07

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 already 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 Vicepresidencia Adjunta de Transferencia de Conocimiento (VATC).

The Technology Transfer Department promotes the exploitation of research results obtained at the CNB for society's benefit and to potentiate the biotechnology sector and basic research.

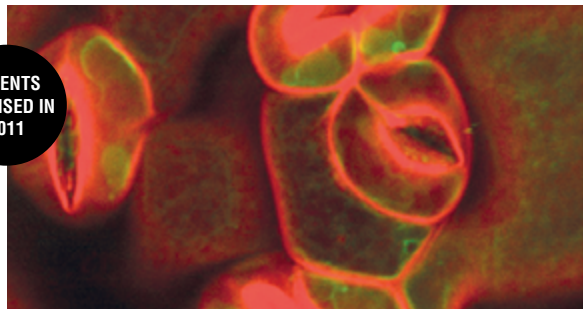
TECHNOLOGY TRANSFER MANAGER

Ana Sanz Herrero

Ana did her PhD research at the CNB, studying plant-pathogen interactions at Dr. Carmen Castresana's group. She has nine years of working experience as a research scientist in biotechnology companies in Spain and in the US, specialised in development of innovative molecular and cell biology products, and two years experience as an independent consultant for biotech companies. Ana Sanz has managed the CNB Technology Transfer Department since September 2012.

Patents and biological materials licensed

PATENTS LICENSED IN 2011



PATENTS LICENSED IN 2011

Procedure to modify plant architecture and improve the crops yield through the control of entering into cell differentiation

Dr Enrique Rojo and colleagues at the CSIC-CNB discovered and characterised the IYO and ART (or AtRTR1) genes in *Arabidopsis*, which they have demonstrated to cooperate as positive regulators of transcriptional elongation, sufficient to initiate the process of cell differentiation. IYO and ART overexpression induce early cell differentiation. The decreased rates of cell proliferation in loss-of-function IYO and ART mutants indicate that these genes are also important in undifferentiated cells to promote cell division. The inventors have transferred *Arabidopsis* IYO to transgenic tomato and shown that plant architecture can be modified, with development of increased lateral branches. They are also characterising an interesting double-embryo phenotype that could have practical applications for increasing crop plant density or affecting overall seed composition (*e.g.*, oil content).

RESEARCH GROUP:
Enrique Rojo de la Viesca

APPLICATION NUMBER AND PRIORITY DATE:
P201130812, 19/05/2011

INTERNATIONAL PCT APPLICATION:
PCT/EP12/059312, PCT/GB12/051146

COUNTRIES SELECTED IN NATIONAL PHASE:
Pending

PRESENT SITUATION:
Exclusive licence to a company (10/11/2011). The application for mammalian cells, PCT/GB12/051146, is in co-titularity with the CNIO (Manuel Serrano's Group) and is available for licensing.

Epidermal development in wild type (Wt) and iyo-1 cotyledons. Protoderm differentiation is delayed in iyo-1 plants and as a result, stomatal patterning is disrupted. The plants express a tonoplast GFP marker (green signal) and are stained with propidium iodide (red signal).

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

The research group lead by Pilar Cubas at CNB-CSIC has discovered the BRC1-like genes which control shoot branching in potato and tomato.

RESEARCH GROUP:
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

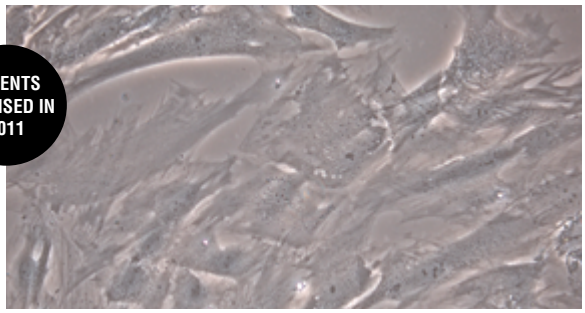
COUNTRIES SELECTED IN NATIONAL PHASE:
EU, US, CN, IN

PRESENT SITUATION:
Exclusive licence to a company (18/05/2011). The licensing agreement also includes a R&D Contract between the company and the same research group

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

Patents and biological materials licensed

PATENTS LICENSED IN 2011



PATENTS LICENSED IN 2011

Stem cell culture media and methods

The group led by Lourdes Planelles at the CNB-CSIC has participated in the discovery of new culture media and methods for pluripotent stem cells, which provide significant advantages over known culture media and methods. The invention also provides related culture medium supplements, compositions and uses. There is great interest in culture media and methods for expanding populations of pluripotent stem cells, particularly adipose-derived mesenchymal stem cells (ASC cells). Clinical applications of pluripotent stem cells require reproducible cell culture methods to provide adequate numbers of cells of suitable quality. Although numerous different culture media and methods have been tested for pluripotent stem cells, a great need remains for further improvements in ASC culture media and methods.

An advantage of the invention is that it can be used to culture pluripotent stem cells at a high proliferation rate, whilst maintaining their undifferentiated phenotype.

RESEARCH GROUP:
Lourdes Planelles

APPLICATION NUMBER AND PRIORITY DATE:
EP10382244, 10/08/2011 (Europe Patent as Priority Patent). Co-titularity with Cellerix (now TiGenix NV)

INTERNATIONAL PCT APPLICATION:
PCT/EP11/065540

COUNTRIES SELECTED IN NATIONAL PHASE:
Pending

PRESENT SITUATION:
Exclusive licence agreement to a company (10/08/2011) R&D Contract between the company and the same research group

Method for extracting gluten contained in heat-processed and non-heat-processed foodstuffs, compatible with an enzyme-linked immunosorbent assay, composition and kits comprising said composition

The method can be used to extract quantitatively the gluten contained in a heat-processed or non-heat-processed food sample before quantification of the gluten by ELISA. Said method is suitable for food analyses, in particular, for foodstuffs intended for coeliac sufferers.

RESEARCH GROUP:
Enrique Méndez Corman

APPLICATION NUMBER AND PRIORITY DATE:
P200101098, 14/05/2001

INTERNATIONAL PCT APPLICATION:
PCT/ES02/00208

COUNTRIES SELECTED IN NATIONAL PHASE:
EU, US, CA

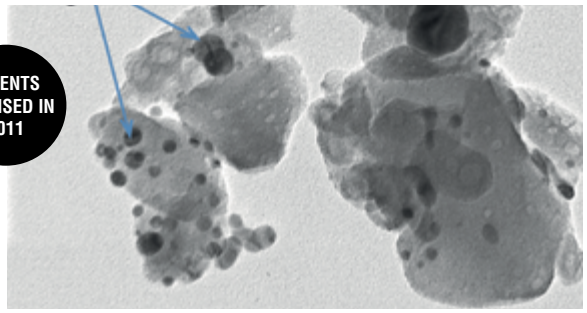
PRESENT SITUATION:
Exclusive licence to a company (28/08/2011)

Adipose-derived mesenchymal stem cells

Coeliac disease is caused by a reaction to gliadin, a prolamin (gluten protein) found in wheat, and similar proteins found in the crops of the tribe Triticeae (which includes other common grains such as barley and rye).

PATENTS LICENSED IN 2011

PATENTS LICENSED IN 2011



Nanostructure calcium silver phosphate composite powder, method for obtaining same, and bactericidal and fungicidal uses thereof

Scientists at the CNB-CSIC participated in the discovery of nanostructured powders formed by a calcium phosphate, having a particle size, and silver nanoparticles adhered to its surface that can be used as universal disinfectants. One advantage provided by the present nanocomposite powders is that nanoparticle agglomeration is avoided because the nanoparticles can be adhered to the substrate surface. A second advantage is its bactericidal and fungicidal efficiency. A third advantage is its low toxicity (far below that of commercial products, very far below toxic levels). Applications include the surgical implants sector, public facilities (toilets and hospitals, transport, etc.), air conditioning equipment, food, dentistry, paints, clothes and packaging (food, domestic, pharmaceutical, medical devices, etc.).

RESEARCH GROUP:
Francisco Malpartida Romero
This scientist is now retired

APPLICATION NUMBER AND PRIORITY DATE:
P200803695, 24-12-2008. Co-titularity with Instituto de Ciencias Materiales (ICMM-CSIC), Nanomaterials and Nanotechnology Research Center (CINN-CSIC), Instituto de Cerámica y Vídrio (ICV-CSIC)

INTERNATIONAL PCT APPLICATION:
PCT/ES09/070628

COUNTRIES SELECTED IN NATIONAL PHASE:
US, CN, EU, JP

PRESENT SITUATION
Licensed to a company, 02/12/2011. Spanish patent has been granted

Nanostructure calcium silver phosphate composite powder

Powder of vitreous composition having biocidal activity

Scientists at CNB have developed a magnetic nanoparticle which can be injected intravenously and targeted to a region of interest using an external magnetic field. It allows obtaining the optimal concentration of an active ingredient in a tumour region, with a reduction of the side effects.

RESEARCH GROUP:
Francisco Malpartida Romero
This scientist is now retired

APPLICATION NUMBER AND PRIORITY DATE:
P200931137, 09/12/2009. Co-titularity with Instituto de Ciencias Materiales (ICMM-CSIC), Nanomaterials and Nanotechnology Research Center (CINN-CSIC), Instituto de Cerámica y Vídrio (ICV-CSIC)

INTERNATIONAL PCT APPLICATION:
PCT/ES2010/070810

COUNTRIES SELECTED IN NATIONAL PHASE:
US, CN, EU, JP

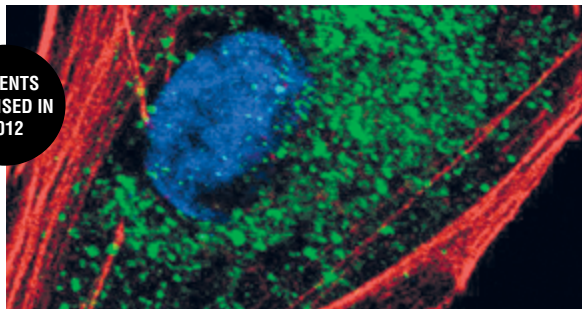
PRESENT SITUATION
Licensed to the same company as the previous patent, 02/12/2011.

Powder of vitreous having biocidal activity

Patents and biological materials licensed

PATENTS LICENSED IN 2012

PATENTS LICENSED IN 2012



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

The research group lead by Pilar Cubas at the CNB-CSIC discovered that the *Solanum pennellii* BRANCHED1-like gene causes reduced basal shoot branching when introgressed into *Solanum lycopersicum*.

This discovery is of great interest to generate improved tomato lines with reduced basal branching, a trait highly desired to avoid pruning of the plants during the time of flowering and fruit production.

RESEARCH GROUP:
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 licence to a company (22/02/2012)

The SpBRC1a gene from Solanum pennellii suppresses the elongation of branches in tomato. Left: Control plant. The red arrow indicates an incipient branch. Centre: Plant without lateral branches that carries a genomic region from Solanum pennellii including its SpBRC1a gene. Right: A Detail of plant in the center.

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

The research group lead by Dr. Mariano Esteban at the CNB has developed a prototype vaccine against HIV based on Modified Ankara Virus (MVA-B). MVA-B efficiently protects mice and macaques against simian immunodeficiency virus (SIV). MVA-B entered phase I clinical trials in 30 healthy individuals in the Gregorio Marañon (Madrid) and Clinic (Barcelona) Hospitals. In this study, 90% of the volunteers developed an immune response against the HIV virus that was maintained after 1 year in at least 85% of the individuals. Phase I clinical trials with HIV-infected volunteers (20 receive the MVA-B vaccine and 10, a placebo) were initiated in 2012 in the Gregorio Marañón, Clinic and IrsiCaixa Hospitals; results will be known in the second half of 2013.

RESEARCH GROUP:
Mariano Esteban Rodríguez

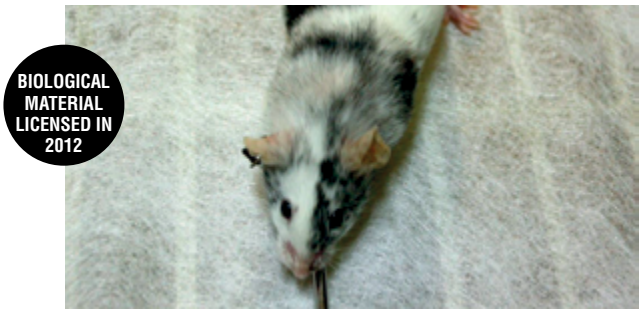
APPLICATION NUMBER AND PRIORITY DATE:
P200501841, 27/07/2005

INTERNATIONAL PCT APPLICATION:
PCT/ES06/070114

COUNTRIES SELECTED IN NATIONAL PHASE:
EU, US

PRESENT SITUATION:
Exclusive licence agreement to a company (30/06/2012)

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 good immunogenicity profile against HIV antigens in phase I clinical trials. In red, phalloidin staining of the cytoskeleton. The cell nucleus appeared in blue.



R5 monoclonal antibody against gliadin for gluten determination

RESEARCH GROUP:
Enrique Méndez Corman

PRESENT SITUATION:
Non-exclusive licence agreement to a company (08/09/2011)

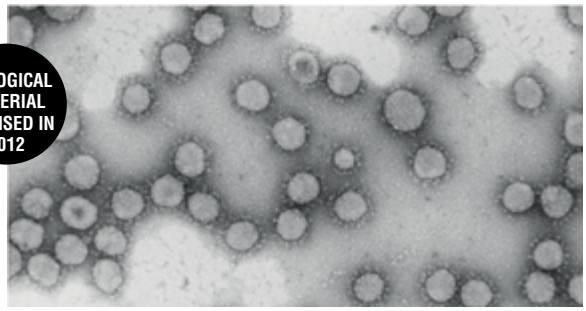
Gliadin is one of the gluten proteins found in wheat and other cereals.

Transgenic mice for use as a model for neurodegenerative diseases

RESEARCH GROUP:
Lluís Montoliú José

PRESENT SITUATION:
Exclusive licence agreement to a company (13/04/2012)

Chimaeric mouse used to generate a new transgenic animal model for sporadic Alzheimer diseases

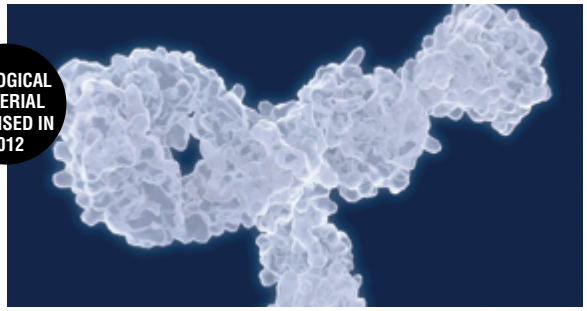


Cell lines producing monoclonal antibodies, against gastroenteritis porcine transmissible virus (GPT) and related coronavirus

RESEARCH GROUP:
Luis Enjuanes Sánchez

PRESENT SITUATION:
Exclusive licence agreement to a company (28/05/2012)

Purified enteric TGEV virus



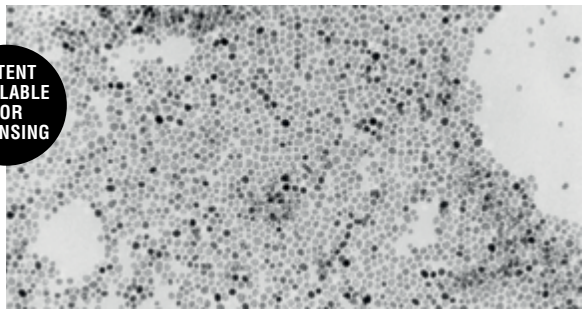
Cell lines producing monoclonal antibodies against IGF-1

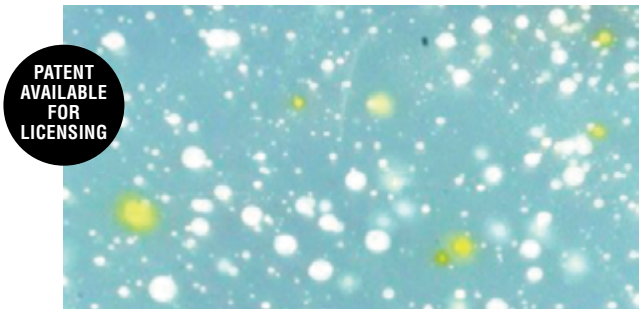
RESEARCH GROUP:
Santos Mañes Brotón

PRESENT SITUATION:
Non-exclusive licence agreement to a company (06/11/2012). They are available for other licensing agreements.

Monoclonal antibodies against IGF-1

Technology offer





Magnetic nanoparticles for use in a pharmaceutical composition

Scientists at the CNB have developed a magnetic nanoparticle which can be injected intravenously and targeted to a region of interest using an external magnetic field. It allows obtaining the optimal concentration of an active ingredient in a tumour region, with a reduction of the side effects.

RESEARCH GROUP:
Domingo Francisco Barber Castaño

APPLICATION NUMBER AND PRIORITY DATE:
P201030138, 02/02/2010

INTERNATIONAL PCT APPLICATION:
PCT/ES11/070056

PRESENT SITUATION:
Patent applications have been abandoned but the know-how is available for licensing and new nanoparticles are under development

MAIN INNOVATIONS AND ADVANTAGES:
This new nanoparticle solves the problems encountered with other therapeutic systems:
Important side effects with the systemic administration of cytokines. Moreover, when using systemic administration, the level of cytokines at the site of action is much lower than the therapeutic concentration needed, and the increase in the level is transitory.
Great therapeutic diversity in the treatments with genetic vectors injected directly into the tumour mass, or with implantation in the tumour of cells genetically modified to produce cytokines.
Significant side effects similar to the systemic administration with the injection of modified tumour cells or irradiated tumour cells as vaccines.

TEM image of magnetite nanoparticles prepared by decomposition of a metal-organic precursor in solution

Bacterial biofilm combined with liquid crystal for the preparation of an electro-optical devices

Scientists at the National Center for Biotechnology in collaboration with the Institute of Materials Sciencie of the CSIC have developed a liquid crystal type that is patterned on the structure of a bacterial biofilm, which has a high degree of porosity and displays electro-optical propierties. The production method and the use of this material for the production of devices with controllable transparency to visible light is described.

RESEARCH GROUP:
Víctor de Lorenzo

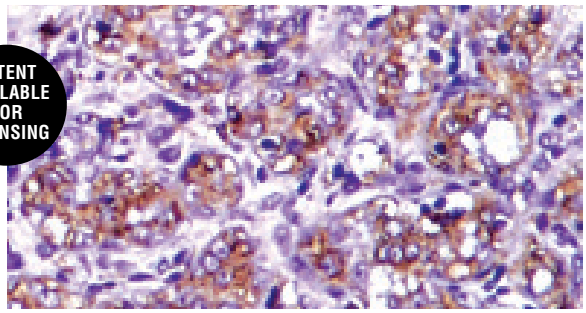
APPLICATION NUMBER AND PRIORITY DATE:
P201030295, 01.03.2010

INTERNATIONAL PCT APPLICATION:
PCT/ES11/070129

PRESENT SITUATION:
Spanish patent has been granted

Environmental bacteria like those shown in the figure (Pseudomonas putida) are prone to form biofilms that provide a complex molecular frame for developing materials with new physical and optical properties

PATENT AVAILABLE FOR LICENSING



Biomarker for cancer diagnosis, prognosis and follow-up, and a cancer diagnosis method based on its quantification in a biological sample

Scientists at the CNB-CSIC have discovered the protein p85ß, a subunit of phosphoinositide 3-kinase, as a protein marker useful for cancer diagnosis, prognosis and follow-up of tumour progression. In colon cancer samples, it was demonstrated that high p85ß protein levels correlate with an advanced cancer grade, whereas in breast cancer samples they correlate with invasive and metastatic tumours. The invention also refers to a method for cancer diagnosis, prognosis and follow-up based on the quantification of p85ß in biological samples. Industrial partners focussed on developing cancer molecular diagnostics are being sought to licence the technology.

RESEARCH GROUP:
Ana Clara Carrera

APPLICATION NUMBER AND PRIORITY DATE:
P201031137, 22/07/2010

INTERNATIONAL PCT APPLICATION:
PCT/ES2011/070451

COUNTRIES SELECTED IN NATIONAL PHASE:
US

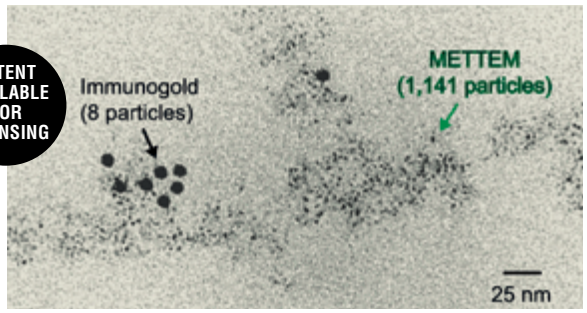
PRESENT SITUATION:
Initiating examination in US.

MAIN INNOVATIONS AND ADVANTAGES:
The PI3KR2 gene expression can be analysed by measuring the level of the mRNA encoding protein p85ß or the level of p85ß protein itself.
In human breast cancer, the p85ß marker allows discrimination between localised and metastatic cancer.
In human colon cancer, the p85ß marker is predictive of tumour grade.

REF. :
CSIC/AH_003

Confirmation of PI3K pathway activation by immunohistochemical analysis of S6 phosphorylation (red) in breast cancer tumour tissue.

PATENT AVAILABLE FOR LICENSING



Method for protein detection by electron and correlative microscopy using a clonable tag based on the protein metallothionein

A group at the National Center of Biotechnology (CNB-CSIC) has developed a method for protein detection by electron microscopy using a clonable marker based on metallothionein (MT) protein. MT is a protein that binds metal ions, such as gold. This method can be applied for protein detection in live cells, both prokaryotic and eukaryotic, in cell organelles, and in virus particles. Moreover, it allows the visualisation of the proteins in their native environment, and it is independent of antigen-antibody recognition.

RESEARCH GROUP:
Cristina Risco

APPLICATION NUMBER AND PRIORITY DATE:
P201031880, 17/12/2010

INTERNATIONAL PCT APPLICATION:
PCT/ES11/070869, PCT/ES2012/070864 (claiming priority the new material introduced in the first PCT Application).

PRESENT SITUATION:
National phase application pending. Spanish patent application has been abandoned.

MAIN INNOVATIONS AND ADVANTAGES:
It allows for *in vivo* protein detection inside cells.
It can be used for protein detection in prokaryotic and eukaryotic cells.
It can be used to detect proteins in cell organelles and in viral particles.
It allows simultaneous detection of several proteins
It is not necessary to have primary antibodies that recognise the proteins of interest.
It is independent of antigen-antibody recognition.
Sensitivity is at least two orders of magnitude higher than immunogold detection.

REF. :
CSIC/AH_004

Immunogold (antibody based method) versus METTEM (metal-tagging transmission electron microscopy).

Technology offer

PATENT AVAILABLE FOR LICENSING

PATENT AVAILABLE FOR LICENSING

Nucleic acids enconding PRRSV GP5-ecto domain and M protein

A group at the CNB-CSIC has developed a vaccine candidate to prevent porcine reproductive and respiratory syndrome virus (PRRSV), based on a recombinant transmissible gastroenteritis virus (TGEV) vector expressing selected PRRSV antigens.

RESEARCH GROUP:
Luis Enjuanes Sánchez

APPLICATION NUMBER AND PRIORITY DATE:
EP10192693, 26-11-2010. Co-titularity with Fort Dodge Veterinaria S.A. (It has been acquired by PFIZER OLOT USL)

INTERNATIONAL PCT APPLICATION:
PCT/EP11/071044

COUNTRIES SELECTED IN NATIONAL PHASE:
Pending

PRESENT SITUATION:
Patent applications have been published

The most relevant porcine virus is PRRSV

Compounds for the treatment of neurodegenerative diseases

Researchers from the CSIC, CIBERNED, CRG and Fundación CIEN have observed that changes in the expression of the protein DREAM (also known as KChIP-3 or calsenilin) in cerebral tissue precedes the onset of pathological symptoms related to Huntington's disease (HD), Alzheimer's disease (AD) and Down's syndrome (DS). These results suggest that DREAM could be an early biomarker as well as a possible therapeutic target in HD, AD and cognitive impairments related to DS. Researchers have identified two series of compounds that bind DREAM in a Ca^{2+}–dependent manner *in vitro*, and inhibit its activity. Chronic administration of these compounds in murine models of HD shows that it delays the appearance of locomotor symptoms and increases the life expectancy of the animals.

RESEARCH GROUP:
José Ramón Naranjo

APPLICATION NUMBER AND PRIORITY DATE:
P201130033, 13/01/2011

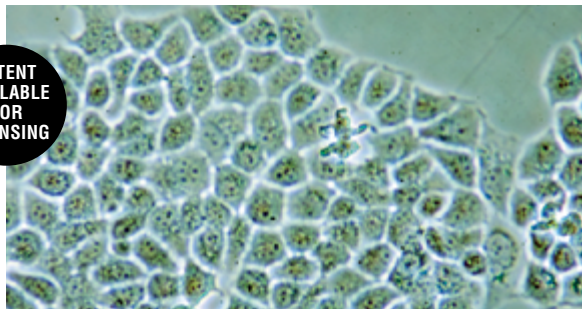
INTERNATIONAL PCT APPLICATION:
PCT/ES12/070020

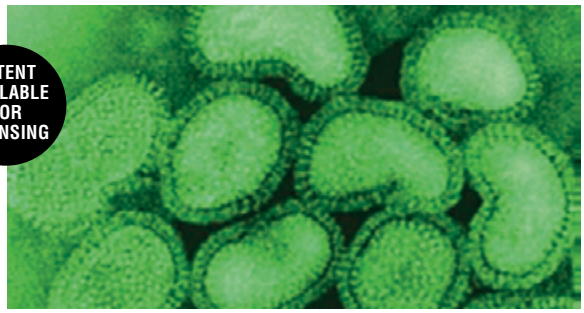
PRESENT SITUATION:
National phases application pending

MAIN INNOVATIONS AND ADVANTAGES:
Identification of DREAM protein as a novel biomarker and target related to neurodegenerative diseases
Description of a family of compounds that inhibits the target
Tested *in vivo* and *in vitro*

REF.:
CSIC/AH_005

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





Test for the determination of the response to treatment with 5-FU of patients with colon or breast cancer

PATENT AVAILABLE FOR LICENSING

Scientists at the National Center for Biotechnology (CNB-CSIC), the Servicio Andaluz de Salud and the Universidad de Granada have identified the RNA-dependent protein-kinase PKR as a marker to assess the response to the treatment of cancer with 5-fluorouracil (5-FU). Identification of mutations in PKR, changes in its activity, or insufficient expression, allows predicting the response to 5-FU alone or combined with other drugs or cytokines, particularly in patients with colon and breast cancer. Industrial partners are sought interested in a patent licence.

RESEARCH GROUP:
Mariano Esteban

APPLICATION NUMBER AND PRIORITY DATE:
P201130247, 24/02/2011

INTERNATIONAL PCT APPLICATION:
PCT/ES12/070115

PRESENT SITUATION:
National phases application pending

MAIN INNOVATIONS AND ADVANTAGES:
Previous studies have tried to analyse the relationship between the status of various enzymes involved in DNA replication with the response to 5-FU. In most cases, the conclusion is unclear, and the analysis was proposed of different markers to predict correctly the response to chemotherapy.
Other studies have analysed the tumour suppressor protein p53 as a marker. However, more than 50% of tumours have mutations or lack p53, which has an essential role in apoptosis and in control of the cell cycle. In these patients, it was demonstrated that functional PKR has a key role, as it is the only known alternative to p53 able to induce cell death. It is thus essential in these cases to determine PKR status to predict the effectiveness of 5-FU.

REF.:
CSIC/AH_012

Breast tumour cell

An improved method to produce influenza vaccine for humans in cell culture

PATENT AVAILABLE FOR LICENSING

Scientists at the National Center for Biotechnology (CNB-CSIC) have generated a new cell line with ten-fold higher yield of influenza virus particle production. The cell line of the invention has silent the CHD6 cellular protein, that acts as viral negative modulator. The use of this cell line would reduce vaccine production costs and would improve the capacity of massive vaccine production in case of pandemic flu. In addition, it would cooperate to change the current manufacture of vaccines in chicken embryonated eggs to efficient cell culture methods, as the former has a number of disadvantages, especially for egg-allergic individuals. Industrial partners interested in a patent licence are being sought.

RESEARCH GROUP:
Amelia Nieto Martín

APPLICATION NUMBER AND PRIORITY DATE:
P201130879, 27/05/2011

INTERNATIONAL PCT APPLICATION:
PCT/ES12/070388

PRESENT SITUATION:
National phases application pending. Spanish patent application has been abandoned.

MAIN INNOVATIONS AND ADVANTAGES:
The cell lines of the invention improve the replication of viral RNA and produce from 5 to 10 times more viral particles per infected cell.
The use of these cell lines reduces the cost of cell culture flu vaccine production and offer the possibility of massive production in case of pandemic flu.

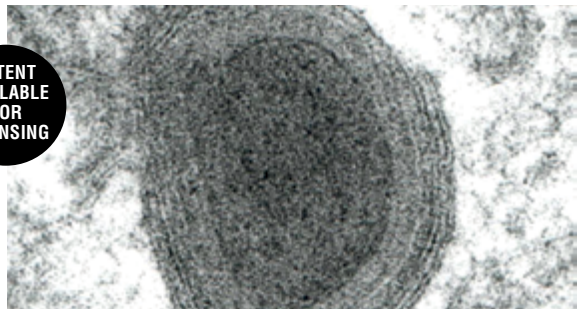
REF.:
CSIC/AH_007

Electron micrograph of influenza virus particles

Technology offer

PATENT AVAILABLE FOR LICENSING

PATENT AVAILABLE FOR LICENSING



Procedure to obtain monoclonal antibodies from complex samples of antigens

Scientists at the CNB-CSIC have discovered a method to select recombinant antibodies from camelids (camelbodies) that were obtained from complex samples of antigens.

RESEARCH GROUP:
Víctor de Lorenzo

APPLICATION NUMBER AND PRIORITY DATE:
P201131152, 06/07/2011

PRESENT SITUATION:
Spanish patent pending

The technology allows massive production of antibodies against mixtures of complex antigens (e.g., a whole cell extract) and their sorting by direct panning of the phage display library on a denaturing 1-D or 2D gels.

Recombinant vectors based on Ankara modified virus (MVA), with a deletion in the 6CL gene, as vaccines against HIV and other diseases

A group at the National Center of Biotechnology (CNB-CSIC) has developed recombinant viruses based on modified Ankara virus (MVA a highly attenuated poxvirus strain) with deletion in the 6CL gene as vaccines against HIV and other diseases such as malaria, leishmaniosis, hepatitis C and prostate cancer. This vector represents an attractive alternative for improving the immunogenicity of prototype vaccine candidates based on MVA. Industrial partners are sought interested in a patent licence.

RESEARCH GROUP:
Mariano Esteban

APPLICATION NUMBER AND PRIORITY DATE:
P201131230, 19/07/2011

INTERNATIONAL PCT APPLICATION:
PCT/ES12/070521

PRESENT SITUATION:
National phases application pending

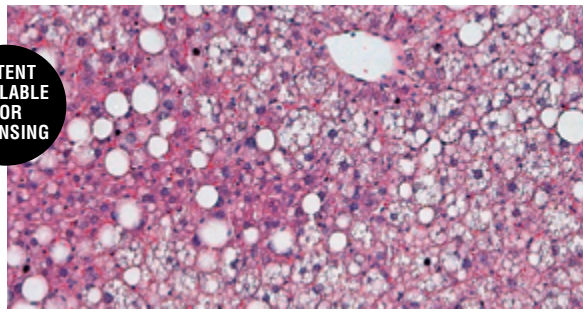
MAIN INNOVATIONS AND ADVANTAGES:
The vector of the invention replicates at the same level as the parental virus and induces innate immune responses, increasing the expression of IFNβ and the genes that are inducible by IFNα/β in human cells.
In mouse, deletion of the C6L gene produces an increase in the humoral and cellular immune responses to HIV antigens.
Deletion of the C6L gene could improve the immunogenicity of other recombinant vectors based on MVA that express other heterologous antigens (from malaria, leishmania, hepatitis C and prostate cancer) to be used as vaccines against these diseases.

REF.:
CSIC/AH_008

Modified Ankara virus (MVA) in CEF cells

PATENT AVAILABLE FOR LICENSING

PATENT AVAILABLE FOR LICENSING



Adjuvant effect of A27 protein from vaccinia virus (14K) and its applications for vaccines

A group at the CNB-CSIC has found the adjuvant-like effect of the immunogenic vaccinia virus protein 14K when fused with the circumsporozoite (CS) protein of *Plasmodium*. The chimaeric protein CS-14K has a pronounced tendency to form oligomers/aggregates, which in turn enhanced the host immune response profile in prime/boost protocols, leading to protection against malaria. The adjuvant effect of the 14K protein was shown in the design of a new vaccine against malaria, but could be used to generate similar fusion proteins as immunogens for other diseases such as HIV, hepatitis C, leishmaniasis and cancer. Industrial partners are being sought interested in a patent licence.

RESEARCH GROUP:
Mariano Esteban

APPLICATION NUMBER AND PRIORITY DATE:
P201131854, 17/11/2011

INTERNATIONAL PCT APPLICATION:
PCT/ES2012/070794

PRESENT SITUATION:
National phases application pending. Spanish patent application has been abandoned

MAIN INNOVATIONS AND ADVANTAGES:
Chimaeric protein of 14K protein improves the overall immunogenicity of the fused antigen, such as *plasmodium* CS, in the absence of any adjuvant.
The activation of type I IFN signalling by 14K fusion protein further validates its use as priming agent.
The use of proteins as priming agents is gaining acceptance due to their better efficiency and safety than DNA vectors.

REF.:.
CSIC/AH_009

Vaccine against malaria

p38 MAPK gamma and delta for use as biomarkers of NAFLD

The present invention provides a precise, non-invasive method to obtain a prognosis for and to diagnose non-alcoholic fatty liver disease. The invention corresponds to a method that analyses the levels of different kinases in blood samples. As such, it can be considered a non-invasive test to diagnose fatty liver disease, which could clearly lead to an improvement in early diagnosis, the ability to follow the disease, and in patient quality of life.

RESEARCH GROUP:
Guadalupe Sabio
This group has moved to the CNIC.

APPLICATION NUMBER AND PRIORITY DATE:
EP12164807, 19/04/2012. European patent was presented as priority patent. Co-titularity CSIC (CNB), CNIC and Salamanca University

INTERNATIONAL PCT APPLICATION:
Pending

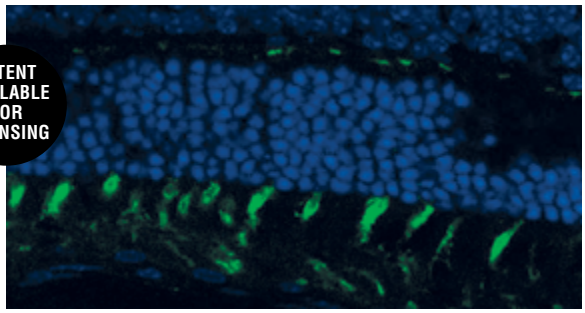
PRESENT SITUATION:
The CNIC is in charge of managing this patent .

MAIN INNOVATIONS AND ADVANTAGES:
The levels of certain kinases in the bloodstream can be used as potential biological markers of hepatic steatosis in humans, without the inconvenience and risks associated with performing liver biopsy.

Micrograph of non-alcoholic fatty liver disease.

Technology offer

PATENT AVAILABLE FOR LICENSING



PATENT AVAILABLE FOR LICENSING

New animal model for achromatopsia

Scientists at the CNB-CSIC have described a new animal model for a retinopathy, achromatopsia disease. Achromatopsia is a rare disease (affects 1-9:100,000 people) and is characterised by reduced visual acuity, nystagmus, photophobia, and total or partial loss of the ability to discriminate between colours.

RESEARCH GROUP:
Lluís Montoliu José
In co-titularity with the Centre for Biomedical Network Research on Rare Diseases (CIBERER), Alcalá de Henares University and Spanish National Cancer Research Center (CNIO)

APPLICATION NUMBER AND PRIORITY DATE:
P201231296, 13/08/2012

PRESENT SITUATION:
International PCT Application pending

MAIN INNOVATIONS AND ADVANTAGES:
This animal model will allow development and validation of new therapies for achromatopsia disease.

REF.:
CSIC/AH_014

Attenuated SARS-CoV vaccines

Scientists at the CNB-CSIC have developed a vaccine candidate to prevent severe acute respiratory syndrome (SARS) in humans. This candidate has been proved to provide one hundred percent protection in three animal model systems.

RESEARCH GROUP:
Luis Enjuanes Sánchez

APPLICATION NUMBER AND PRIORITY DATE:
EP05013727, 24/06/2005

INTERNATIONAL PCT APPLICATION:
PCT/EP06/006091

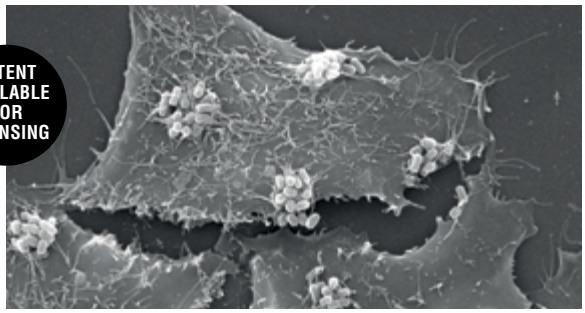
COUNTRIES SELECTED IN NATIONAL PHASE:
CN, HK

PRESENT SITUATION:
Patent examination in each country.

REF.:
CSIC/AH_016

Histological section of an adult mouse retina displaying the cone photoreceptor cells (green) and the nuclei of all cells (blue)

BSL3 containment laboratory at the CNB-CSIC



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

Scientists at the CNB-CSIC have 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 functionality by the 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:
Luis Angel Fernández Herrero

APPLICATION NUMBER AND PRIORITY DATE:
P200700644, 12/03/2007

INTERNATIONAL PCT APPLICATION:
PCT/ES08/070045

COUNTRIES SELECTED IN NATIONAL PHASE:
EU, US. EU application has been abandoned

PRESENT SITUATION:
Spanish patent has been granted (12/03/2007). Patent examination in US

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 the transfer of the protein-encoding gene by viral infection or transfection.

REF.:
CSIC/AH_015

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

Diagnosis and treatment procedure for diseases with alteration of p38 kinase, the elements required and its applications

Scientists at the CNB-CSIC have developed a method to assess disease activity of rheumatoid arthritis (RA) based on measurement of the phosphorylation status on p38 Tyr^{323}. They have shown that phosphorylation of p38 on Tyr^{323} was higher in T cells from patients with active RA (P = 0.008 vs. healthy controls) than in patients with RA in remission or patients with ankylosing spondylitis. Tyr^{323} p38 phosphorylation was associated with disease activity determined by the Disease Activity Score in 28 joints (DAS28) (P = 0.017).

RESEARCH GROUP:
Jesús Mª. Salvador
Carlos Martínez-A

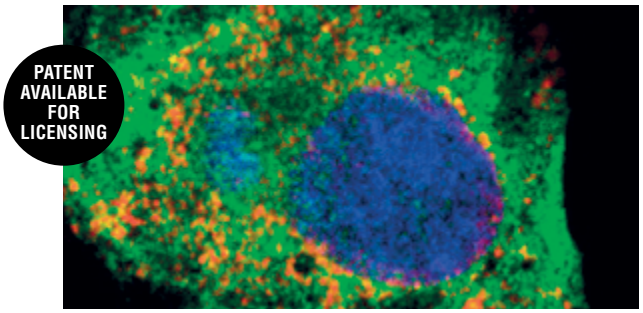
APPLICATION NUMBER AND PRIORITY DATE:
P200702770, 22/10/2007

INTERNATIONAL PCT APPLICATION:
PCT/ES08/070193

PRESENT SITUATION:
The Spanish patent application has been granted. The scientists have new biological materials and know-how regarding this technology.

REF.:
CSIC/AH_011

Rheumatoid arthritis is an autoimmune disease that attacks the joints and other body parts.



Potato plants able to tuberise under heat stress conditions and the method to produce them

A group at the National Center of Biotechnology (CNB-CSIC) has identified and sequenced the potato gene *SP6A*, orthologue to the *Arabidopsis thaliana* FLOWERING LOCUS T (FT) gene, and has demonstrated that the gene encodes a protein that acts as the tuberisation-inducing signal in potato plants. Transgenic potato plants have been generated which carry a construct consisting of a heat shock promoter from soybean, induced at temperatures higher than 35ºC, fused to the *SP6A* potato gene sequence and it has been demonstrated that they are able to tuberise under heat stress conditions (night temperatures above 25ºC).

RESEARCH GROUP:
Salomé Prat

APPLICATION NUMBER AND PRIORITY DATE:
P200930114, 29/04/2009

INTERNATIONAL PCT APPLICATION:
PCT/ES10/070265

COUNTRIES SELECTED IN NATIONAL PHASE:
EU BR, US, AU, IN

PRESENT SITUATION:
Patent examination in each country

MAIN INNOVATIONS AND ADVANTAGES:
The overexpression of the potato *SP6A* gene under the control of a heat-inducible promoter notably improves tuber production yield under heat stress conditions.
Under heat stress conditions, while control potato plants showed a 30% reduction in tuber production, transgenic plants expressing the potato *SP6A* gene showed only a slight reduction in tuber production (8% yield reduction for the transgenic line with the highest level of 6SPA gene expression).
The use of a heat-inducible promoter allows expression of the gene only under high temperature conditions that would otherwise negatively affect generation and growth.

REF.:
CSIC/AH_001

In heat conditions, control potato plants showed a 30% reduction in tuber production (left), while transgenic plants expressing the potato Sp6A gene showed only a slight reduction in tuber production (right).

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/II clinical trials are expected to be initiated in 2013/14.

RESEARCH GROUP:
Mariano Esteban

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

INTERNATIONAL PCT APPLICATION:
PCT/US10/032966

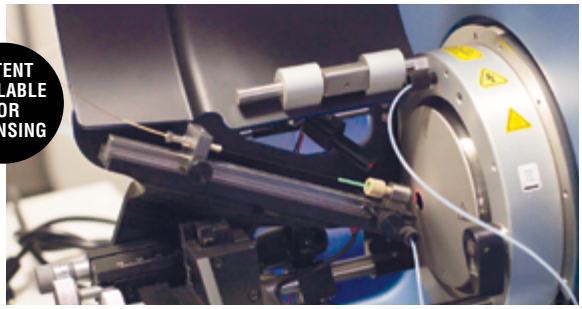
COUNTRIES SELECTED IN NATIONAL PHASE:
EU, US, CA

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

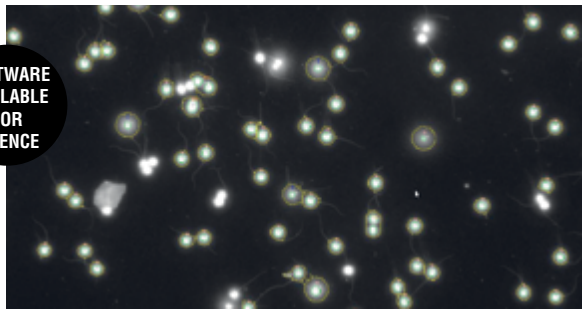
REF.:.
CSIC/AH_010

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.

PATENT AVAILABLE FOR LICENSING



SOFTWARE AVAILABLE FOR LICENCE



Method for identifying peptides and proteins from mass spectrometry data

In the course of large-scale proteomics projects, millions of peptide ion collision spectra (MS/MS) may be generated, which must be matched to theoretical spectrum models inferred from known peptide sequences in order to identify proteins

A number of database search engines using different scoring systems have been and are being developed to this end. Scientists at the National Center for Biotechnology 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, remarkably increases the number of proteins identified. The process may be extended by integration of additional sources of information besides primary search engine results.

RESEARCH GROUP:
Juan Pablo Albar

APPLICATION NUMBER AND PRIORITY DATE:
P200930402, 01/07/2009

INTERNATIONAL PCT APPLICATION:
PCT/ES10/070445

COUNTRIES SELECTED IN NATIONAL PHASE:
EU, US

PRESENT SITUATION:
Patent examination in each country

MAIN INNOVATIONS AND ADVANTAGES:
It is extremely flexible and remarkably increases the number of proteins identified.
High level of accuracy in terms of error rate control.

REF.:
CSIC/AH_002

High throughput, proteome-wide identification of proteins using tandem mass spectometry requires computational methods to interpret and filter large sets of peptide ion collision data.

Automatic classification of spermatozoids from microscopic images

This is image processing software that automatically classifies the quality of a sperm sample.

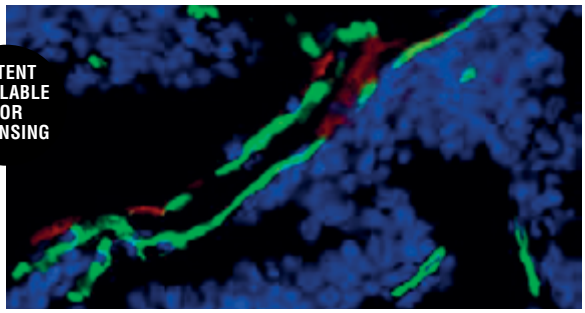
The software has been integrated into a customised microscope especially designed for high-throughput analysis of these kinds of samples.

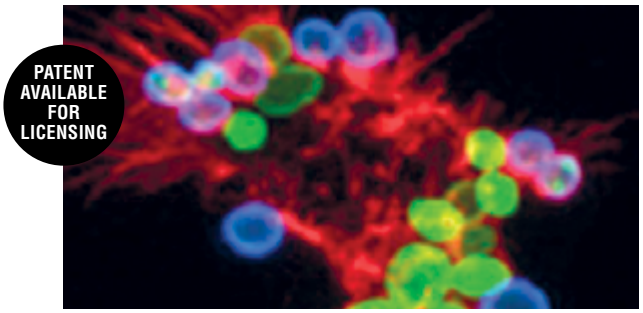
RESEARCH GROUP:
Carlos Óscar Sánchez Sorzano
In co-titularity with Roberto Marabini Ruiz (UAM) and Halotech DNA S.L.

PRESENT SITUATION:
Licence pending

Segmented sperms are highlighted in yellow with centers in green. The objective is to measure the rate of fragmented sperm cells over normal ones.

Technology offer





Use of SOD-3 for adjuvant immunotherapy of cancer

The group lead by Santos Mañes has demonstrated that the forced expression of the extracellular superoxide dismutase, also known as SOD3, in the tumour microenvironment increases the number of cytotoxic T lymphocytes infiltrating breast tumours, thus favouring the immune-based eradication of neoplastic cells. SOD3 is expressed at high levels in the mammary epithelium but its expression is drastically decreased in breast tumours. SOD3 or compounds emulating its enzymatic activity, or drugs that increase SOD3 expression in tumours might thus be useful to elaborate new pharmaceutical compositions for the prophylaxis and immunotherapy of cancer.

RESEARCH GROUP:
Santos Mañes

APPLICATION NUMBER AND PRIORITY DATE:
P201031015, 30/06/2010

PRESENT SITUATION:
Spanish patent is pending

Antibody anti-dectin-1, hybridoma producer of this antibody and its applications

The CSIC and the Biomedical Research Foundation of the La Princesa Hospital have developed an antibody to detect dectin-1 protein.

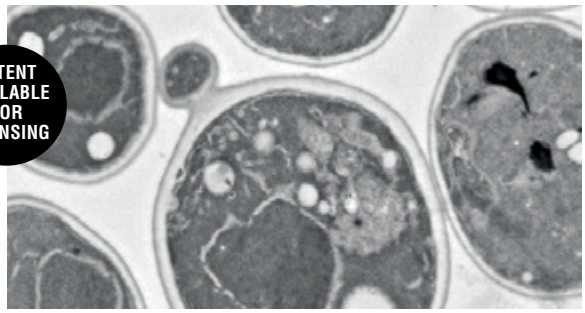
RESEARCH GROUP:
Leonor Kremer Barón

APPLICATION NUMBER AND PRIORITY DATE:
200801766, 11/06/2008

PRESENT SITUATION:
Spanish patent has been granted (07.02.2011)

SOD3 staining (red) in normal glands and breast tumors; blood vessels are stained in green.

Phagocytosis and killing of Candida albicans by human monocyte-derived dendritic cells expressing dectin-1. Confocal microscopy images showing extracellular yeast cells (blue), extracellular and internalized yeast cells (green), and actin (red).



Monoclonal antibody against the protein GAPDH from *Candida famata*

PATENT AVAILABLE FOR LICENSING

The CSIC and the Universidad Autónoma Foundation have developed a monoclonal antibody to detect GAPDH protein from *Candida famata*. This antibody could be useful for the diagnosis of infections produced by the microorganism and for its follow-up.

RESEARCH GROUP:
Leonor Kremer Barón

APPLICATION NUMBER AND PRIORITY DATE:
200930966, 06/11/2009

PRESENT SITUATION:
Spanish patent has been granted (11-06-2012)

Yeast samples were fixed and embedded in Eppon resin following standard procedures. Ultrathin sections were prepared and stained with uranyl acetate and lead citrate. Pictures were obtained in a Jeol Jem 1010 EM equipment operated at 100 kv.

Method for extracting hydrolised and native gluten

PATENT AVAILABLE FOR LICENSING

CSIC has developed a method for extracting gluten from food. The invention can be used to extract gluten from food that has been subjected to different thermal and/or hydrolytic treatments and in which the gluten-forming proteins can be hydrolysed and the structure thereof modified. The method is compatible with enzyme immunoassay systems for gluten quantification, such as competitive ELISA, as well as with other techniques used in gluten analysis.

RESEARCH GROUP:
Juan Pablo Albar Ramírez

APPLICATION NUMBER AND PRIORITY DATE:
P200930445, 13.07.2009

INTERNATIONAL PCT APPLICATION:
PCT/ES2010/070487

PRESENT SITUATION:
Spanish patent has been granted (28-01-2011)

Method to extract gluten proteins from food that has been subjected to different thermal and/or hydrolytic treatments.