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

XI Encuentro de Cooperación Farma-Biotec

Miércoles, 2 de julio de 2014

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 miércoles día 2 de julio 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.

Con objeto de **concretar** del modo más preciso posible los **encuentros bilaterales** que los representantes de los laboratorios farmacéuticos asistentes deseen realizar con algunos de los investigadores ponentes, se incluye en la **última página** de este documento un formulario simple que nos pueden devolver directamente escaneado o copiar su contenido a un correo-e.

Amelia Martín Uranga

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Agenda prevista

La organización de la jornada pretende dar tanto énfasis 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	*1. Empleo de péptidos inhibidores de la Calcineurina para el tratamiento de enfermedades inflamatorias y autoinmunes*	Completada prueba de concepto	***Juan Miguel Redondo*** CNIC
10:00 10:30	*2. Métodos de utilización de una variante de la calcineurina para el tratamiento de la hipertrofia cardíaca*	Completada prueba de concepto	***Enrique Lara*** CNIC
10:30 11:00	*3. Kit de predicción de la respuesta clínica a una terapia contra el cáncer colorrectal*	Completadas pruebas in-vivo	***Jaime Feliú Batlle*** Hospital La Paz
11:00 11:30	*4. Nuevos compuestos eficaces para el tratamiento de enfermedades inflamatorias que cursen con niveles altos de TNF- α.*	Completadas pruebas in-vivo	***Teresa Bellón Heredia*** Hospital La Paz
11:30 12:00	Café, refrescos, contactos directos		
12:00 12:30	*5. Test plasmático, no invasivo, para diagnóstico de adenomas avanzados y cáncer colorectal*	Iniciando fase clínica	***Rocío Arroyo*** Amadix
12:30 13:00	*6. Compuestos epigenéticos para el tratamiento del cáncer*	Completadas pruebas in-vivo	***Julen Oyarzabal*** CIMA
13:00 13:30	*7. Kit basado en biomarcadores predictivos de respuesta a tratamiento con quimioterapia cáncer colorectal*	Completadas pruebas in-vivo	***Rocío García-Carbonero*** Hosp. Virgen del Rocío
13:30 14:00	*8. Anticuerpos para diagnóstico/tratamiento de enfermedades que median con alteración de respuesta inflamatoria*	Completadas pruebas in-vivo	***Javier Miñano Sánchez*** Hosp. Nª Sª de Valme
14:00- en adelante	Aperitivos y refrescos. Contactos informales y **reuniones bilaterales concertadas**		

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 pta.**
Fecha: **Miércoles día 2 de julio de 2014**

GOBIERNO DE ESPAÑA
MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD

CNIC, Centro Nacional de Investigaciones Cardiovasculares

PROFILE

The Spanish National Centre for Cardiovascular Research (CNIC) is an international research centre of excellence which mission is to improve cardiovascular health in the population, generating scientific knowledge and efficiently translating that knowledge to the clinic. The CNIC's three main areas of activity are Basic Research of excellence, Translational Medicine, and Training. CNIC is a Public-Private Research Foundation equipped with the most advanced technology at an international level. The institution was distinguished with the "Severo Ochoa" award in 2011. The Gene Regulation in Cardiovascular Remodeling and Inflammation Lab, headed by Dr. Redondo is part of the Vascular Biology and Inflammation Department, one of three strategic departments where research at the CNIC is organized.

SPEAKER

Juan Miguel Redondo, PhD, made his postdoctoral training in Immunology at different national (CBMSO, Hospital de la Princesa) and international centers (Harvard Medical School and Duke Medical Centre), after graduating in Biochemistry and getting his PhD in Sciences by the Universidad Autónoma de Madrid. Since 1995, Dr. Redondo manages his own lab, initially at the CBMSO and since November 2001 at CNIC, in which he develops his research on gene regulation in cardiovascular and inflammatory diseases. Since 2010 Dr. Redondo is the Head of the Department of Vascular Biology and Inflammation at CNIC, composed of a total of 105 researches divided into 9 research groups.

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PRODUCT

Development of Novel Anti-Calcineurin Drugs for the Treatment of Inflammatory and Autoimmune Diseases.

MECHANISM OF ACTION

The identified inhibitors act directly on Calcineurin, and they do not require a previous binding with the ciclophylins (unlike CsA and FK506, that need to bind these proteins to exert its inhibitory effect). This mechanism of action largely diminishes the potential secondary effects associated with the other treatments using CsA and FK506.

TARGET INDICATIONS

Autoimmune and inflammatory diseases, pathologies where angiogenesis plays a basic role (chronic inflammatory diseases and ischemic retinopathies), immunosuppression, and diseases characterized by a pathologic vascular remodeling (atherosclerosis, aneurism and restenosis).

CURRENT STATUS

- A proof of concept of the activity and specificity of these compounds has been already developed.
- In vivo experiments based on the lentiviral-mediated expression of the LxVP peptide indicates that this mode of inhibition of CN results in prophylactic and therapeutic inhibition of a number of inflammatory diseases, such rheumatoid arthritis and delayed type hypersensitivity.
- The identified permeable compounds inhibit the CN activity and CN-dependent luciferase reporter expression in living cells and are expected to display similar anti-inflammatory properties that those exerted by the expressed LxVP in vivo (Escolano et al., EMBO J. 2014 May 16;33(10):1117-33)

INNOVATIVE ASPECTS

- The interaction of CN with their substrates is mediated by two conserved motifs, LxVP and PxIxIT. However, only the in vivo expression of LxVP inhibits the phosphatase activity of CN. As occurs with the immunosuppressive drugs CsA and FK506, the in vivo expression of the LxVP peptide down-regulates the activity of CN which results in the inhibition of the expression of pro-inflammatory mediators.
- We have identified a set of hits selected based on the mode of action of the LxVP peptide. As the peptide does, these permeable drugs identified inhibit the phosphate activity of CN and the NFAT-regulated transcription of reporter constructs.
- These molecules are expected to be the hits that will evolved to highly specific Calcineurin inhibitors safer that those currently used for transplantation, and with the potential to be efficacious new anti-inflammatory compounds

IPR

• "Selective peptides that inhibit the biological activity of calcineurin". EPO and USPTO applications pending.

• "LxVP-mediated calcineurin inhibition in macrophages". PCT application (PCT application date: 18/10/2013).

PARTNERING OPPORTUNITIES

We are seeking for a pharmaceutical partner to co-develop and/or invest in the pharmaceutical development of these new leads for inflammatory and auto-immune diseases. We have already raised a part of the funding required for drug development.

CNIC, Centro Nacional de Investigaciones Cardiovasculares

PROFILE

The Spanish National Centre for Cardiovascular Research (CNIC) is an international research centre of excellence which mission is to improve cardiovascular health in the population, generating scientific knowledge and efficiently translating that knowledge to the clinic. The CNIC's three main areas of activity are Basic Research of excellence, Translational Medicine, and Training. CNIC is a Public-Private Research Foundation equipped with the most advanced technology at an international level. The institution was distinguished with the "Severo Ochoa" award in 2011.

SPEAKER

Enrique Lara-Pezzi obtained PhD in Biochemistry and Molecular Biology from Universidad Autónoma de Madrid (2000). After a first postdoctoral period he worked at European Molecular Biology Laboratory, Italy (2003-2006). With funding from the EC Marie Curie Programme, he subsequently moved to Nadia Rosenthal's laboratory at the Heart Science Centre, Imperial College London (2006-2009). Dr Lara-Pezzi joined the CNIC in 2009 as a Group Leader to study molecular mechanisms of heart failure.

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PRODUCT

Usage of the calcineurin variant CnAβ1 with gene therapy to treat heart failure

MECHANISM OF ACTION

Overexpression of CnAβ1 in cardiomyocytes will be achieved with a single intracoronary injection of an adeno-associated viral vector serotype 9 (AAV9) carrying the CnAβ1 cDNA. Specific overexpression in cardiomyocytes will be further ensured by the cardiac-specific troponin T promoter and by direct injection into the coronary trunk. This will decrease the probability of CnAβ1 expression in other organs. The viral vector lacks the viral genes encoding the packaging proteins so the recombinant virus cannot replicate on its own. The AAV mostly remains as episomal DNA, eliminating the risk of side effects on endogenous genes due to random integration into the host's genome.

TARGET INDICATIONS

The efficacy of CnAβ1 overexpression is indicated for the treatment of post-infarction heart remodeling and ischemic heart failure as well as for the treatment of non-ischemic heart remodeling and heart failure caused by decompensated cardiac hypertrophy.

CURRENT STATUS

- We have proof of concept of the efficacy of the viral product AAV9-CnAβ1 in mouse models of myocardial infarction and aortic stenosis.
- The efficacy of CnAβ1 overexpression for the treatment of cardiac remodeling and heart failure had already been proved in different transgenic mice.
- We will now test the efficacy of AAV9-CnAβ1 in a preclinical pig model of myocardial infarction

INNOVATIVE ASPECTS

- We propose to improve heart remodeling and prevent or reverse heart failure by overexpressing the calcineurin splicing variant CnAβ1 using gene therapy.
- CnAβ1 is a natural human protein expressed in the heart at low levels, so the chance of immune rejection is very low. AAV themselves cause no disease and induce only a mild immune reaction if any.
- As opposed to drug regimes that require administration of several tablets daily, AAV9-CnAβ1 would be effective with just a single dose.
- Considering cardiac remodelling is a progressive chronic condition, a single injection offers a significant financial advantage over drug regimes that involve daily administration for years.
- Furthermore, AAV9-CnAβ1 is much cheaper and less invasive than the available treatments for end-stage heart failure (i.e. left ventricular assist devices (LVADs) and transplantation). In addition, AAV9-CnAβ1 requires no immunomodulatory therapy.

IPR

Two patents have been filed so far: EP12382329.6 (Date of application: 17/08/2012) - "Methods of using the Calcineurin A variant CnAB1 for the treatment of cardiac hypertrophy and EP14155721.5 (Date of application: 19/02/2014) - "AAV vectors for the treatment of ischemic and non-ischemic heart disease".

PARTNERING OPPORTUNITIES

Cooperation with industry will be beneficial in order to implement preclinical studies to determine the product's safety and efficacy in a pig model of post-infarction heart failure, and for the development, prospective clinical trials to be held, and commercialisation of the product.

IdiPAZ Institute for Health Research

PROFILE

The inventions arise from the joint collaboration between **IdiPAZ Institute for Health Research**, IMDEA (Instituto Madrileño de Estudios Avanzados), Autonoma University of Madrid and Infanta Sofía University Hospital. The three institutions are world´s leading centers in the field of biomedical research. The IdiPAZ Institute for Health Research is especially well known for a high level in basic, clinical and epidemiological research and in health services. The main scientific aim is the translation of scientific findings to clinical applications to improve regular healthcare practice.

SPEAKER

Jaime Feliu M.D., PhD. is currently the Head of the Medical Oncology Department at La Paz University Hospital and Professor of Medicine in the Autonoma University in Madrid. Dr. Feliu main research interest includes basic and clinical research in gastrointestinal cancer, focused on molecular-targeted therapies and molecular biology. He is author of more than 250 national and international research publications, books and books chapters in this field.

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PRODUCT

Test for the prediction of prognosis and response in colorectal cancer patients

MECHANISM OF ACTION

ColoLipidGene is based on the combined analysis of four metabolic-related genes and constitutes a robust and potent prognostic biomarker of stage II CRC patients. ColoLipidGene biomarker might reflect the potential energetic capacity of the tumoral cells revealing the potential aggressiveness of the tumor. In addition, since ColoLipidGene is constituted by metabolic "druggable" enzymes, these results point at these molecules as relevant targets for anticancer therapy.

On the other hand, the kit for neoadjuvant rectal cancer treatment makes it possible to discriminate between the different grades of pathological response, based on the tumor regression grade value. The prediction of response to treatment makes it possible to adequate treatments and to act more or less aggressively. With this tool, the non-response to an antitumor therapy is predicted with a high sensitivity, (80%). This high sensitivity is very relevant, , since as there is a very low likelihood of benefit, these patients should leave the usual protocol of preoperative treatment and be operated directly, avoiding unnecessary delays in local treatment, which increase the risk in these patients of developing distant metastasis and local complications, such as intestinal obstruction.

TARGET INDICATIONS

ColoLipidGene is a biomarker that could provide definitive stratification to predict the risk of relapse for all stage II colon cancer patients. On the other hand, the kit for rectal cancer is another biomarker that helps in the prediction of response to treatment and makes possible to adequate treatments and to act more or less aggressively. In addition, since ColoLipidGene is constituted by metabolic "druggable" enzymes, these results point at these molecules as relevant targets for anticancer therapy

CURRENT STATUS

1. COLOLIPID test:

- In a first step it was determined the expression profile of 83 lipid metabolism-related genes by real time qPCR in tumor samples from a training set of 77 patients with stage II colorectal cancer. The association between the expression profile of lipid metabolism-related genes and clinical outcome was determined using univariate and multivariate Cox regression analyses using c-index methodology to identify a metabolic signature as a new marker of prognosis of these patients.
- Results showed that the combined analysis of 4 lipid-related genes, constitutes a metabolic-related signature (ColoLipidGene) able to accurately stratify stage II CRC patients with 5-fold higher risk of relapse with a strong statistical power in the three independent groups of patients assayed.
- The value of this metabolic signature was further confirmed in an independent validation set of 119 patients and followed a second validation in an additional set of 120 patients with stage II colorectal cancer from different hospitals located in different regions.

2. Kit for rectal cancer:

- In vitro studies in more than 50 human samples were carried out with promising results. The genomic fingerprint showed predictive value of response to treatment in colorectal cancer and enabled a significant discrimination between the different grades of pathological response.

INNOVATIVE ASPECTS

- sAXL in serum is increased in heart failure (HF) patients with reduced ejection fraction (HF-REF, n=192) when compared to controls (n=67, P<0.0001).
- Furthermore, sAXL levels correlated with numerous parameters associated with worse HF prognosis but not with echocardiographic parameters.
- Therefore, its behavior differs from brain natriuretic peptides (BNPs), the "gold standard" biomarkers of HF.
- Cox regression analysis indicated that high sAXL values at enrollment time were related to the major HF events (all-cause mortality, heart transplantation and HF hospitalizations) at one year follow-up (P<0.001), adding predictive value to high BNP levels.
- Preliminary results with other groups of patients sustains the role of sAXL in HF, as we also find higher sAXL values in HF patients with preserved ejection fraction (HF-PEF) and we do not find higher values in patients suffering from other cardiovascular pathologies such as acute myocardial infarction or atrial fibrillation.

IPR

Two different patent families: Spanish patent P201130863 -granted in February 2014 with a very favourable IET report- and PCT/ES2012/070379 international patent application; Spanish patent P201231918 –under prosecution- and PCT/ES2013/070864 international patent application

PARTNERING OPPORTUNITIES

We would like to find any party interested in partnering, licensing or investing in the technology: Investors to finance the subsequent phases of the research project; Patent licensees; Partners interested in getting involved in the subsequent phases of the research project, etc

IdiPAZ Institute for Health Research

PROFILE

The invention arises from the joint collaboration between the University of Alcalá and the **Institute for Health Research of Hospital la Paz-IdiPAZ**. The first is responsible for the synthesis and chemical characterization of compounds and the second for in vitro testing in cellular systems and in vivo testing in animal models. Both institutions are leader centers at national and international level in the field of quality research. The IdiPAZ Institute for Health Research is especially noteworthy for the generation of results in the area of basic, clinical and epidemiological biomedicine and health services. One of its main research objectives is to have practical applications for improving health problems, health care, and all issues arising in regular healthcare practice.

SPEAKER

Teresa Bellón has a PhD degree in Biology (Universidad Autónoma de Madrid). Her research experience has been developed in the Centro de Investigaciones Biológicas (CSIC), the Jefferson Cancer Institute (Philadelphia, PA, USA), the Immunology Service of La Princesa Hospital (Madrid, Spain), and at present she works at La Paz University Hospital. She is author of more than 60 national and international research publications and acts as principal investigator in many research projects. She is also Vice-President of the Spanish Consortium for the study of SCARs PIELenRed.

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PRODUCT

New therapeutic agents with efficacy in the treatment of inflammatory disorders characterized by high levels of TNF- a.

MECHANISM OF ACTION

One of the selected compounds is able to inhibit the expression of TNF-α at the transcriptional level in human primary monocytes, which suggest that the mechanism could be related to the activity of some transcription factor and could also regulate the expression of additional cytokines. The effect seems to be independent of p38 MAPK or c-jun activation. Preliminary data suggest that NFκB activity could be affected.

TARGET INDICATIONS

These new agents are intended to be used as active ingredients in drugs that could be located primarily within the nephrology/rheumatology therapeutic area. The main indication for which these agents have demonstrated efficacy is the treatment of immune-mediated inflammatory diseases (IMIDs) or autoimmune disorders associated with high levels of TNF-a. Metabolic diseases and insulin resistance are related to a low grade inflammation. The compound could be used also in this therapeutic area.

CURRENT STATUS

- In addition to TNF-α, 1 μM of the selected compound down-regulated the production of IL-1β and IL-6 in THP-1 cells stimulated with LPS as well. We explored the response to additional inflammatory stimuli such as poly I:C (an analogue of ssRNA) and the compound also inhibits the production of TNF-α and IL-12 in response to poly I:C stimulation

by in vitro differentiated human dendritic cells

- Metabolic diseases are related to a low grade inflammation. We have explored the action of the compound on human mature adipocytes generated in vitro from human mesenchimal stem cells. We found a dose-dependent downregulation of IL-6 and leptin production by human adipocytes stimulated with LPS.
- In vivo studies in animal models previously treated with low doses of the compositions of the invention (2mg/kg) show significantly less TNF-a production when challenged with a potent proinflammatory stimulus such as LPS (lipopolysaccharide). This result indicates that the compounds have antiinflammatory efficacy when administered in vivo.
- Long term (1 month) treatment of mice with low doses of the compound showed no toxicity over kidney, lung or liver.

INNOVATIVE ASPECTS

- New generation of inhibitors of tumor necrosis factor-alpha (TNF-a) production and, therefore, useful for the prevention and/or treatment of inflammatory diseases such as rheumatoid arthritis, osteoarthritis, Crohn's disease, ulcerative colitis, asthma, bronchitis, chronic obstructive airways disease, psoriasis, allergic rhinitis, ankylosing spondylitis, hidradenitis supurativa, dermatitis and any other inflammatory condition which curses with high levels of TNF-a.
- These new compounds, besides showing a marked efficacy in inhibiting production of proinflammatory cytokines or signaling -strategy that has proved to be the most effective in treating inflammation- allow at the same time their oral administration, unlike recent antiinflammatory protein-based biological therapies.
- On the other hand, the majority of drugs currently available in the market for the treatment of inflammatory disorders, such as steroidal anti-inflammatory agents (hormones), nonsteroidal anti-inflammatory agents (NSAIDs) show numerous side effects, which make worth to explore the potential of new drugs.

IPR

Spanish patent P201331143 filed in July 2013. Shortly it will be internationally extended through PCT route.

PARTNERING OPPORTUNITIES

We would like to find any party interested in partnering, licensing or investing in the technology: Investors to finance the subsequent phases of the research project; Patent licensees; Partners interested in getting involved in the subsequent phases of the research project, etc.

AMADIX

PROFILE

Amadix is a biotechnology company focused on developing innovative diagnostic tools in oncology, either to improve the diagnosis of different types of cancer through a non-invasive test, or to support the physician´s decisions for administration of the right treatment for patients. The company identifies and in-licenses breakthrough discoveries in cancer diagnosis and develops them into marketable products, thus helping patients avoid unnecessary invasive procedures while reducing healthcare costs. In December 2012 Amadix acquired Transbiomed (the first spin-off of Vall d´Hebrón Research Hospital (VHIR), Barcelona, Spain, providing the company with existing and new diagnostic opportunities as well as direct access to Valld´Hebron cutting-edge technology and facilities for the development of different programs under an agreement with the Vall d´Hebron Hospital.

SPEAKER

Rocío Arroyo, CEO, is an entrepreneurial executive with more than 15 years of experience in the Pharmaceutical and Biotechnology industry. Prior to joining Amadix, she filled the position of General Manager in Bionostra Biotechnology Applications in the Oncology area, and a range of positions in Eli Lilly, in a variety of therapeutic areas from oncology and gynecology to urology and endocrinology. She holds a BSc in Pharmacy from the Complutense University (Madrid, Spain), where she also completed graduate courses in Pharmacology, and a MBA from the IE Business School (Madrid, Spain).

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PRODUCT

***miColon* - Non-invasive screening test for Advanced Adenomas and Colorectal Cancer in blood**

MECHANISM OF ACTION

Through this product Amadix will develop an innovative diagnostic test (miColon) based on validated innovative biomarkers (miRNAs signature), to identify those patients who have advanced adenomas and CRC in a simple blood test. miRNAs regulate crucial cellular processes such as development, proliferation and apoptosis. Recently it has been shown that miRNAs can also be detected in serum and plasma, showing a bigger stability than other types of biological molecules. Plasma levels in individuals with CRC are different than in healthy individuals. Therefore, the detection of miRNAs as biomarkers in plasma represents a promising new strategy for the diagnosis of cancer.

TARGET INDICATIONS

Colorectal cancer (CRC).

CURRENT STATUS

- miColon is based on an exhaustive previous discovery phase, to assess a valuable miRNA expression profiling able to discriminate patients with Advanced Adenomas, CRC and healthy individuals.

- This discovery phase was followed by clinical validation through a prospective study including 273 patients from 2 different cohorts (Hospital Clinic in Barcelona and Hospital Donostia, San Sebastián). The objective was to show the clinical utility of a set of 6 miRNA for Advanced Adenomas and Colorectal Cancer Diagnosis.

INNOVATIVE ASPECTS

- The main objective of this product is to develop and launch non-invasive screening test for Advanced Adenomas and CRC which can be reached by high number of individuals and would be a cost-effectiveness strategy to decrease the rise in chemotherapy costs in CRC and aging of the population. The test is based on quantification of a profile of 6 micro RNAs using quantitative RT-PCR.
- Our preliminary data, already supported by in-depth Intellectual Property assessment, demonstrates that being a non-invasive blood test, this micro RNAs profile possesses a higher sensitivity to detect advanced adenomas and CRC compared with the test currently introduced in the market. The test would end in a marketable product that either though a kit or as a Laboratory Developed Test would become health care and commercial implementation for a very important clinical applicability. The envisioned screening test would be able to replace existing tests with lower sensitivity and less cost-effectiveness.
- *miColon* would not only contribute to reduce the mortality rate of these patients, offering a superior performance in terms of higher sensitivity and specificity. This product would lead also to a higher rate of participation and patient's compliance versus fecal tests in a cost-effective way for patients and healthcare providers. Experts conclude that probably the new techniques based on DNA/RNA detection will be the most cost-saving strategy in the next 2-3 years.

IPR

- This project is protected by patent applications filed in the main international markets all around the world (Brazil, Canada, China, India, Japan, Korea, Mexico, USA, Europe, Australia and Russia).
- The provisional patent application US61/550,148 was filed on October 21th 2011.
- An international patent application PCT/IB2012/003035 was filed on October 20th 2012, claiming the priority right of the above cited US patent application.
- The PCT application was duly published on June 27th, 2013, with publication number WO/2013/093635. This PCT application entered national phase in the above cited countries/regions on 21 April 2014.

PARTNERING OPPORTUNITIES

License agreement to develop and commercialize the product.

CIMA, Center for Applied Medical Research

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. These groups are interested in the functional analysis and drug activity of epigenetic agents, either demethylating or histone deacetylase inhibitors, both in vitro and in vivo models of hematological malignancies, and discovery of the corresponding therapeutic agents.

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 15 published patents.

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PRODUCT

New epigenetic agents: therapeutic approach in cancer

MECHANISM OF ACTION

Novel MoA has been identified and validated. First - in - class. Dual and reversible inhibitors against two epigenetic target classes. Hitting two different epigenetic target classes simultaneously leads to improvement in efficacy against certain cancer cell lines. Proprietary molecules show low nM efficacy (GI50<150 nM) against cell lines from different cancer types; for example, hematological (ALL or/and ABC - DLBCL) and solid tumors (bladder, hepatocelullar carcinoma, glioblastoma or/and melanoma).

TARGET INDICATIONS

Therapeutic Scope: epigenetics is an emerging area covering a broad range of mode of actions. However, only four drugs are currently approved and eleven agents are in early-stage trials.

Indication: cancer, a wide range of neoplastic diseases in where the epigenetics targets addressed are implied.

CURRENT STATUS

- Validation process. Chemical probes were discovered and utilized for in-vitro cellular Proof-of-Concept-Functional response. These proprietary molecules impact on the corresponding epigenetic marks (EC50) and inhibit proliferation of cancer cell lines (GI50)
- Lead compound, CM - 272, was tested in-vivo efficacy study: Mice inoculated with ALL CEMO - 1 cell line, hematologic cancer, were treated with CM - 272 (2.5 mg/Kg, i.v.) for 28 days. These mice showed a significant increase in survival probability compared to

untreated animals (untretated 70 days vs treated 100 days; p=0,0009).

INNOVATIVE ASPECTS

Novel proprietary compounds binding two epigenetic targets:

- more effective than reference epigenetic compounds vs different cancer cell lines.
- HDAC-independent.

Multifactorial optimization process, from initial proprietary hits to lead compounds:

- Hitting two independent targets at low nM range (IC50<100nM).
- In-vitro efficacy in cellular assays: epigenetic marks (EC50) and proliferation (GI50), both at low nM range.
- Optimal solubility, P450s profiling, hERG and plasma protein binding (unbound fraction).
- Cellular permeability. There is still room for improvement.
- Therapeutic window, efficacy vs toxicity, >1 log unit (to be improved).
- Acceptable pharmacokinetics.
- In-vivo proof-of-concept.

IPR

Patent application for novel proprietary compounds is 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.

IBIS, Instituto de Biomedicina de Sevilla

PROFILE

IBiS is a comprehensive and multidisciplinary biomedical research facility focused on translational research on the most prevalent diseases, with the aim to promote rapid transfer of knowledge to the clinical setting, improving the quality of clinical and epidemiological research. To favor a real translational research, the IBiS is located in the campus of the **Virgen del Rocio University Hospital (HUVR)**, one of the largest university hospitals in Spain, and it is functionally tied to it. The HUVR provides health and coverage to over half million people and acts as a hospital of reference in some of its specialized areas. The HUVR is one of the largest and most reputed health complexes in the Spanish National Health System, for its large volume of medical activity, its infrastructure and its technological facilities.

SPEAKER

Dr. Rocío García-Carbonero is a consultant in Medical Oncology as well as an associate Professor at Universidad de Sevilla and Co-Principal Investigator of the Molecular Oncology & Developmental Therapeutics Laboratory at IBiS, biomedical research facility focused on translational research on the most prevalent diseases. Member of the executive board of the Spanish Society of Medical Oncology (SEOM), European Society for Medical Oncology (ESMO) National representative and Member of the Scientific Advisory Comittee (SAC) for Oncology of the European Medicines Agency (EMA) (2008-present), among other Scientific Committees and research cooperative groups.

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PRODUCT

Selected miRNAs as biomarkers for Advanced Colorectal Cancer (CRC) Response to Chemotherapy

MECHANISM OF ACTION

Evidence has been provided that there is an overlapping set of microRNAs (miRNAs) whose levels are predictive of both, the clinical outcome of chemotherapy (oxaliplatin, fluoropyrimidine and irinotecan) and the response related to the tumour burden. 6 miRNAs showed variable profiles of expression in the different responses to chemotherapy of patients with advanced CRC through qRT-PCR analysis. These miRNAs exhibited significant differences in expression in responder vs non-responder patients. Furthermore, it was found that some of these miRNAs were differentially expressed in both progression-free survival and overall survival. It indicates these miRNAs are suitable predictors of response.

TARGET INDICATIONS

The current diversity of post-surgery treatments for metastatic CRC (chemotherapy and monoclonal antibodies) makes it necessary to have a method to predict the response of patients to treatments, and thereby facilitate the choice of the most appropriate therapy in each case. Our research group has developed a method to predict the efficiency of current chemotherapy treatments. The method and kit, based on identified biomarkers, enable the assignation of patients according to their expected response and encourages

the implementation of personalized therapies.

CURRENT STATUS

- These biomarkers have been validated in a study conducted in 61 patients who had undergone surgery for CRC: 39 patients were used to study the miRNA expression profile and 22 to test the results.
- Patients were divided into two groups according to the type of chemotherapy regimens they underwent: (i) based on oxaliplatin and fluoropyrimidine, and (ii) based on irinotecan and fluoropyrimidine

INNOVATIVE ASPECTS

- To date, somatic changes with a response to therapy in CRC, such as KRAS, BRAF, adenomatous polyposis coli (APC) and TP53 mutations have been described. The diagnostic systematization of the analysis of such mutations is another step towards personalized medicine.
- The present technology provides methods and tools for predicting survival of CRC patients, in particular overall survival or progression-free survival.
- Moreover, it allows foreseeing the response of patients to chemotherapy, supports the choice of the appropriate therapy and ultimately prolongs life and/or improves its quality.
- Since it is applied on classical chemotherapy, not in biological therapy such as molecular antibodies, our diagnostic tool can be applied in combination with Ras, Raf APC or p53 mutations to select the most adequate therapy for a given patient.

IPR

This technology is covered by an International Patent Application, filed on April 3rd, 2013, which claims priority from a Spanish patent application. Such patent application might give protection to the following embodiments:

- A method of predicting response of a human subject to chemotherapy, wherein the subject is suffering from advanced CRC, and wherein the method comprises using, as an indicator, expression levels of one or more of the identified miRNAs, wherein the result is indicative of response if the levels of the corresponding miRNAs are increased or decreased depending of the case.

- A kit comprising at least one oligonucleotide(s) capable of hybridizing with any one, two or more, and preferably all, of the identified miRNAs.

Entry into national phases is expected by October, 2014.

PARTNERING OPPORTUNITIES

The research group is looking for a partner interested in a license and/or a collaboration agreement to further develop and exploit this innovative technology. It is also open to establishing partnerships for co-development of the technology before reaching the market and highly interested in applying to different funding calls, mainly to Horizon 2020.

IBIS, Instituto de Biomedicina de Sevilla

PROFILE

The **IBiS** is a comprehensive and multidisciplinary biomedical research facility focused on translational research in the most prevalent diseases, with a view to promote the rapid transfer of knowledge to the clinical setting. The Clinical and Experimental Pharmacology Research Unit is broad-based, and includes basic research of molecular mechanisms underlying normal and abnormal physiology to define novel therapeutic targets; translational research; and clinical research to examine the behavior of novel therapeutics in humans. The members of the research group belong to the **University of Seville** and the **University Hospital of Valme**, one of the largest hospitals in Seville.

SPEAKER

Dr. Javier Miñano is the Principal Investigator of the Experimental & Clinical Pharmacology Unit of Nuestra Señora de Valme University Hospital (Seville, Spain) & Principal Investigator of the Pharmacology: Neurodegeneration and Neuroprotection research group affiliated to IBiS. He is also Professor of the Pharmacology, Paediatry and Radiology Department at the Universidad de Sevilla since 2001.

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PRODUCT

Antibodies for the Diagnosis, Prevention and Treatment of Diseases Involving Alteration of the Inflammatory Response

MECHANISM OF ACTION

N-PCT, unlike PCT, katacalcin or calcitonin, has demonstrated that it is a highly conserved peptide with a structural homology over 90% in all mammal species studied, which suggests an important role on a biological level.

It is observed that N-PCT is increased in the case of administration of bacterial endotoxin suggesting a role in the inflammatory response. Furthermore, it has been demonstrated that the central administration of N-PCT simulates the inflammatory responses that occur in sepsis (lethargy, fever, anorexia, weight reduction), indicating its importance in the inflammatory response via mechanisms dependent on the activation of POMC neurons and prostaglandin synthesis.

Therefore, it is a protein that has awoken great interest as secondary mediation in the systemic inflammatory response syndrome. Furthermore, it has been showed that N-PCT is overexpressed in the presence of Aβ42.

TARGET INDICATIONS

Diagnosis, treatment and prevention of diseases, which occur with alteration of the systemic inflammatory response or metabolic stress, such as sepsis, septic shock, postoperative complications, lung injury or neurodegenerative diseases, specifically Alzheimer's disease.

CURRENT STATUS

Promising results have been obtained in some in vivo studies performed in Wistar rats:

- Prophylactic or therapeutic neutralization of endogenous N-PCT with monoclonal or specific polyclonal antibodies, decreases the early production of proinflammatory cytokines (e.g., IL-1β and TNF-α), increases the late production of protective anti-inflammatory factors (e.g., IL-10 and ACTH) and reduces the mortality of rats after a lethal dose of endotoxin. None of the animals treated with anti-N-PCT showed signs of systemic infection.
- Peptides binding to the N-PCT or anti-N-PCT antibodies restore lung CALC-I mRNA and procalcitonin levels, reduce lung injury, decrease neutrophil infiltration, bacterial load and proinflammatory cytokines in lung tissues, while increasing the expression of antiinflammatory cytokines, inhibit NF-kB activation, and significantly improve survival in a murine model of lethal polymicrobial sepsis.
- Anti-N-PCT induces in vitro neuroprotection through the regulation of Aβ42 induced citotoxicity in SK-SY-5Y neuroblastoma cells as well as in vivo neuroprotection in domoic acid animal model, improves of abnormal behaviour in treated APP/PS1 mice and decreases pro-inflammatory cytokines release in APP/PS1 mice.

INNOVATIVE ASPECTS

The present antibodies show a high specificity to N-procalcitonin (N-PCT), a target of great importance due to its involvement in the inflammatory response of numerous diseases such as sepsis, metabolic stress, cardiogenic shock, post-operative complications, peritonitis, transplantation, autoimmune diseases, obesity, diabetes, bacterial meningitis, neoplasias or neurodegenerative diseases, which are obtained by using peptides derived from the fragmentation of procalcitonin (PCT), and which have the following advantages:

- Currently available diagnostic systems lack specificity due to cross-reactions with other molecules, such as PCT. Besides they may also require the use of two antibodies. For instance, N-PCT is the most abundant CALCA gene product in the plasma of septic patients and has the greatest specificity for differentiating patients with systemic inflammatory response syndrome (SIRS) from those with sepsis, when compared with other biomarkers such as IL-2, IL-6, IL-8, CRP and TNF-α.
- The methodological approach, based on the synthesis of antibodies and peptides derived from N-PCT, provides a reliable and very specific way to detect those diseases involving an alteration of the inflammatory response or metabolic stress.
- These antibodies may be also useful for the treatment of diseases such as sepsis, acute lung injury, acute respiratory distress syndrome or Alzheimer's disease. Currently, none of these pathologies have an effective treatment in the market.

IPR

- US patent application, filed in June, 2012, which may provide protection to the isolated nucleotides, peptides, antibodies obtained from said peptides and their use for the early diagnosis and treatment of diseases that develop alterations of the inflammatory or metabolic stress.
- International Patent Application, filed in November, 2013, claiming priority from a Spanish patent application, which might provide protection for the use of said peptides or antibodies in the treatment of lung injury, including sepsis-derived lung injury or septic shock (Second medical use).
- Spanish patent application filed in January, 2014, which may provide protection for the use of said peptides or antibodies in the prevention or treatment of a neurodegenerative disease, specifically Alzheimer's disease (Second medical use).

PARTNERING OPPORTUNITIES

The research group is looking for a partner interested in a license and/or a collaboration agreement to further develop and exploit this innovative product. We also offer this know how to improve the properties of research molecules in different therapeutic areas. It is also open to establishing partnerships for co-development of the technology before reaching the market and highly interested in applying to different funding calls, mainly to Horizon 2020.

In this moment, it would be necessary to design and produce a humanized antibody for subsequent proof of efficacy in human and perform the relevant regulatory toxicology studies with these antibodies before beginning the clinical phase. With regard to the diagnostic use of this product, the development of the kit per se as well as the scaled-up production of the antibodies should be carried out.

CÓMO CONCRETAR LOS ENCUENTROS BILATERALES

De acuerdo con la experiencia acumulada en los encuentros Farma-Biotech realizados hasta ahora, los momentos en los que se pueden producir conversaciones informales las compañías farmacéuticas y los investigadores proponentes de nuevos fármacos en desarrollo (los descansos entre ponencias y el cóctel al final de la jornada) a veces son insuficientes para establecer una conversación más detallada, especialmente cuando se ha despertado un interés específico hacia el fármaco en desarrollo.

Con ese motivo se van a facilitar, adicionalmente, encuentros bilaterales con aquellos ponentes con quienes se desee mantener una breve charla (en principio de hasta 15 minutos) programándola de antemano.

En la tabla siguiente complete por favor la información que se pide y remítanos sus respuestas por correo-e a amuranga@farmaindustria.es

Su nombre:

Su empresa:

Desea mantener una reunión personal con uno o varios ponente (SI/NO):

(Si manifiesta NO tener interés no es necesario seguir respondiendo este cuestionario)

El horario preferido:

Entre 11:30 y 12:00:

Entre 14:00 y 15:00:

Más tarde de las 15:00:

Desea reunirse con los investigadores de los siguientes fármacos:

(Anote por favor el nº de orden de cada ponencia que le interese según la agenda del acto)