ ischemia.

IPR

This approach has been subjected to patent: IP: 27/5/2014 European patent application nº EP14382190.8 for "Prevention and/or treatment of ischemia/reperfusion injury"

PARTNERING OPPORTUNITIES

We have an open approach to collaboration with pharma and expect proposals from interested partners. In particular: call for industry expressions of interest, evaluate our product in conjunction with the industry and look for strategic partners and funds.

Centro de Investigación Biomédica de La Rioja (CIBIR)

PROFILE

CIBIR was inaugurated in August 2005 on the initiative of the Government of the Autonomous Community of La Rioja working through its Department of Health. Fundación Rioja Salud (FRS) is the entity responsible for the management and coordination of CIBIR. CIBIR, closely linked to the main reference hospital of the area, has 7 research units grouped into 4 strategic areas: infectious diseases, oncology, neurodegenerative diseases, and antibiotic resistance.

SPEAKER

Alfredo Martínez obtained a PhD in Cell Biology by the University of Navarra (Pamplona, Spain). He performed postdoctoral training in Dublin (Trinity College), London (Hammersmith Hospital), and Vancouver (University of British Columbia), and spent 11 years at the National Cancer Institute (NIH, Bethesda, MD, USA) as a staff scientist. He returned to Spain to work at the Cajal Institute (Madrid) and since 2008 he is Group Leader at CIBIR (Logroño, Spain). He is also full professor of Cell Biology.

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PRODUCT

Adrenomedullin inhibitor to treat/prevent osteoporosis

MECHANISM OF ACTION

We have discovered a novel therapeutic target for osteoporosis. Inhibition of this target can be accomplished through different strategies (monoclonal antibodies, small molecules, siRNA, etc). We have evidence that a small molecule that binds the target with high affinity (dissociation constant [Kd] = 7.8 x 10-9 M) was able to completely prevent osteoporosis in an ovariectomized mouse model.

Adrenomedullin is a 52 amino acid peptide that binds to a membrane receptor composed by a 7-transmembrane domain polypeptide known as calcitonin receptor-like receptor (CLR) and a single transmembrane domain protein known as receptor activity modifying protein (RAMP). Adrenomedullin regulates bone deposition through an indirect mechanism that implicates insulin and ghrelin regulation. Knockout mice for adrenomedullin are characterized by higher bone density than their wild type littermates.

TARGET INDICATIONS

Osteoporosis and conditions where bone mass is reduced (osteomalacy, arthritis, Cushing´s syndrome, eating disorders, gastric bypass, prolonged immobility, drugs that reduce bone mass, etc). Also indicated for persons subjected to microgravity (as in space flights).

CURRENT STATUS

- First, we created an inducible knockout for adrenomedullin (complete abrogation of the gene from conception results in 100% embryo lethality), producing viable adult mice lacking adrenomedullin expression. These animals present higher bone density than their wild type littermates.

- Second, we used a blocking small molecule in a mouse model of osteoporosis based on ovariectomy. In this experiment, the small molecule completely prevented the loss of bone mass due to the lack of estrogens.
- Furthermore, analysis of these mice showed no toxicity due to the application of the small molecule.
- At the moment we are beginning preclinical characterization of the small molecule for approval by the Spanish regulatory agency.

INNOVATIVE ASPECTS

- The mechanism of action defined by adrenomedullin and its receptors is completely new and thus different from all currently existing clinical targets for osteoporosis.
- In addition, we have found no toxicity after looking for markers of blood, renal, or hepatic toxicity.
- Furthermore, we have a complete battery of molecules that can target the peptide/receptor interaction, thus we can act at different levels through the cascade of events.

IPR

A European patent was filled out on March 2015 (application number: 15382111). It covers all potential applications of adrenomedullin inhibitors as they relate to bone mass preservation.

PARTNERING OPPORTUNITIES

Fundación Rioja Salud plans to create a start-up small company to develop this new drug and to carry it out through preclinical testing, regulatory approval, and the initial clinical phases (phase 1, phase 2). We would be delighted to collaborate with the industry through a co-development or any other formula that suits both partners.

CSIC-CIBERER

PROFILE

The research group is interested in the regulation of the activity of the AMPK complex by glucose and also by alternative mechanisms (i.e., small chemical compounds). At present he is also studying of the molecular basis of Lafora disease, a progressive myoclonus epilepsy, since he described that AMPK plays a role in regulating the major proteins affected in the disease, namely laforin (a dual specificity phosphatase) and malin (an E3-ubiquitin ligase).

SPEAKER

Dr. Pascual Sanz studied Pharmacy at the Faculty of Pharmacy of the Univ. of Valencia and obtained his Ph Degree in 1986. He moved to the Dept. of Biological Chemistry at the Univ. California at Los Angeles (UCLA, USA) for a post-doctoral stay (1987-1989) and then gained a position at the Institute of Agrochemistry and Food Technology (IATA-CSIC), where he worked on biotechnology improvement of baker's yeast from 1990 to 1998. Then, he went to the Univ. Columbia at New York (USA) for a second post-doctoral stay (1998-1999) and returned to the Institute of Biomedicine of Valencia (IBV-CSIC), where he is leading the group of Nutrient Signaling since then.

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PRODUCT

Novel AMPK activators for the treatment of Type 2 Diabetes and related metabolic diseases

MECHANISM OF ACTION

The new indol-derivative compounds are activators of the AMPK complex.

AMPK is an enzyme that controls whole-body energy metabolism. Compounds that target AMPK affect energy production processes such as glycolysis, lipid oxidation and gluconeogenesis.

In addition, activation of AMPK reduces the expression of lipogenic enzymes such as fatty acid synthase (FAS) and acetyl CoA carboxylase (ACC) suppressing in this way the proliferation of prostate cancer cells.

TARGET INDICATIONS

Diabetes, obesity and metabolic syndrome, as well as neurodegenerative, inflammatory diseases and some types of cancer.

CURRENT STATUS

We have synthesized and tested new indol-derivative compounds in mammalian HEK293 cells. Our results indicate that these compounds are water soluble and are able to be internalized inside the cells where they promote the activation of endogenous AMPK complex.

When we performed a dose-response experiment we noticed that these compounds had a potency of more than 100 fold higher than phenformin.

Even at the highest dose tested these compounds did not show any sign of toxicity in the regular cell viability assays.

The program is currently in optimization phase with several-like candidates that fulfill the product profile.

INNOVATIVE ASPECTS

- The synthesized family of indol heterocyclic compounds activate AMPK complex both in vitro and when added to mammalian cultured cells. In cells treated for one hour with these compounds, activation of AMPK [defined as the levels of phosphorylated catalytic AMPKalpha subunit (pT172) and one of its substrates (phospho-acetylCoA-Carboxylase)] is more than 100 fold higher than the one observed with 5 mM phenformin (a regular AMPK activator).
- At the concentration of use, the new compounds do not show any sign of toxicity (determined by regular cell viability assays). Therefore, the product activates rapidly endogenous AMPK complex present in the human embryonic kidney (HEK293) cells studied so far.
- Metformin is the most common used drug for the treatment of type2 diabetes. However, metformin activates AMPK by an indirect mechanism: it affects mitochondrial respiratory chain thus increasing the AMP/ATP ratio which ends with an activation of AMPK complex.
- In addition, metformin has recognized effects that are independent of AMPK action. The use of compounds that could affect specifically AMPK complex would allow a better therapeutic choice with fewer side effects.

IPR

The product is protected by an international PCT patent application (PCT/ES2015/070677) covering the priority patent application P201431364.

PARTNERING OPPORTUNITIES

We are open to any kind of collaboration with a Pharma industry interested in our product.

Universidad de Santiago de Compostela

PROFILE

The research group is focused in the study of molecular mechanisms involved in obesity and metabolism. In the challenge to decipher the complex and multiple pathways causing obesity, we use different approaches such as genetically engineered mice, pharmacological tools and in vitro assays. We have also a close collaboration with several clinical groups in order to understand the translational potential of our preclinical data.

SPEAKER

Rubén Nogueiras Pozo, doctor in 2003 by the University of Santiago de Compostela. Postdoctoral stays in Germany, Switzerland and USA. IP from different national, regional and international projects (ERC Starting Grant) that allow to have a group that combines experienced researchers (postdocs) and young researchers in training (PhD).

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PRODUCT

Repurposing of the use of Doxorubicin

MECHANISM OF ACTION

Doxorubicin is an antibiotic currently used in chemotherapy at very high doses. Our results indicate that at very low doses, this compound inhibits the amount of triglycerides in obese mice and mice that were induced liver damage. These effects were not associated with any change in the expression of markers of cardiotoxicity and hepatotoxicity.

Doxorubicin is an activator of p53, and our data indicate that the hepatic effects of this compound at very low doses are not observed in p53-deficient mice treated with doxorubicin.

TARGET INDICATIONS

Liver disease, particularly steatohepatitis

CURRENT STATUS

Doxorubicin administration chronically (2 months, intraperitoneal administration) in obese mice and mice that were induced liver damage, the results showed that hepatic profile of mice improves, decreases of the body weight and increases sensitivity to insulin.

We have also achieved similar results through oral administration of doxorubicin.

In neither case changes of expression or levels of circulating markers of hepatotoxicity or cardiotoxicity, major side effects of doxorubicin used in high dose chemotherapy, were observed.

INNOVATIVE ASPECTS

- Hepatic steatosis and steatohepatitis currently have no approved treatment. They are classified as orphan diseases.
- Also because doxorubicin has for years used in the clinic, all its features bioavailability, toxicology, etc. are known.

IPR

European patent submitted. Submission number: 300173808

PARTNERING OPPORTUNITIES

We are open and willing to have any kind of collaboration, from scientific advise to go on with the right assays in the project to a co-development. Our group has a broad experience in establishing public-private partnerships.