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

XIX Encuentro de Cooperación Farma-Biotech

Jueves, 12 de noviembre de 2020

La jornada tiene por objeto establecer un punto de encuentro para 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 estas jornadas 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 jueves día 12 de noviembre en Madrid.

En Farmaindustria venimos siguiendo el **desarrollo de proyectos avanzados** de investigación en nuevos fármacos, tanto en centros de investigación como en pequeñas empresas biotecnológicas, y consideramos que los **ocho que han sido seleccionados** para su presentación en esta jornada han alcanzado un **grado de madurez suficiente**, lo que permite estudiar posibles **acuerdos de cooperación** con la industria farmacéutica en condiciones ventajosas técnico-económicas. Consecuentemente, pensamos que esta jornada reviste especial interés para las compañías farmacéuticas invitadas, incluyendo responsables de sus **unidades de desarrollo de negocio** e inversiones.

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 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.

Debido a las circunstancias especiales originadas por la pandemia del Covid19, esta jornada se organizará en formato online. Se **enviará con antelación la documentación de cada proyecto**, en inglés, incluido el PowerPoint de cada presentación, a todos los participantes inscritos, a fin de que puedan analizar mejor cada proyecto y formular dudas y preguntas a través del correo-e los días previos a la celebración de la jornada. Este mecanismo permitirá **una mayor flexibilidad en las presentaciones**, de modo que los ponentes no usarán su tiempo simplemente para repetir lo que ya está escrito en la documentación enviada, sino que podrán hacer más énfasis en los aspectos concretos de mayor interés de los representantes de las compañías farmacéuticas participantes. Por lo tanto, la presencia online durante toda la jornada suministrará más valor añadido que la mera lectura previa de la documentación.

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

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Agenda

El programa Farma-Biotech, patrocinado por FARMAINDUSTRIA*, pretende dar énfasis tanto a las presentaciones como a la interacción personal entre los asistentes, para lo cual todas las jornadas hasta el presente se han realizado de modo presencial. Sin embargo, las circunstancias actuales derivadas de la pandemia del covid19 aconsejan que esta próxima jornada tenga lugar, excepcionalmente, de modo telemático. Aunque este formato plantea ciertas barreras para la interacción interpersonal, haremos lo posible para obtener el máximo provecho del desarrollo de la jornada.*

Hora	Presentación	Estado de Desarrollo	Ponente
09:00	Se abre la sesión online para ajustes de conexión		
09:30 09:45	*Bienvenida y presentación de la jornada*		***Javier Urzay*** FARMAINDUSTRIA
09:45 10:00	*Indicaciones para la operativa de la jornada*		***Amelia Martín/Javier Villoslada*** FARMAINDUSTRIA
10:00 10:30	*Inhibidores de ship-1 para tratamiento profiláctico y/o prevención de enfermedades infecciosas*	Prueba de concepto	***Carlos del Fresno*** CNIC
10:30 11:00	*Vacuna oral para el tratamiento de alergia al cacahuete*	Entrando en Fase I	***Maite Agüeros*** INNOUP FARMA
11:00 11:30	*Nuevo miRNA para el diagnóstico de cardiomiopatías*	Pruebas en pacientes	***Pilar Martín*** CNIC
11:30 12:00	*Tratamiento de tumores iniciados y dependientes de la expresión de oncogenes de fusión*	Pruebas preclínicas	***Sandra Rodríguez*** CNIO
	DESCANSO		
12:15 12:45	*Tratamiento sintomático de la corea de Huntington y Disquinesia Tardía*	Completada Fase II	***María Zimina*** SOM BIOTECH
12:45 13:15	*Uso de la obestatina para la mejora de la reparación del nervio periférico*	Prueba de concepto	***Jesús Pérez Carmiña*** IDIS
13:15 13:45	*Cribado para cáncer colorrectal que mejora los estándares del sistema actual FIT*	Pruebas en pacientes	***Toni Castell*** IDIBAPS-CIBERER
13:45 14:15	*miRNAs en plasma para el diagnóstico precoz de la enfermedad de Alzheimer*	Pruebas en pacientes	***José Rodríguez Álvarez*** UAB
	FINAL. Desconexión de la sesión online		

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: **Formato telemático por videoconferencia. Se facilitará la conexión con suficiente antelación.**
Fecha: **Jueves día 12 de noviembre de 2020.**

La Plataforma Tecnológica Española Medicamentos Innovadores cuenta con apoyo financiero del Ministerio de Ciencia e Innovación a través de la Agencia Estatal de Investigación

PRESENTACIONES QUE TENDRÁN LUGAR EN ESTA JORNADA

CNIC

PROFILE

Within **CNIC** (*Spanish National Center for Cardiovascular Research*) the **Immunobiology lab,** led by Dr. David Sancho, focus on the study of myeloid cells, in particular macrophages and dendritic cells, trying to understand cellular, molecular and metabolic features related to the capacity of these cells to modulate immunity. These studies cover relevant pathologies such as metabolic disorders (obesity), cancer and infections of diverse etiology.

SPEAKER

After his degree in Biology, **Dr. Carlos del Fresno** performed his doctoral thesis in the Research Unit of La Paz Hospital, Madrid, where he obtained his PhD in Biochemistry, Biomedicine and Molecular Biology. Since 2013 he takes part of the Immunobiology laboratory at the Spanish National Center for Cardiovascular Research (CNIC). Altogether he can credit more than 12 years as biomedical researcher.

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PRODUCT

Ship-1 inhibitors for prophylactic treatment and/or prevention of infectious diseases

MECHANISM OF ACTION

SHIP-1 inhibitors are small molecules that specifically target the phosphatase SHIP-1. It is well described that the inhibition of this molecule boosts immunogenic processes. Our novelty is the application of SHIP-1 inhibitors in the context of the prophylaxis generated by the trained immunity. This trained mechanism prompts prophylactic immune responses against infections, that are boosted by the SHIP-1 inhibitors.

Trained immunity is a recently described process by which innate immune cells, such as macrophages, develop a state that allows them to perform improved inflammatory responses against infections. Of note, this state is long-lasting. A key molecular pathway to generate this prophylactic trained state is the PI3K/Akt, and the SHIP-1 phosphatase inhibits this pathway. Therefore, the underlying mechanism of our product is the inhibition of a trained immunity repressor. Thus, we have described that SHIP-1 inhibitors improve the prophylaxis generated by inducers of trained immunity, allowing better outcomes after infections.

TARGET INDICATIONS

The therapeutic area where SHIP-1 inhibitors can be applied in combination with the prophylactic effect of trained immunity is to fight infections. Due to the wide-ranging effect of this prophylaxis against virus, bacteria and fungi, there is a broad potential application of our product in the clinical practice. Importantly, this prophylactic effect could be extended to other non-infectious pathologies such as cancer.

CURRENT STATUS

- In 2018 we published the basis for the development of our product (Saz-Leal, et al., Cell Reports, 2018). There, we showed that both the genetic deletion of SHIP-1 or its chemical inhibition, improved trained immune responses triggered by ß-glucans.

- These ß-glucans are compounds of fungal origin that are well known for their capacity to induce trained immunity. We showed that their combination with SHIP-1 inhibitors, protected mice against lethal infections in a prophylactic manner.
- We confirmed that these SHIP-1 inhibitors also enhanced inflammatory responses in human blood cells, supporting their potential use in the clinical practice. Thus, those SHIP-1 inhibitors constitute the product we are presenting in here.

INNOVATIVE ASPECTS

- To the best of our knowledge, our product is the only chemical with the capacity of improving trained immune responses.
- As indicated before, trained immunity is a quite novel process that is still under intense investigation, in an attempt to understand it deeply. Based on our solid expertise in SHIP-1, immunity and infectious processes, we were the first research group to publish the capacity of improving trained immune responses.

IPR

The technology is currently protected under international application PCT/EP2019/064871 entitled 'Enhanced trained immunity in myeloid cells by SHIP-1 inhibition' filed on the 6th June 2019. The patent applicants are the CNIC, Syracuse University and the Research Foundation for the State University of New York.

PARTNERING OPPORTUNITIES

We are looking for a partner interested in a license of the patent application. We would like to explore diverse ways of cooperation with pharmaceutical partners ranging from extending our knowledge on the effect of SHIP-1 inhibitors in additional pathological settings where trained immunity could be important, to testing our product in clinical trials.

INNOUP FARMA

PROFILE

InnoUp Farma, with two candidates in clinical phase, is a company dedicated to nanotechnology innovation, that seeks to develop solutions for the administration of oral drugs. InnoUp has a technology platform, protected by international patents, based on the use of nanoparticles. One of our projects using this platform enables oral administration of anti-cancer drugs with low oral bioavailability. Another ongoing project based on our platform uses nanoparticles as an adjuvant in immunotherapy and vaccination.

SPEAKER

Dr. Maite Agüeros, is co-founder & CEO of InnoUp Farma. PhD in Pharmacy. Executive Master in Business Administration (E-MBA). Over 18 years of experience in nanomedicines research and 7 years of experience in the pharmaceutical industry. Co-inventor of 5 international patents.

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PRODUCT

INP20: oral vaccine for peanut allergy

MECHANISM OF ACTION

The main research on the field has focused on the use of peanut immunotherapies to prevent life-threatening reactions.

The vaccine proposed by InnoUp is based on increasing knowledge about the potential of immunological adjuvants to improve the limitations of the forms of immunotherapy being investigated. The use of this approach in INP20 allows to administrate lower doses of antigen leading to decreased side effects; the possibility of being administered every few weeks or months rather than daily exposures; and induce a long-lasting protective effect.

On the other hand, the progress in nanomedicine has allowed InnoUp to encapsulate peanut extract in protein nanoparticles acting as immunoadjuvants designed to improve mucosal allergen delivery, modify host immunity and enhance safety and efficacy of the vaccine.

TARGET INDICATIONS

Peanut immunotherapy.

CURRENT STATUS

- INP20 is manufactured by a validated and reproducible process at an industrial scale. It has already obtained the authorisation of the Spanish Agency of Medicines and Health Products to make clinical studies in patients allergic to peanuts, with a Phase I study in execution at the University of Navarra Clinic and Complejo Hospitalario de Navarra.
- INP20 is currently being tested in a double-blind phase I clinical trial to assess its safety and determine the therapeutic dose. To date, all the patients who have been administered INP20 have tolerated the treatment perfectly and have not had any adverse effects.
- On the other hand, it is very important to note that INP20 manufacturing process has been previously scaled from the laboratory to an industrial manufacturing plant with GMPs and a very reproducible process has been obtained, which results in a stable product over time.

- In addition, before starting the clinical phase, all relevant toxicity studies were carried out, obtaining very satisfactory results that indicate that INP20 is safe.

INNOVATIVE ASPECTS

- INP20 is a powder for extemporaneous reconstitution in water that is administered orally for the treatment of peanut allergy. It consists of protein nanoparticles that encapsulate peanut protein extract inside.
- To date, there is not long-term efficacious marketed treatment and no rigorous and adequately controlled trial has demonstrated the development of permanent tolerance to peanut.
- The solution developed by InnoUp is based on nanoparticles made from a food protein what guarantees safety, by a very simple nanoprecipitation method, that has been scaled up to a semi-industrial and continuous process.
- This innovative solution mechanism of action is to obtain tolerance based on the ability of nanoparticles to present the allergens and to obtain long term regulatory immune responses that can protect the allergic patient from dangerous allergic reactions.
- InnoUp's strategy, if the results of this study are satisfactory, would be to develop vaccines for other food allergens.

IPR

InnoUp has a portfolio of patents to protect its developments in the best possible way. They are already granted in many countries. The current expiration is in 2035, and an action plan has also been established to extend the protection.

The scope of protection of patents is very broad since it was not necessary to incorporate limitations in the main product claim and it was granted as it was originally drafted.

PARTNERING OPPORTUNITIES

Raise funds from strategic partner or venture capital to fund clinical development plan for INP20 and INP12. License-out development and commercialisation global rights.

CNIC

PROFILE

The ***Centro Nacional de Investigaciones Cardiovasculares*** **(CNIC)** is a leading international research center dedicated to understanding the basis of cardiovascular health and disease and to translating this knowledge into improved patient care. Martín´s laboratory work lines focuses on: i. Study of the molecular mechanisms of pathophysiology in myocarditis; ii. Search and validation of new Biomarkers for myocarditis and ischemic cardiomyopathies; and iii. study of new Biomarkers as predictive for the development of immune-related adverse events and fatal myocarditis during Immune Checkpoint Inhibitors cancer therapy

SPEAKER

Dr. Pilar Martín is the head of the Regulatory Molecules of Inflammatory Processes Group at the CNIC. A recognized immunologist, she has acquired wide experience in translational research involving micro-RNAs in cardiovascular diseases, including atherosclerosis, acute myocardial infarction and myocarditis. Her recent works have been published in Circulation, Nature Immunology or the New England Journal of Medicine, among others.

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PRODUCT

MyoBiomark: a novel circulating microRNA for the detection of acute myocarditis

MECHANISM OF ACTION

MyoBiomark is a novel circulating microRNA with a high diagnostic value (area under the curve `AUC´ of 0.927, 95% CI, 0.879-0.975; p<0.0001) for discriminating acute myocarditis from myocardial infarction patients.

We identified miR-721 in preclinical models as an exclusive marker of myocarditis, which was translated to its homologue novel miRNA in human plasma. The diagnostic ability to discriminate myocarditis was confirmed in plasma from four different patient cohorts (n= 151) with different comparators including myocardial infarction (n= 150), MINOCA (n= 20), autoimmune diseases (n= 152) and healthy volunteers (n= 80).

TARGET INDICATIONS

MyoBiomark provide a non-invasive unique tool for the clinically challenging diagnosis of myocarditis in plasma samples.

Due to the absence of discriminating tools at the Emergency Room, all patients presenting symptoms of myocardial infarction (MI) undergo triage for urgent coronary arteriography and antithrombotic therapy.

However, about 10-20% of all patients with MI criteria are misdiagnosed as they present myocardial infarction with non-occlusive coronary artery (MINOCA) disease, most of them finally diagnosed as myocarditis with weeks of delay, leading to inappropriate clinical management and prognostic implications.

CURRENT STATUS

- After experimental autoimmune myocarditis, Th17 cells boost myocardial inflammation and progression to dilated cardiomyopathy. We have identified mmu-miR-721, by smallRNA-

microarrays and qPCR, as specific for Th17 cells that is secreted to the plasma of mice with acute autoimmune and viral myocarditis, but not with acute myocardial infarction.

- We have cloned, sequenced and validated the human homologue in the chromosome 8 as hsa-miRNA-Chr8:96 (MyoBiomark) in four independent cohorts of myocarditis patients. The microRNA retained its diagnostic value when adjusted by age, gender, ejection fraction and troponins.
- The results of the discovery and development of **Myobiomark** are about to be published in the New England Journal of Medicine. Moreover, the CNIC leads a Prospective Registry for the validation of the new diagnostic marker in patients with clinical suspicion of myocarditis, from the clinical trials coordination unit (UCEC, CNIC).
- The Prospective Registry (Instituto de Salud Carlos III CEI authorization code: CEI PI 23_2020-v3) is being carried out in Hospital Virgen de la Arrixaca (Murcia), Hospital de la Princesa, HM Hospitales and Hospital Clínico San Carlos (Madrid), Hospital Clínico de Salamanca and Hospital General de Valencia.

INNOVATIVE ASPECTS

- Differential diagnosis of myocarditis is usually established after ruling-out coronary artery disease by coronary angiography (or CT scan) and confirming the presence of Lake-Louise criteria in cardiac magnetic resonance (CMR) imaging. Although CMR has improved the diagnosis of acute myocarditis, it also has limitations as the lack of accessibility in many hospitals and the ambulatory setting, pregnant women, and the sensitivity to detect oedema and vascular permeability decreases over time.
- Endomyocardial biopsy remains the gold standard diagnosis for myocarditis, and would be indicated in patients with clinical suspicion, but it is not routinely performed due to its risk as an invasive method and its limited sensitivity. **Myobiomark** has been validated in plasma from a biopsy-proven myocarditis cohort (AUC 0.999, 95% CI, 0.977-1.000; p= 0.0182).

IPR

The technology was originally protected under European Patent application EP15382596.3 entitled "Method for diagnosing cardiomyopathies" on December 12th, 2015. Currently, the USA application (US15/780,888) is still pending while the European Patent (EP3384043B1) was granted on January 23rd, 2020. The CNIC is the only applicant in the patent family.

PARTNERING OPPORTUNITIES

The CNIC is looking for an industrial partner interested in licensing the patent family and completing the necessary steps for the diagnostic kit to reach the market. If the company needs it, the CNIC is open to collaborate through a Research and Development Contract.

CNIO

PROFILE

cnio stop cancer

Within CNIO, the main interest of the *Molecular Cytogenetic and Gene Editing* (**MC&GE Unit**) is the study of how the fusion of two different genes—a class of oncogenes that provide immense diagnostic and therapeutic advantages because of their tumour-specific expression—and the amplification of (onco)genes can cause cancer. In addition, the group is developing new genome editing tools as therapeutic approaches to treat human cancer. Dr. Rodríguez-Perales is working on translational projects with an innovative edge trying to develop and valorised products that can tackle unmet medical needs.

SPEAKER

Dr Sandra Rodriguez is a geneticist with a robust knowledge of the fields of Molecular Cytogenetic and Gene Editing (MC&GE) in cancer. She is currently the Head of the MC&GE Core Unit at the CNIO. After her PhD training she focused on the discovery and study of new chromosomal rearrangements in cancer, she carried out postdoctoral work on modifications of the mouse genome to reproduce cancer chromosome translocations. In 2014, she developed the first genome engineering approach able to reproduce cancer translocations in human cells (Nature Commun, 2014). She has contributed to the field with more than 50 publications in international scientific journals and is an inventor on 2 patents.

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PRODUCT

Gene editing therapy for human cancers driven by fusion genes (FuGe) and oncogene amplifications

MECHANISM OF ACTION

Chromosome rearrangement plays a causal role in tumorigenesis mainly by contributing to the generation of novel fusion oncogenes or oncogene amplification. Fusion oncogenes (FOs) are chimeric genes resulting from in-frame fusions of the coding sequences of two genes involved in a chromosomal rearrangement and are common in many cancer types being powerful drivers of tumour development.

Because their expression is exclusive to cancer cells and their elimination induces cell apoptosis in FO-driven cancers, FOs are attractive therapeutic targets. Gene amplification is a relatively frequent event in cancer genomes and overexpression is a requisite for amplified genes to function as driver alterations. We have developed a gene editing strategy for the treatment of tumours driven by FOs and gene amplifications.

Based on the use of an innovative CRISPR-based gene editing approach, we have developed a feasible, efficient and non-patient-specific strategy based on gene editing that specifically targets FOs and gene amplifications only in cancer cells.

Through targeting two locus in both genes involved in these gene rearrangements we accomplished a robust disruption of the FO and amplified genes specifically in cancer cells while sparing wild-type gene expression in non-cancer cells.

TARGET INDICATIONS

Gene editing technique can potentially treat all tumours driven by fusion or amplified (onco)genes, including leukaemia, sarcoma and many epithelial cancers including prostate, colorectal, breast or melanoma. In particular, we are developing a strategy against high-risk neuroblastoma.

CURRENT STATUS

- Concept tests show how the treatment of tumors bearing these fusion genes with our new CRISPR-based approach leads to tumor cell death in culture and to a decrease in tumor size and mortality in mice xenografted with human sarcoma or leukemia cells (in press at Nat. Comm.).
- Although the approach has proven successful in vitro and in mouse models of XXX, the process remains complex, and several techniques need further development. The technical challenges identified so far include increasing the efficiency, specificity and safety of the system. To address this, different molecular carriers (or "vectors"), such as adeno and adeno-associated virus, nanocages and virus capsids, will be tested to deliver our CRISPR-based approach to cancer cells. These vectors will have to efficiently release our system to overcome any immune-related barrier and be produced in a feasible manner for clinical use.

INNOVATIVE ASPECTS

- The product is based on a novel engineered Gene Editing Cassette (CnioGEC) capable of removing the gene fusions, and thereby inducing cell death specifically in the tumour cells. The ability to precisely manipulating cancer cell genomes to correct or eliminate cancer-causing aberrations by highly efficient CRISPR/Cas9 genome editing has provided us new possibilities to develop FO- and oncogene amplification-targeted options to eliminate cancer cells.
- FOs and gene amplifications are attractive targets for directed therapy; however, therapeutic targeting of specific FOs and amplified genes has remained challenging. The reasons include both difficulties in specifically recognizing and targeting the resultant chimeric protein and the nature of FO products, which are intracellular, necessitating effective approaches for delivery of therapeutic molecules targeting the chimeric transcripts/proteins inside the cell.
- Likewise, the development of genome editing approaches offers new possibilities to directly and specifically targeting and modifying the genomic sequence of cancer cells.

IPR

There is a patent application with patent publication number WO2020/079243 A1 with priority number EP18382746.8 and international application number PCT/EP2019/078408. The priority date is 18-10-2018. The patent will enter in national phases in 2021 and the institution will likely enter examination in the major markets (USA, Europe with wide country coverage, Japan and Canada).

PARTNERING OPPORTUNITIES

Our current strategic approach with industry will be to establish a co-development collaboration so we can continue leveraging our know-how or the system and the indication and use in parallel the capabilities of industry to develop a delivery system for our CRISPR-based technology to start defining a clinical-grade product for further testing in both small animal system and in future clinical trials.

SOM BIOTECH

PROFILE

SOM Biotech is a clinical-stage biopharmaceutical company focused on the accelerated discovery of therapies through a proprietary artificial intelligence-based computational technology (SOMAI PRO). SOM Biotech has an extensive portfolio of programs in orphan diseases including orphan CNS. Two programs of the company achieved positive Phase 2a results, and two were out-licensed.

SPEAKER

Dr. Maria Zimina has a Ph.D. in Biotechnology and finished an MBA program. Before joining SOM Biotech, she was working as a researcher in the area of Biotechnology and Biomedicine, and as a Business Development Project Manager at a Research Institute of Biotechnology.

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PRODUCT

SOM3355: Chorea movements associated with Huntington's disease.

MECHANISM OF ACTION

SOM3355 is a Vesicular monoamine transporter (VMAT) 2, and Vesicular Monoamine Transporter 2 inhibitor. Its specific interaction with VMAT2 and inhibition of VMAT1 provides a balanced change in monoamine signalling, ameliorating the motor symptoms of Huntington's disease but preserving mental well-being.

TARGET INDICATIONS

SOM3355 is a drug for Chorea in Huntington's disease with positive results of Clinical Phase 2a PoC. It is the only safe VMAT2(-) not related to serious adverse events like depression, suicide, parkinsonism, or neuroleptic syndrome. Being a previously developed drug for hypertension, it has a lot of safety data from previous clinical trials and pharmacovigilance studies and is considered as a NCE in the US.

The drug is eligible for Orphan Drug Designation and has the potential opportunity for an extension of indication in Tardive dyskinesia. It has the potential peak sales of $1,3B (US and EU)

Possible additional indication: Tardive dyskinesia.

CURRENT STATUS

- SOM3355 obtained positive results of the Phase 2a PoC trial in patients with Chorea in Huntington's disease in a double-blind, randomized, placebo-controlled study with 32 patients from 4 hospitals in Spain.
- The primary endpoint was an improvement in any active drug period in the Total Maximal Chorea score (TMC) of at least 2 points compared with the placebo period. The results provided the confirmation of the expected effects of SOM3355 on the chorea symptoms related to VMAT2 inhibition.

- The drug also showed an excellent safety profile: no suicidality, no depression-induced, and no concern about QT prolongation. Currently, the company is planning the Clinical Phase 2b/3, Pre-IND with FDA is scheduled for the end of this year.

INNOVATIVE ASPECTS

- Existing VMAT-2 inhibitors increase depression and suicidality in patients with Huntington's disease, and cause parkinsonism, and neuroleptic syndrome. SOM3355 is a drug extensively developed for hypertension only available today in some Asian countries. Its excellent safety profile has been proved as by the previous clinical (more than 1300 patients) and pharmacovigilance studies, so by the clinical trial performed by SOM Biotech in Huntington's disease.
- In addition to having a better safety profile than competitors, SOM3355 is a racemic drug. One of its enantiomers can be developed as an add-on product at a higher dose improving the efficacy and safety profile.

IPR

SOM3355 has the Method of Use Patent (WO 2014/202646 A1). It was filed in 2014, and already granted in many countries (Australia, China, Russia, Japan, Singapur, Mexico, Israel and US)

PARTNERING OPPORTUNITIES

The main focus of the company is the out-licensing of the program or its co-development.

IDIS

PROFILE

INSTITUTO DE INVESTIGACIÓN SANITARIA
SANTIAGO DE COMPOSTELA

Wihtin the *Instituto de Investigación Sanitaria* (IDIS), the **Cellular Endocrinology Group** works in collaboration with Yolanda Pazos-Randulfe, leader from **Digestive Pathology Group**, also belonging to IDIS. Both Groups works to understand the molecular and cellular mechanisms that regulate myogenesis and determine nerve-muscle communication under pathological conditions related to muscular atrophy. Located at the IDIS within *Hospital Clínico Universitario de Santiago* at the CHUS, both Groups employ molecular and cellular approaches to determine the function and roles played by autocrine/paracrine regulatory factors in the regeneration functions.

SPEAKER

Dr. Jesus Perez-Camiña is PhD in Chemistry and is currently leader from the Group of Cellular Endocrinology within IDIS focused on the identification of therapies directed at myopathies related to the processes of skeletal muscle and peripheral nerve regeneration.

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PRODUCT

Use of obestatin peptide as a factor to improve peripheral nerve repair.

MECHANISM OF ACTION

Use of obestatin for the regeneration of peripheral nerve injuries, improves nerve and neuromuscular function recovery, by enhancing remyelinization and thus the regeneration of the damaged nerve, counteracting the severe loss of function and the atrophy of the innervated muscle.

Obestatin peptide directs proliferation and migration of Schwann cells that sustain axonal regrowth and later remyelinate regenerated axons. This action supports the preservation of skeletal muscle by the maintenance of neuromuscular synapses through the axonal regulation of calpain-calpastatin proteolytic system.

This encompasses the control of skeletal muscle homeostasis by regulation of the ubiquitin proteasome system and the autophagy machinery. Thus, obestatin peptide promotes nerve repair through integration of multiple molecular cues of neuron-Schwann cells crosstalk aimed to promote axon growth and guide axons back to their targets.

TARGET INDICATIONS

Peripheral nerve regeneration associated to traumatisms.

Peripheral nerve injury is a high-incidence clinical problem, significantly affects the patient's quality of life and causes an enormous socioeconomic burden. It still stands as one of the most challenging tasks in neurosurgery, as functional neuromuscular recovery is rarely satisfactory.

CURRENT STATUS

- Critical roles for the obestatin/GPR39 system in regulating the plasticity of SCs, as well as in preserving neuromuscular synapses during peripheral nerve regeneration, have been

identified. We found that obestatin directs different stepwise from the repair program of Schwann cells, including proliferation and migration, that guide regrowing axons and later remyelinate regenerated axons.

- Importantly, this action supports the preservation of skeletal muscle by the maintenance of neuromuscular synapses. This provides the necessary signals and spatial cues for the regulation of autophagy and ubiquitin-proteasome systems in skeletal muscle.
- These results serve as a therapeutic approach to skeletal muscle atrophy related to peripheral nerve injury. Thus, we demonstrated the feasibility of obestatin peptide as a factor to improve peripheral nerve repair in both in vitro and in vivo models corresponding to the POC to verify its practical potential.

INNOVATIVE ASPECTS

- Direct nerve repair with epineural end-to-end sutures is still the gold standard treatment for severe neurotmesis injuries but only in the cases where well-vascularized tension-free coaptation can be achieved. However, when peripheral nerve injury originates a significant gap between the nerve stumps, nerve grafts are required, with several associated disadvantages.
- To circumvent these facts, scaffolds were developed by tissue engineering to stimulate optimum clinical outcome. Nerve conduit tailoring involves reaching ideal wall pores, surface coating with extracellular matrix materials, and adding of growth factors or cell-based therapies. Also, the intraluminal cues are employed such as the filling with hydrogels, inner surface modification, topographical design, and the introduction of neurotrophic factors, antibiotics, anti-inflammatories and other pharmacological agents.
- Obestatin can be added to the group of neurotrophic factors/growth factors for its use as a pharmacological agent in third-generation nerve conduits, as well as for its use mixed with hydrogels for a perineural application.
- Obestatin will also improve therapies based on Schwann cells treatments for nerve regeneration.
- Comparing to other studied neurotrophic factors, obestatin might include many of the single positive aspects of any of them, namely enhanced axonal regeneration and remyelination, neuroprotection, rescue of functional neuromuscular junctions, which ameliorates the atrophy of the innervated muscle increasing its recovery and functionality.

IPR

European Patent Request EP18382680 : Obestatin For Use In The Treatment Of Peripheral Nerve Damages Or Injuries.

PARTNERING OPPORTUNITIES

We are fully committed to ensuring the translation of our research results into a manufacturing scale product. The optimization and development of the product needed could be done by the research team. We are seeking for a collaboration with the pharmaceutical industry to address the market access through a license agreement of the technology.

IDIBAPS-CIBER

PROFILE

The *Gastrointestinal and Pancreatic Oncology Research Team* belongs to the leading biomedical research center in Spain **IDIBAPS** and to the Centro de Investigación Biomédica en Red (**CIBER**). The goal of the group is to improve current preventive, diagnostic and therapeutic approaches through the understanding of molecular mechanisms involved in gastrointestinal and pancreatic neoplasms. Major contributions include evaluation of CRC screening strategies and identification of biomarkers for both hereditary and sporadic cancers.

SPEAKER

Dr. Antoni Castells' research activity is focused on colorectal cancer (CRC) prevention. He is co-coordinator of the CRC Screening Program of Barcelona and leads the Spanish COLONPREV project (N Engl J Med 2012; J Natl Cancer Inst 2013). He is a founding member of the Alliance for the Prevention of CRC, and is on the advisory board for CRC screening of the International Digestive Cancer Alliance and of the World Gastroenterology Organization Task Force on Digestive Oncology, among others.

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PRODUCT

miRFec: non-invasive method for colorectal cancer screening.

MECHANISM OF ACTION

miRFec is a new non-invasive diagnostic method based on the combination of three fecal biomarkers (two microRNAs and hemoglobin) that is able to identify individuals with CRC or its precursor lesion –advanced adenoma (AA)– with better performance than the current non-invasive method FIT (only based on fecal hemoglobin).

Indeed, it shows higher sensitivity for AA, thus representing an attractive approach for CRC prevention, and higher specificity that results in a reduction of false-positives from FIT, thus reducing the number of unnecessary colonoscopies. Therefore, miRFec could improve effectiveness and cost-effectiveness of population-based CRC screening programs

By analyzing the whole miRNome in 124 tissues from CRC or AA patients, we found 200 and 324 miRNAs significantly deregulated in CRC and AA tissues, respectively. More precisely, 7 and 5 of these miRNA were found to be detectable and also deregulated in feces. Indeed, MIR421 and MIR27a-3p were significantly upregulated in fecal samples from patients with CRC or AA (n=767).

miRFec is based on the combination of fecal levels of these miRNAs and hemoglobin, showing that is more accurate than fecal hemoglobin concentration alone. Analysis of these two miRNAs might be added to current fecal test –FIT– for a better detection of CRC or AA, resulting in a widely distributable and cost-effective tool for population-based CRC screening.

TARGET INDICATIONS

The miRFec has been designed for population-based, CRC screening in average-risk population (i.e. men and women older than 50 years-old). Other potential applications include diagnosis of CRC, screening of familial CRC, colonoscopy triage or prioritization on

individuals with a fecal immunochemical test (FIT) positive result, and surveillance of patients with colorectal polyps and cancer.

CURRENT STATUS

- The results obtained so far are published in two articles in high-impact scientific journals (Identification and Validation of microRNA Profiles in Fecal Samples for Detection of Colorectal Cancer. Duran-Sanchon S, et al. Gastroenterology 2020 Mar;158:947-957; Fecal MicroRNA-Based Algorithm Increases Effectiveness of Fecal Immunochemical Test-based Screening for Colorectal Cancer. Duran-Sanchon S, et al. Clin Gastroenterol Hepatol 2020:S1542-3565(20)30262-7).
- In summary, we studied **767 individuals** with a FIT positive result who underwent colonoscopy examination. In this cohort, miRFec was able to differentiate patients with CRC from those with normal colonoscopy or non-significant lesions with an AUC of 90% and is application would have avoided 34% of unnecessary colonoscopies.

INNOVATIVE ASPECTS

- CRC is the third most common incident cancer and the second leading cause of cancer-related death in the world. Evidences have shown that CRC screening is effective and cost-effective in average-risk population. Most extended worldwide CRC screening strategies relies on a two-step approach, starting with stool tests (i.e. FIT) and continuing with colonoscopies if an abnormal result is obtained.
- Current stool tests have a suboptimal sensitivity for AA (20-30%) and a high rate of false-positive results, which leads to a significant number of unnecessary colonoscopies. miRFec shows **better performance than FIT** to detect CRC and AA patients, and is being simpler than Cologuard®, a fecal DNA-based CRC screening test.

IPR

This technology was protected by a European Patent Application in 2019, which was extended to PCT on July 14th, 2020 (PCT/EP2020/069918). Those documents and further information still not published can be provided after the execution of an NDA.

PARTNERING OPPORTUNITIES

We are looking forward to establish a strong collaboration for the clinical validation of miRFec in a prospective, multicenter, comparative, parallel study, as well as to evaluate a potential partnership with a company with expertise in regulatory affairs (in vitro diagnostic/screening tests) for future commercialization of this technology. This collaboration may be organized through different cooperation models, including license agreement, research cooperation agreement, or creation of a new company.

UAB-INc-CiberNed

PROFILE

During the last years, the basic objective of our research team has been the study of the cellular and molecular mechanisms involved in the alteration of synaptic activity and learning and memory dysfunction associated to early stages of Alzheimer's disease as a way to identify novel therapeutic targets and biomarkers for earlier diagnosis and functional recovery.

SPEAKER

Prof. José Rodríguez Alvarez has a long-lasting experience as a principal investigator in the field of neurodegeneration and in the management of academic and research teams. With extensive international collaborations, Prof. Rodríguez-Alvarez has published more than 60 research papers in international journals and has been the Principal Investigator of 18 research projects. Currently he is Group Leader in the Institute of Neurosciences (UAB), CIBERNED and visiting Professor at the Dpt Neuroscience in the Albert Einstein College of Medicine (NY, USA).

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PRODUCT

Blood-based biomarker for early diagnosis of Alzheimer's disease.

MECHANISM OF ACTION

The project deals with the development of a molecular kit blood-based for a cost-effective diagnosis of AD at early stages. This molecular kit will be based on a molecular signature obtained by the combinational analysis of plasma levels of three synaptic transmission-associated miRNAs (miR-92a-3p, miR-181c-5p and miR-210-3p).

The detection of these miRNAs by standard techniques such as RT-qPCR and RT-ddPCR will allow a specific molecular diagnosis of AD at earlier, preclinical, stages.

The levels in plasma of these three miRNAs would be a reliable biomarker for early diagnosis of AD. These miRNAs have different synaptic targets. For example, miR-92a-3p targets NRX3 (encodes for neurexin-3a) and GRIA1 (encodes for GluA1), miR-181c-5p targets NPTXR (encodes for neuronal pentraxin-1 receptor) and miR-210-3p targets NPTX1 (encodes for neuronal pentraxin-1), NPTXR, and GRINA (NMDAR-associated protein 1). All these genes, related to synaptic structure and/or function, have been shown to be down-regulated in AD human brain or in experimental models of AD.

TARGET INDICATIONS

This molecular kit could be used as a diagnostic tool in routine clinical screening and would help:

a) to provide the basis improving the non-pharmacologic therapy including the modification of lifestyle risk factors associated with AD progression.

b) to select AD patients in early stages for future clinical trials and c) to facilitate an eventual early and effective therapeutic intervention.

Early diagnosis offers also several emotional and social benefits, opening, for instance, many training, education and support programs available to individuals and family members.

CURRENT STATUS

- In our laboratory we have examined plasma levels of specific miRNAs related to synaptic proteins regulation and we have discovered and up-regulation in the expression levels of miR-92a-3p,miR-181c-5p and miR-210-3p in AD subjects.
- Moreover, we found that the mild-cognitive impairment (MCI) patients that eventually developed AD had higher plasma levels of these miRNAs compared to patients that do not progress to AD-dementia. We also found that the expression levels of these miRNAs could be specifically used as a potential biomarker for AD, as no changes in their expression levels were observed in frontotemporal dementia patients (FTD).

INNOVATIVE ASPECTS

- Nowadays there is no solution in the market for early and cost-effective diagnosis of AD. Available biomarkers, such as amyloid-β or tau detection by positron emission tomography (PET) and in the cerebrospinal fluid (CSF) have a high economical cost and require invasive procedures, making them unsuitable for routine screening.
- Blood biomarkers would provide an **easy**, minimal invasive, and **cost-reduced** method that could present a significant breakthrough in routine screening for incipient AD.
- Some companies are developing blood biomarkers for early AD based on Aβ (Pre-diagnostics AS, Norway; Araclon Biotech-Griffols, Spain; AgenT, France) or mtDNA (ADmit therapeutics, Spain).Only one company is currently developing a system based on blood miRNAs (DiamiR, USA) for eAD but, in contrast with our miRNAs signature, it does not have the potential to differentiate between mild-cognitive impairment (MCI) subjects that will or will not develop AD.

IPR

Industrial Property Rights comprises a patent family protecting not only the miRNAs combinations which are present in our diagnostic method but also all the components needed for their measurement in plasma samples and the future molecular kit that will be used for the tests. Priority patent was filed in June 2018, EP18382427.5. In 2019 the international protection was extended through the following filing: WO2019238807A1

PARTNERING OPPORTUNITIES

The TTO is leading the commercialization activities of this project. We are looking for a private partner either to continue the development of this asset through a license or collaboration agreement.