

7 / Innovation

The Centro Nacional de Biotecnología (CNB-CSIC) has traditionally been involved in transferring the knowledge generated through its basic research to society. In the past two years, CNB scientists have applied for several patents, some of which have been licensed. In addition, the centre has a number of biological materials (such as antibodies and proteins) that, although not protected by patent, have been commercialised to companies through licensing agreements.

The CNB is one of the CSIC research institutes with its own Technology Transfer Department, which works in close collaboration with the CSIC Deputy Vice-presidency for Knowledge Transfer.

The Technology Transfer Department promotes the use of our research results for society's benefit, to potentiate the biotechnology sector as well as basic and clinical research.



TECHNOLOGY TRANSFER MANAGER

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PATENTS,
KNOW-HOW
AND
BIOLOGICAL
MATERIALS
LICENSED

DDA1 gene for mitigating negative ABA effects on growth during abiotic stress

Improved germination, seedling establishment, root growth and enhanced crop growth under stress conditions

Dr Vicente Rubio's research group found that PYL8, a receptor for the water-stress hormone ABA, is specifically targeted for ubiquitin-mediated degradation by DDA1 protein, which previously had no known function. The inventors showed that DDA1 binds to PYL8 *in vivo* and mediates its degradation through the proteasome, and that DDA1 overexpression in transgenic plants reduces plant sensitivity to ABA. The commonly observed ABA repression of seed germination, seedling establishment and root growth is much reduced in DDA1-overexpressing plants. These plants are also less sensitive to NaCl- or mannitol-mediated inhibition of seed germination compared to wild type. DDA1 is highly conserved in vascular plants, including all important crop species.

RESEARCH GROUP:

Dr Vicente Rubio

APPLICATION NUMBER AND PRIORITY DATE:

European patent application EP13382197.5, 29/05/2013

INTERNATIONAL PCT APPLICATION:

PCT/EP2014/061214, 29/05/2014 (published as WO/2014/191539)

PRESENT SITUATION:

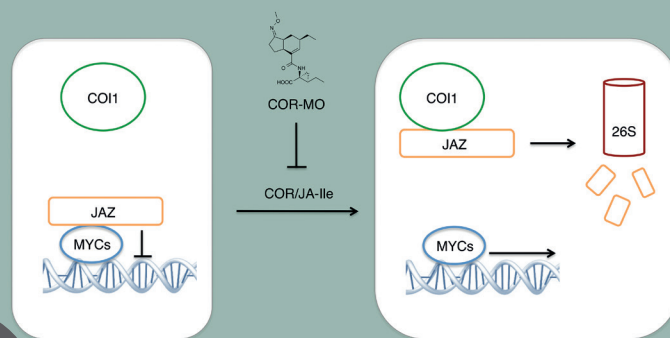
Exclusive license agreement to Plant Bioscience Limited (PBL) (11/01/2013) but sublicensing rights are available from PBL

REFERENCE:

Irigoyen *et al.* Targeted degradation of abscisic acid receptor PYL8 is mediated by ubiquitin ligase substrate adaptor DDA1 in Arabidopsis. *Plant Cell* 2014; 26:712-28



Plants that overexpress DDA1 gene are more resistant to abscisic acid-mediated abiotic stress such as drought.



Control of plant pathogens using novel coronatine derivatives

Modifications in coronatine confer potency and specificity for protecting plants against bacterial pathogens and enhance plant defences

Dr Roberto Solano's research group, with the company Lipidox, has designed, synthesised and characterised a novel, potent, highly specific antagonist of jasmonic acid perception. These coronatine derivative compounds competitively inhibit binding of JA-Ile to its co-receptor and thereby provide a tool to potentiate crop defences against biotrophic and hemi-biotrophic pathogens.

RESEARCH GROUP:

Dr Roberto Solano

APPLICATION NUMBER AND PRIORITY DATE:

European patent application EP13382362.5, 18/09/2013

INTERNATIONAL PCT APPLICATION:

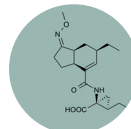
PCT/EP2014/069796, 17/09/2014. The International Patent Application has been published as WO2015/040061

PRESENT SITUATION:

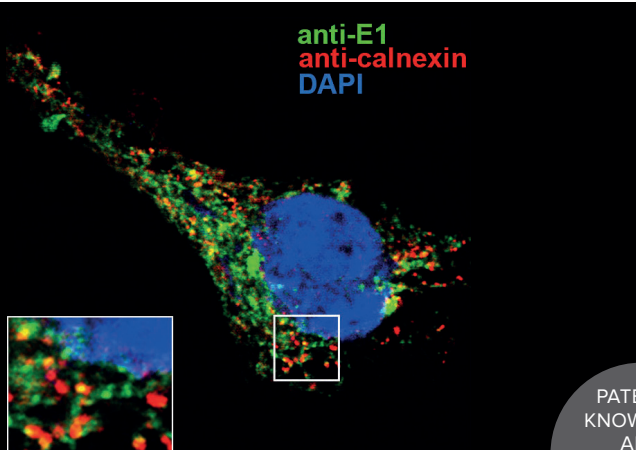
Exclusive license agreement to Plant Bioscience Limited (PBL) (31/05/2013) but sublicensing rights are available from PBL

REFERENCE:

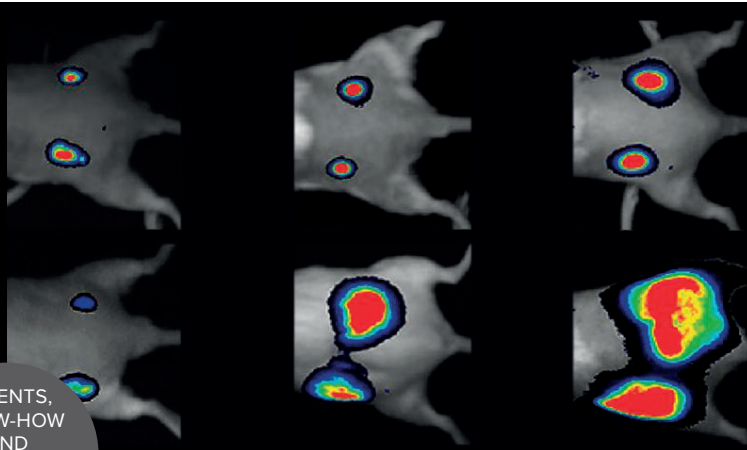
Monte *et al.* Rational design of a ligand-based antagonist of jasmonate perception. *Nat Chem Biol* 2014; 10:671-6



Coronatine derivative (COR-MO) efficiently antagonises JA-Ile perception by the COI1-JAZ co-receptor interaction and blocks jasmonate signaling. (+)-7-iso-jasmonoyl-L-isoleucine (JA-Ile) is a plant hormone involved in plant development and stress response that signals through a COI1-JAZ co-receptor complex.



anti-E1
anti-calnexin
DAPI



PATENTS,
KNOW-HOW
AND
BIOLOGICAL
MATERIALS
LICENSED

Hepatitis C virus (HCV) vaccine candidate based on recombinant modified Ankara virus (MVA) expressing the near full-length HCV genome

Dr Mariano Esteban's research group has developed a vaccine prototype for hepatitis C virus (HCV) based on an attenuated vaccinia vector (MVA) that expresses all HCV proteins except the C-terminal domain of NS5B protein. The main advantage of this MVA-HCV vector is that in a single product it is possible to amplify the *in vivo* immune response to all HCV antigens. In two murine models (BALB/c and humanised HLA-A2), vaccination with MVA-HCV vector mainly induces activation of CD8⁺ T lymphocytes, although CD4⁺ T cells are also produced. The antigenic response is produced to all HCV proteins, but unlike other viral vectors, MVA-HCV vaccination preferentially activates p7 and NS2 antigen responses. Moreover, MVA-HCV induces a broad response to HCV antigens that is polyfunctional (activates various cytokines) and durable.

RESEARCH GROUP:

Dr Mariano Esteban

APPLICATION NUMBER AND PRIORITY DATE:

P201330467, 02/04/2013

INTERNATIONAL PCT APPLICATION:

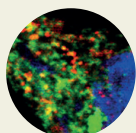
PCT/ES2014/070246, 31/03/2014. 09/10/2014 published as WO 2014

PRESENT SITUATION:

Exclusive license agreement to Plant Bioscience Limited (PBL) (6/05/2014) but sublicensing rights are available from PBL

REFERENCE:

Gómez *et al.* High, broad, polyfunctional, and durable T cell immune responses induced in mice by a novel hepatitis C virus (HCV) vaccine candidate (MVA-HCV) based on modified vaccinia virus Ankara expressing the nearly full-length HCV genome. *J Virol* 2013; 87:7282-300



Expression of hepatitis C (HCV) protein E1 by the vaccine candidate MVA-HCV in human HeLa cells as revealed by confocal microscopy. E1 protein (green), endoplasmic reticulum (red) and DNA (blue).

Human CCR9 monoclonal antibodies for diagnosis and therapy of cancer and other diseases

Dr Leonor Kremer's research group, in collaboration with scientists from the Centro de Investigaciones Biológicas (CIB-CSIC), developed monoclonal antibodies that bind specifically to the human CCR9 chemokine receptor. These antibodies inhibit CCR9⁺ tumour growth in an *in vivo* mouse xenograft model. The results show the potential of the 91R monoclonal antibody as a therapeutic agent for treatment of CCR9-expressing tumours.

RESEARCH GROUP:

Dr Leonor Kremer

APPLICATION NUMBER AND PRIORITY DATE:

EP13382469.8, 25/11/2013

INTERNATIONAL PCT APPLICATION:

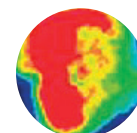
PCT/EP2014/075578, 25/11/ 2014

PRESENT SITUATION:

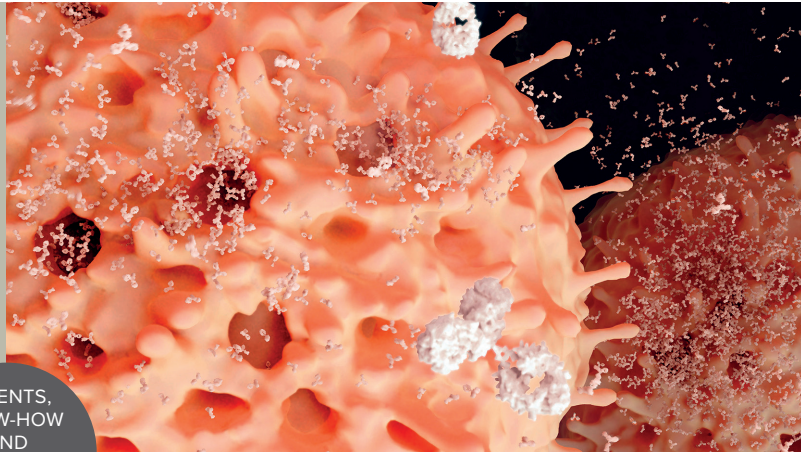
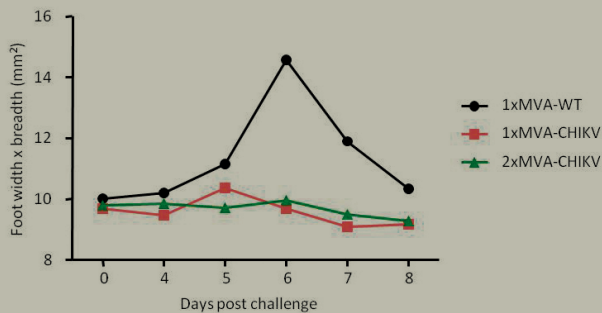
Exclusive license agreement to SunRock Biopharma SL, 30/09/2014

REFERENCE:

Chamorro *et al.* Antitumor effects of a monoclonal antibody to human CCR9 in leukemia cell xenografts. *mAb.* 2014; 6:1000-12



Bioluminescence image showing growth of tumours derived from human T cell acute lymphoblastic leukaemia cells implanted in immunodeficient mice, in response to treatment with 2an anti-human CCR9 mAb (top) or a control mAb (bottom)



PATENTS,
KNOW-HOW
AND
BIOLOGICAL
MATERIALS
LICENSED

Chikungunya vaccine candidate based on recombinant modified Ankara virus (MVA)

Dr Mariano Esteban's research group, in collaboration with Dr Peter Liljeström from the Karolinska Institute, has developed a vaccine candidate to chikungunya virus (CHIKV), an emerging pandemic that affects approximately 5 million people, based on an attenuated poxvirus vector expressing the CHIKV structural genes. Immunisation with MVA-CHIKV induces strong, broad, polyfunctional adaptive CHIKV-specific T cell immune responses in mice. Immunisation with MVA-CHIKV induces neutralising antibodies to CHIKV. MVA-CHIKV is highly immunogenic and effective, as a single dose protects mice against chikungunya infection. MVA-CHIKV triggers an innate immune response in human macrophages and dendritic cells, inducing type I IFN, proinflammatory cytokines, and chemokine expression.

RESEARCH GROUP:

Dr Mariano Esteban

APPLICATION NUMBER AND PRIORITY DATE:

PCT/EP2014/076310, 02/12/2014

PRESENT SITUATION:

Exclusive license agreement to Plant Bioscience Limited (PBL) (14/07/2014) but sublicensing rights are available from PBL

REFERENCE:

García-Arriaza *et al.* A novel poxvirus-based vaccine, MVA-CHIKV, is highly immunogenic and protects mice against chikungunya infection. *J Virol* 2014; 88:3527-47

Cell lines producing monoclonal antibodies against the CCR2 human receptor

RESEARCH GROUP:

Dr José Miguel Rodríguez Frade and Mario Mellado

PRESENT SITUATION:

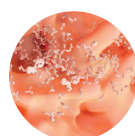
Exclusive license agreement to a company (06/05/2013)

REFERENCE:

Frade *et al.* Characterisation of the CCR2 chemokine receptor: functional CCR2 receptor expression in B cells. *J Immunol* 1997; 159:5576-5584



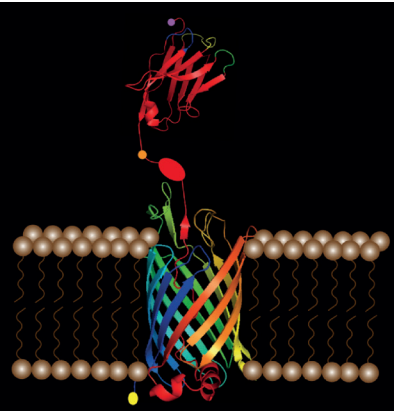
Immunisation with MVA-CHIKV protects mice against CHIKV infection. Foot swelling in animals immunised with one dose of MVA-WT or one or two doses of MVA-CHIKV and challenged with a total of 10⁶ PFU of CHIKV subcutaneously in both feet.



Monoclonal antibodies against CCR2



PATENTS,
KNOW-HOW
AND
BIOLOGICAL
MATERIALS
LICENSED



R5 monoclonal antibody to gliadin for gluten determination through a flow-through kit

RESEARCH GROUP:

Dr Enrique Méndez

PRESENT SITUATION:

Exclusive license agreement to two companies (Inmunología y Genética Aplicada SA and Institute for Environmental Health, Inc.)

REFERENCE:

Valdés I, García E, Llorente M, Méndez E. Simple sandwich ELISA based on the use of a single monoclonal antibody (RE) as the coating and means of detection. A quantitative cocktail gluten-extraction procedure for heat-processed foods was also tested. *Eur J Gastroenterol Hepatol* 2003; 5:465-74

Know-how and biological materials related to methods for recombinant antibody expression, selection and purification

Dr Luis Ángel Fernández's research group has know-how and biological material related to the expression of recombinant antibodies on the *Escherichia coli* cell surface (bacterial display), know-how related to the selection methods from an antibody library of recombinant antibodies able to bind specifically to an antigen (bacterial display, magnetic cell sorting (MACS), or fluorescent cell sorting (FACS)), as well as know-how and materials for the purification of recombinant antibodies from bacterial cells.

RESEARCH GROUP:

Dr Luis Ángel Fernández Herrero

PRESENT SITUATION:

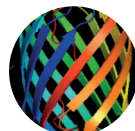
License agreement to Bacmine SL

REFERENCES:

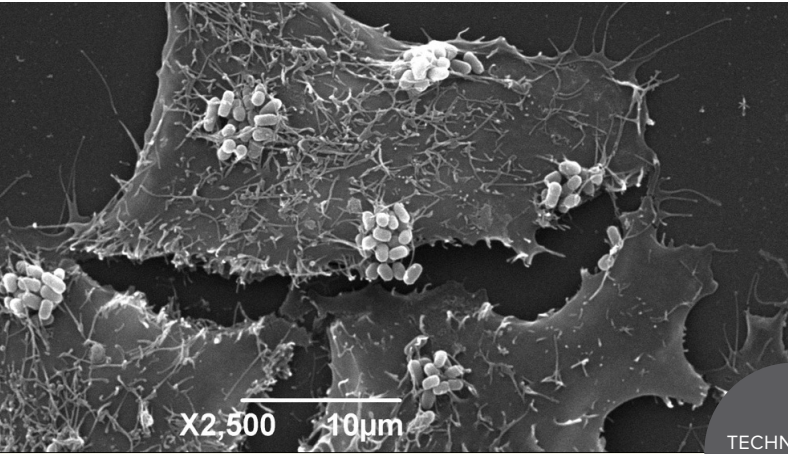
- Salema *et al.* Selection of single domain antibodies from immune libraries displayed on the surface of *E. coli* cells with two beta-domains of opposite topologies. *PLoS One* 2013; 8:e75126
- Salema & Fernández. High yield purification of nanobodies from the periplasm of *E. coli* as fusions with the maltose-binding protein. *Protein Expr Purif* 2013; 91:42-8



Gliadin is one of the gluten proteins found in wheat and other cereals.



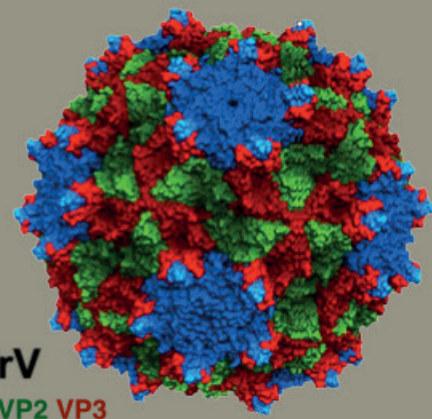
Surface display of a nanobody on the outer membrane of E. coli anchored to the intimin beta-barrel.



X2,500 10μm

TECHNOLOGY
OFFER

TrV
VP1 VP2 VP3



INNOVATION / 99

An engineered bacteria to deliver intracellular single-domain antibodies into human cells

Dr Luis Ángel Fernández's research group has developed non-invasive *Escherichia coli* bacteria bearing functional molecular syringes assembled by a Type III protein secretion system (T3SS). These bacteria can secrete and translocate single-domain antibody (sdAb) fragments with full capacity to bind to their cognate antigens to the cytoplasm of human cells. They have shown their function by formation of antigen-sdAb complexes in the cytoplasm of infected cells. The use of live bacteria has great potential for *in vivo* delivery of therapeutic proteins.

RESEARCH GROUP:

Dr Luis Angel Fernández Herrero

APPLICATION NUMBER AND PRIORITY DATE:

P200700644, 12/03/2007

INTERNATIONAL PCT APPLICATION:

PCT/ES08/070045

PRESENT SITUATION:

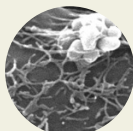
Spanish patent has been granted (12/03/2007). US Patent has been granted and published as US 8,623,349 B2 (Jan 7, 2014)

MAIN INNOVATIONS AND ADVANTAGES:

Non-invasive *E. coli* cells carrying a Type III protein secretion system remain extracellular and can inject specifically the desired single-domain antibodies. The levels of intracellular sdAb (10^5 - 10^6 molecules per cell) are appropriate to modulate the activity of regulatory and cell-signalling proteins. Injection of sdAb does not require bacterial invasion or the transfer of genetic material, differing from other approaches that need to transfer the protein-encoding gene by viral infection or transfection

REFERENCE:

Blanco Toribio A. *et al.* Direct injection of functional single-domain antibodies from *E. coli* into human cells. PLoS One. 2010:e15227



Scanning electron micrograph of human HeLa cells infected *in vitro* with attenuated EPEC bacteria carrying a functional T3SS that injects sdAb into the cytoplasm of the human cell.

Recombinant triatoma virus (TrV): a new platform for the development of chimaeric VLP vaccines and a potential insect biocide

Dr Francisco Rodríguez's research group, in collaboration with the Biophysics Foundation of Bizkaia and University of the Basque Country, has developed virus-like particles (VLP) derived from triatoma virus (TrV). These VLP can be used as adjuvant or epitope carrier for vaccine design. The present invention also relates to a process of obtaining an infectious TrV as a biological agent to control Chagas disease vectors.

RESEARCH GROUP:

Dr José Francisco Rodríguez

APPLICATION NUMBER AND PRIORITY DATE:

EP14382001.7, 03/01/2014

INTERNATIONAL PCT APPLICATION:

PCT/EP2015/050054, 05/01/2015

PRESENT SITUATION:

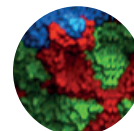
Companies interested in a patent license are being sought

MAIN INNOVATIONS AND ADVANTAGES:

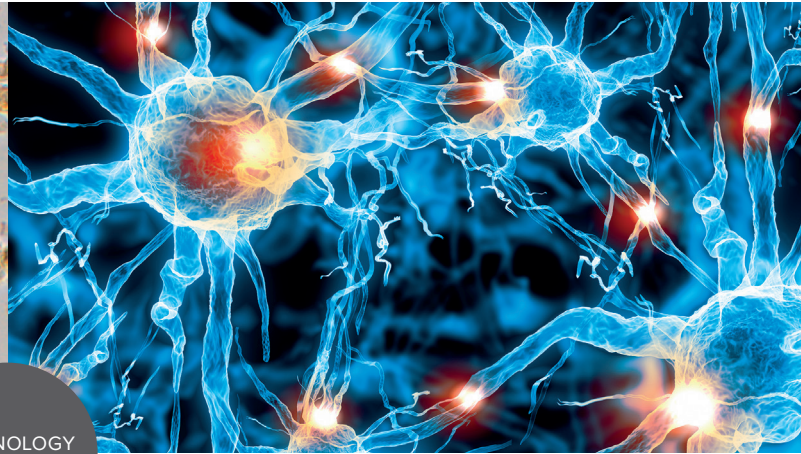
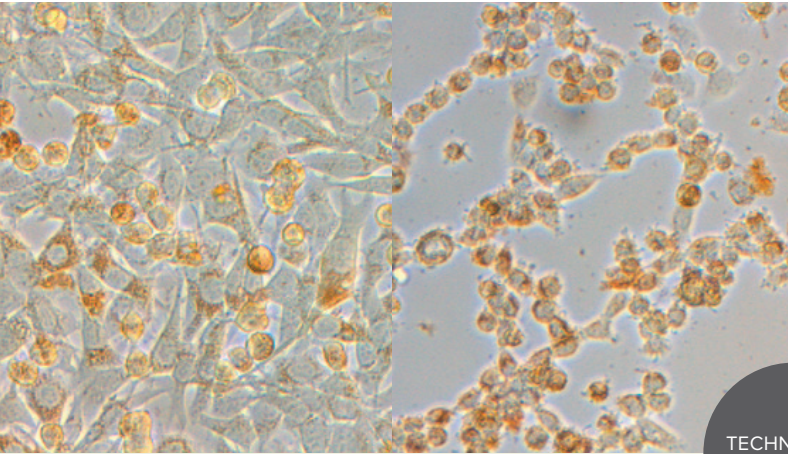
- The TrV-VLP allow epitope exposure on the internal or external surface of the VLP by insertion or substitution of amino acids, facilitating their recognition by the immune system and/or increasing their immunogenicity
- TrV capsids are stable over a very wide acidic pH range and after lyophilisation
- Production of TrV-VLPs bearing different epitopes through expression in insect cells by infection of recombinant baculoviruses
- Recombinant TrV could also be used as biological agent to control Chagas disease vectors

REFERENCE:

Sánchez-Eugenía R *et al.* *Triatoma virus* structural polyprotein expression, processing and assembly into virus-like particles. J Gen Virol. 2015 Jan;96(Pt 1):64-73.



Crystallographic structure of triatoma virus. The capsid structure of TrV is icosahedral of about 30 nm in diameter and is made of three structural proteins (ranging from 28 to 37 kDa) folded with a standard jelly-roll topology.



TECHNOLOGY
OFFER

100 / INNOVATION

Device to induce hyperthermia in cells through magnetic nanoparticles

Dr Domingo Barber's research group has developed an instrument that generates a controlled alternating magnetic field to induce hyperthermia in cells through magnetic nanoparticles.

RESEARCH GROUP:

Dr Domingo Barber

APPLICATION NUMBER AND PRIORITY DATE:

P201431531, 17/10/2014

INTERNATIONAL PCT APPLICATION:

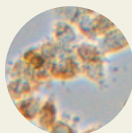
Pending

PRESENT SITUATION:

Companies interested in a patent license are being sought

MAIN INNOVATIONS AND ADVANTAGES:

- A unique "non-contact"-based method for precise measurement of the temperature reached by the nanoparticles inside cells (with precision up to 0.01°C)
- Frequency and amplitude of the magnetic field can be programmed automatically. It allows changes in parameters such as frequency, amplitude, pulse code modulation, or a combination of these, all digitally controlled in real time
- User-friendly software for data capture, representation and analysis to control magnetic field parameters and nanoparticle temperature
- Equipment is compact and user-friendly, and requires no parts exchange when working in a wide frequency/potency range, making it ideal for hyperthermia research
- Can be used in materials sciences to analyse the heating properties of materials and nanoparticles (SAR curves).



Microscopic images showing Panc02 murine pancreatic adenocarcinoma cells treated by magnetic nanoparticles (left) or by magnetic nanoparticles together with alternating magnetic field (right), generated by the patented device for 60 min., with frequency of 250 kHz (right). Pictures were taken 3 h post-treatment.

Novel compounds to modulate DREAM activity

Dr José Ramón Naranjo's research group, in collaboration with scientists from the Institute for Chemical Medicine (IQM-CSIC), have developed compounds with a nuclear structure derived from phenylacetamide, able to modulate the calcium neuronal sensor DREAM; they can be preventive or therapeutic compounds for treatment of diseases with altered DREAM expression.

RESEARCH GROUP:

Dr José Ramón Naranjo

APPLICATION NUMBER AND PRIORITY DATE:

P201431898, 22 Dec 2014

INTERNATIONAL PCT APPLICATION:

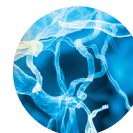
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PRESENT SITUATION:

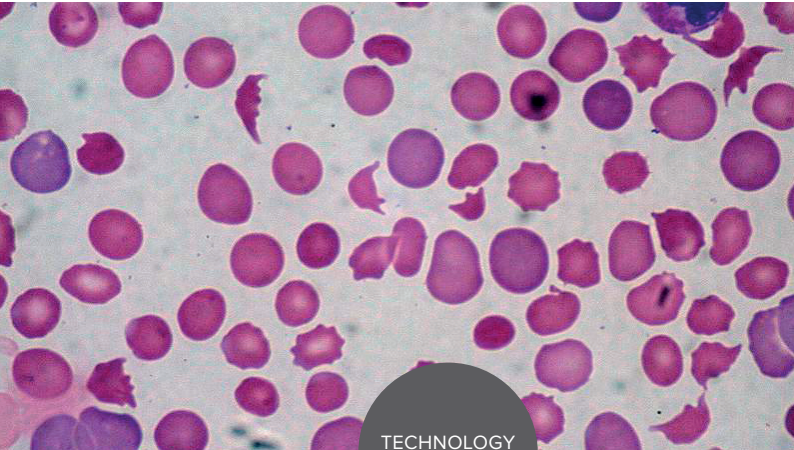
Companies interested in a patent license are being sought

MAIN INNOVATIONS AND ADVANTAGES:

The concept of DREAM as a therapeutic target is novel and the development of various compounds able to bind to and modify DREAM activity could open new avenues for the treatment of DREAM-related neurodegenerative disorders.



Targeting neurodegenerative diseases from Down syndrome to Alzheimer's disease by stimulating protective mechanisms.



TECHNOLOGY
OFFER

Nanosensor and nanobody to detect fibrinogen in blood

Abnormally high fibrinogen levels in plasma are associated with cardiovascular diseases, whereas abnormally low concentrations are linked to risk of bleeding. Dr Luis Ángel Fernández's research group developed a nanobody (single-domain antibody) to detect fibrinogen specifically in plasma. In collaboration with scientists from the Universidad Complutense of Madrid, they developed a fibrinogen-immunosensing device based on this nanobody and the use of magnetic beads. In this biosensor, free fibrinogen in solution and immobilised fibrinogen compete for binding to a fixed amount of specific biotinylated nanobody. Captured biotinylated nanobody is labelled with streptavidin-horseradish peroxidase. The magnetic beads are then captured by a magnet on the surface of screen-printed carbon electrodes, followed by amperometric detection at -0.20V by measuring the catalytic current generated by H₂O₂ addition, using hydroquinone as a redox mediator.

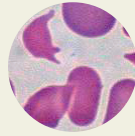
RESEARCH GROUP:
Luis Ángel Fernández Herrero

PRESENT SITUATION:
Companies interested in licensing the nanobody and/or the immunosensor are being sought

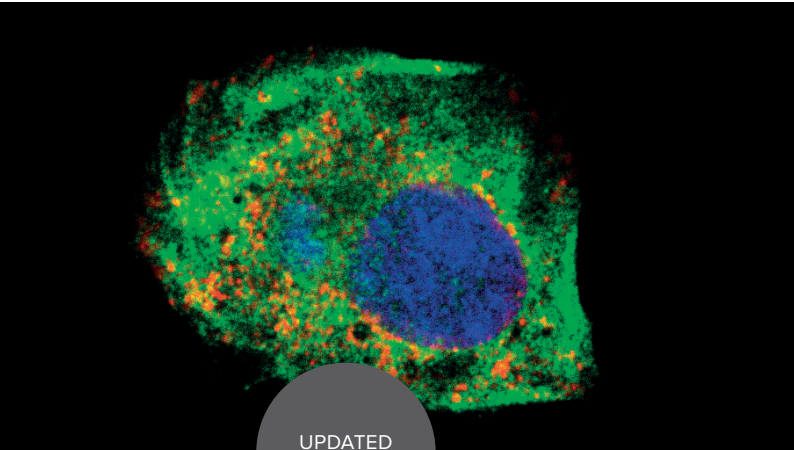
- MAIN INNOVATIONS AND ADVANTAGES:**
- The nanobody is produced in bacteria at lower cost than conventional monoclonal antibodies
 - The assay can be performed in diluted plasma samples, with a total analysis time of 90 min and a detection limit of 0.044 mg ml⁻¹ fibrinogen. Only 0.01 ml plasma is needed.
 - The nanobody could be used to develop other diagnostic materials such as ELISA kits

REFERENCE:
Campuzano *et al.* Disposable amperometric magnetosensors using nanobodies as biorecognition element. Determination of fibrinogen in plasma. Biosens Bioelectron 2014; 52:255-60

BIOLOGICAL
MATERIALS
AVAILABLE FOR
LICENSING



Detection of human fibrinogen concentration in plasma by an ELISA-based method.



UPDATED
INFORMATION

Modified immunisation vectors

This invention refers to two vaccine prototypes against HIV/AIDS, referred to as NYVAC-gp140(ZM96) and NYVAC-gag(ZM96)-pol-nef (CN54), based on the attenuated modified vaccinia virus Copenhagen strain with deletion of 18 viral genes (NYVAC). The viral vectors have shown good behaviour in animal models, triggering specific immune responses to HIV antigens in preclinical trials. Phase I clinical trials are complete and Phase II clinical trials are expected to begin in 2016.

RESEARCH GROUP:
Dr Mariano Esteban

APPLICATION NUMBER AND PRIORITY DATE:
61/174024, 30/04/2009. Co-titularity with Arizona State University (USA), Centre Hospitalier Universitaire Vaudois (Switzerland), Leiden University Medical Center (The Netherlands), Université de Montréal (Canada), Sanofi Pasteur Ltd (France)

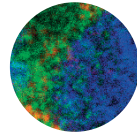
INTERNATIONAL PCT APPLICATION:
PCT/US10/032966

COUNTRIES SELECTED IN NATIONAL PHASE:
EU, US, CA

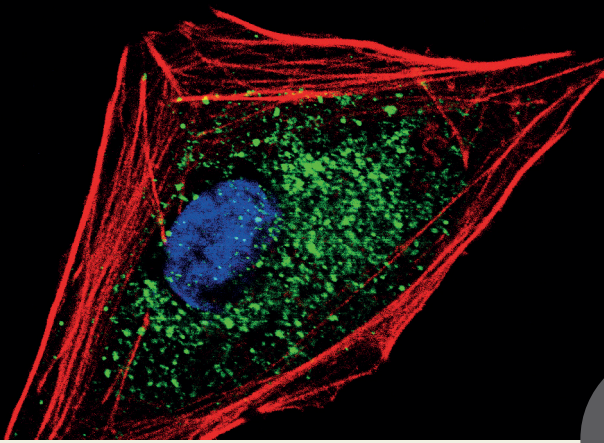
PRESENT SITUATION:
Patent examination in each country. Patent compromised to Sanofi Pasteur Ltd.

REFERENCE:
Perdiguerro *et al.* Virological and immunological characterisation of novel NYVAC-based HIV/AIDS vaccine candidates expressing clade C trimeric soluble gp140(ZM96) and Gag(ZM96)-Pol-Nef(CN54) as virus-like particles. J Virol 2015; 89:970-88

PATENTS
LICENSED
BEFORE
2013



Confocal microscopy showing production of VLPs from HIV-1 expressed by the HIV/AIDS vaccine candidate NYVAC-Gag-Pol-Nef. In green are the cytoplasmic VLPs and fusion protein, in red the endoplasmic reticulum and in blue, the nuclei.



UPDATED
INFORMATION

Recombinant vectors based on Ankara modified virus (MVA) as preventive and therapeutic vaccines against HIV

The research group lead by Dr Mariano Esteban has developed a prototype vaccine against HIV based on modified Ankara virus (MVA-B) expressing four antigens (Env, Gag, Pol, Nef) of HIV-1, clades B and C. During a phase I clinical trial in 30 healthy individuals, 90% of the volunteers developed an immune response against the virus that was maintained after 1 year. A phase I clinical trial with HIV-infected volunteers showed an increase in Gag-specific T cell responses, but it had no major impact on the latent reservoir or the rebound of plasma viral load after interruption of HIV therapy. MVA-C is in phase I clinical trials by the UK-HVC group.

RESEARCH GROUP:

Mariano Esteban Rodríguez

APPLICATION NUMBER AND PRIORITY DATE:

P200501841, 27/07/2005 and P200600762 (24.03.2006)

INTERNATIONAL PCT APPLICATION:

PCT/ES06/070114

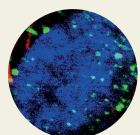
COUNTRIES SELECTED IN NATIONAL PHASE:

EU, US

PRESENT SITUATION: Exclusive license agreement to Laboratorios del Dr. Esteve S.A. y la Fundación Irsi-CAIXA. (30/06/2012). EU Patent has been granted (EP1921146 B1) and validated in 22 countries. US Patent has been granted (US 8,871,219 B2, 28/10/2014).

REFERENCE:

- García F, *et al.* Safety and immunogenicity of a modified pox vector-based HIV/AIDS vaccine candidate expressing Env, Gag, Pol and Nef proteins of HIV-1 subtype B (MVA-B) in healthy HIV-1-uninfected volunteers: A phase I clinical trial (RISVAC02). *Vaccine* 2011; 29:8309-16.
- Gómez CE *et al.* The HIV/AIDS vaccine candidate MVA-B administered as a single immunogen in humans triggers robust, polyfunctional, and selective effector memory T cell responses to HIV-1 antigens. *J Virol* 2011; 85:11468-78.
- Mothe B *et al.* Safety and immunogenicity of a modified vaccinia Ankara-based HIV-1 vaccine (MVA-B) in HIV-1-infected patients alone or in combination with a drug to reactivate latent HIV-1. *J Antimicrob Chemother* 2015; 70:1833-42.



Confocal microscopy showing expression of the cytoplasmic HIV-1 Env protein (in green) induced by the candidate HIV/AIDS vaccine vector MVA-B. This vaccine has shown a good immunogenicity profile against HIV antigens in phase I clinical trials. In red, phalloidin staining of the cytoskeleton. The cell nucleus appears in blue.

Genes regulating plant branching, promoters, genetic constructs containing same and uses thereof

The research group led by Dr Pilar Cubas has discovered the BRC1-like genes that control shoot branching in potato and tomato.

RESEARCH GROUP:

Dr Pilar Cubas Domínguez

APPLICATION NUMBER AND PRIORITY DATE:

P200900088, 13/01/2009 and its divisional P201030915 DIV, 14/06/2010

INTERNATIONAL PCT APPLICATION:

PCT/ES09/070538, PCT/ES2010/070538

COUNTRIES SELECTED IN NATIONAL PHASE:

EU, US, CN. China patent granted (No 200880158052)

PRESENT SITUATION:

Exclusive license to NINSAR (18/05/2011). The contract with NINSAR finalised in 2014 and a new licensing agreement was signed with Semillas Fitó SAU and BHN Seed.

REFERENCE:

Martin-Trillo M *et al.* Role of tomato BRANCHED1-like genes in the control of shoot branching. *Plant J.* 2011; 67:701-14



The SIBRC1b gene from *Solanum lycopersicum* suppresses the formation of basal branches in tomato. Centre: Control plants. Left and right: Tomato plants with the SIBRC1b gene partially inactivated.

(a)



UPDATED
INFORMATION

SpBRANCHED1a of *Solanum pennellii* and tomato plants with reduced branching comprising this heterologous SpBRANCHED1a gene

The research group led by Dr Pilar Cubas discovered that the *Solanum pennellii* BRANCHED1-like gene causes reduced basal shoot branching when introgressed into *S. lycopersicum*.

RESEARCH GROUP:

Dr Pilar Cubas Domínguez

APPLICATION NUMBER AND PRIORITY DATE:

EP11166057.7, 13/05/2011

INTERNATIONAL PCT APPLICATION:

PCT/EP2012/058892

COUNTRIES SELECTED IN NATIONAL PHASE:

EU

PRESENT SITUATION:

Exclusive license to NINSAR (22/02/2012). The contract with NINSAR finalised in 2014 and a new licensing agreement was signed with Semillas Fitó SAU and BHN Seed.

REFERENCE:

Martin-Trillo M *et al.* Role of tomato BRANCHED1-like genes in the control of shoot branching. *Plant J.* 2011; 67:701-14

PATENTS
LICENSED
BEFORE
2013

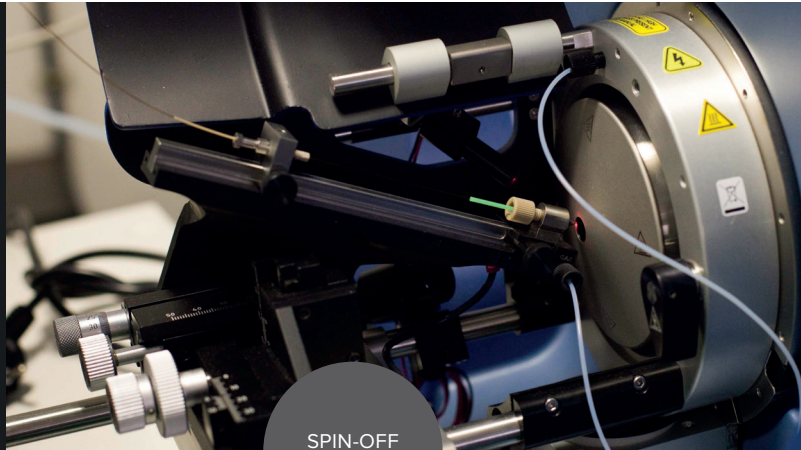


The SpBRC1a gene from *S. pennellii* suppresses the elongation of branches in tomato. Left: Control plant. The red arrow indicates an incipient branch.

(b)



SPIN-OFF
COMPANIES



INNOVATION / 103

Proteobotics

Contact: Antonio Ramos. proteobotics@gmail.com

Proteobotics was created in 2013 by Antonio Ramos, a scientist in Dr Juan Pablo Albar's group. It specialises in identifying peptides and proteins using mass spectrometry data. The company received a 2014 Innovation Award from the Fundación Alberto Elzaburu.

In large-scale proteomics projects, millions of peptide ion collision spectra (MS/MS) are generated that must be matched to theoretical spectrum models inferred from known peptide sequences to identify proteins. A number of database search engines using different scoring systems have been and are being developed to this end. CNB scientists have developed a generalised meta-search process that, by integrating partial evidence from any number and type of such database search engines into a single consensus reconstruction, increases remarkably the number of proteins identified. The process can be extended by integration of additional sources of information besides primary search engine results.

MAIN INNOVATIONS AND ADVANTAGES:

- It is extremely flexible and greatly increases the number of proteins identified
- Great accuracy in terms of error rate control

CNB-CSIC COLLABORATION:

Proteobotics signed an option to license a CSIC patent for a method to identify peptides and proteins from mass spectrometry data (P200930402, 01/07/2009). The patent was granted in Europe and is under examination in the US. The company has also signed a collaboration agreement with the CNB-CSIC.



Method for identifying peptides and proteins from mass spectrometry data. High throughput, proteome-wide identification of proteins using tandem mass spectrometry requires computational methods to interpret and filter large sets of peptide ion collision data.