You became the first Professor and Chairman of Genomic Medicine at Camilo José Cela University, Spain, in 2013. How did your previous experience prepare you for this role?

I was educated at the Osaka University Medical School in Japan. My supervisor was Professor Tsuyoshi Nishimura, one of the fathers of dementia research in the country and an expert in ageing and neurodegenerative disorders. Together with my friend Masatoshi Takeda, I started a series of experiments on the neurochemistry and molecular biology of Alzheimer’s disease, early diagnostic procedures, and novel therapeutic strategies in animal models. In collaboration with Professors Hiroshi Wada, Takehiko Watanabe, Atsuhi Yamatodani and Hiroyuki Fukui, I investigated the role of brain histamine in ageing and the pathogenesis of this form of dementia. After almost a decade in Japan, I returned to Spain and focused my research on neurogenetics and genomics.

Can you introduce the EuroEspes Biomedical Research Center at the Institute of Medical Science and Genomic Medicine, Spain?

In the early 1990s a group of colleagues and I decided to create an institute of technology that specialised in the genomic medicine of central nervous system disorders. Consequently, in 1995, I founded the EuroEspes Biomedical Research Center. For the past 20 years, EuroEspes has been dedicated to providing medical services for patients with brain disorders; researching ageing, neurodegenerative disorders and dementia; identifying biomarkers for central nervous system disorders; and developing new therapies.

EuroEspes Publishing Co. released the World Guide for Drug Use and Pharmacogenomics in 2012 and is soon to launch the EuroPharmaGenics (EPG) Database. How do you hope these resources will impact the field of pharmacogenomics?

The World Guide for Drug Use and Pharmacogenomics is the world’s first practical pharmacogenomics guide. It is a multidisciplinary, systematic exercise to put in order the myriad data on genetics, genomics, pharmacology, drug metabolism, therapeutics and pharmacogenomics. Its 3,000 pages cover 1,395 US Food and Drug Administration-approved drugs and 447 genes of relevance to pharmacogenomics, based on 17,947 references and a collation of international websites and databases.

In the coming weeks, the online version of the EPG Database, with updated fields, will be launched. The main aim of both tools is to serve as an educational aid for the medical and scientific communities, so they can become familiar with the practical use of pharmacogenomics.

Since its inception, EuroEspes Biomedical Research Center has been making swift progress in the fields of dementia, Alzheimer’s and other age-related brain disorders. How do you envision the company will advance its R&D activities in the near future?

Our research projects for the coming five years include the following: implementation of a prevention programme for cerebrovascular disorders; characterisation of genotype-phenotype correlations in dementia and other central nervous system disorders; development of an intelligent pharmacogenetic card (iPC); development of 10 novel nutraceuticals for prevalent disorders, including cancer and diseases of the heart and brain; and identification of genes associated with human intelligence.

@ INNOVATION@
Understanding how a person’s genetic makeup interacts with their environment to determine the progression of a disease is the first step to effective prevention and treatment. Genetics is also relevant for determining the patient’s response, and this pharmacogenomic information is becoming ever more important in therapeutic planning by medical professionals.

Ramón Cacabelos is the first Professor of Genomic Medicine at the Camilo José Cela University, Spain. His groundbreaking research in the field of genetics and pharmacogenomics has resulted in significant advances in understanding the genetic variations controlling an individual’s risk of disease and corresponding response to treatments. Such research has already begun to enhance the field of personalised medicine for improved efficacy and reduced side effects.

Too little too late

Alzheimer’s disease, the most common form of dementia, is a complex neurodegenerative condition. Despite its reputation as a disorder that affects the elderly, progressive neuron death in at-risk patients begins after the brain’s maturation at around 30-35 years of age. This slow neurodegeneration period means that by the time symptoms are detected in an older person, billions of neurons have already been lost beyond repair.

Researchers at EuroEspes Biomedical Research Center have developed world-leading pharmacogenomic approaches to account for genetic variability in a patient’s response to the treatment of Alzheimer’s disease.

Cacabelos and his team have extensive experience in applying genomic medicine to this disease in order to identify its causes, characterising defective genes involved in its pathogenesis and discovering biomarkers that will enable early detection of neuronal death.

All in the genes

Over 600 genes have been implicated in determining the vulnerability of neurons to premature death in Alzheimer’s. Cacabelos and his team have extensive experience applying genomic medicine to this disease in order to identify its causes, characterising defective genes involved in its pathogenesis, and discovering biomarkers that will enable early detection of neuronal death. “The only way to effectively fight dementia is to identify people at risk many years before disease onset and implement a preventive programme to avoid premature neuronal death,” Cacabelos explains. “Genomics, transcriptomics, proteomics and metabolomics are the most advanced scientific resources for the identification of biomarkers to categorise people at risk.” Understanding the genomic profile of a patient susceptible to the development of Alzheimer’s disease means that both prevention and treatment approaches can be targeted to the individual for a more successful outcome.

Dementia drugs

Central nervous system disorders are a major problem in ageing populations, but only 20-30 per cent of patients respond well to conventional pharmacological treatments. Research by Cacabelos, EuroEspes and others has found that genetics accounts for up to 95 per cent of the individual variability in drug efficacy and around 50 per cent of adverse pharmaceutical effects, which highlights the importance of personalised medicine in this area.

Cacabelos has extensive experience in developing therapies for Alzheimer’s, which has been greatly enhanced by his research into the disease’s pharmacogenomics. The therapeutic
TWENTY YEARS IN THE MAKING
Since its foundation, EuroEspes has made huge progress in the fields of genomic medicine, pharmacogenomics and personalised treatment. So far, the company has:

- Been involved in over 150 research projects
- Collaborated with more than 100 scientists and physicians within national and international groups
- Published over 600 papers in international medical journals, provided 500 book contributions and given 600 international presentations
- Contributed to the development and clinical research of several drugs, some of which are now commercialised worldwide
- Registered several patents including a genetic kit for the diagnosis of Alzheimer’s disease, a cell culture system for drug primary screening, the EB101 vaccine against Alzheimer’s disease and several nutraceuticals, which are now on the market

response to anti-dementia drugs is genotype-specific, Cacabelos discovered that polymorphic variants in the APOE-TOMM40 region of the genome are involved in determining a person’s risk, the age at which symptoms appear and the response to conventional pharmaceuticals.

A PERSONALISED APPROACH
These findings are currently being translated into practical personalised treatment plans for individuals. The EuroEspes Pharmacogenetic Card (EPC), our latest development, is a device which contains the pharmacogenomic profile of an individual, together with a list of almost 1,000 US Food and Drug Administration-approved drugs, showing what kind of treatment a person can take and what sort of drugs the carrier of the EPC must avoid,” Cacabelos details.

The EPC contains information on the most important and representative genes for each of the five major pharmacogenetic categories: pathogenic, mechanistic, metabolic, transporter and pleiotropic genes. “We have also designed specific EPCs for pharmaceutical categories and pathologies, for example drugs used to treat brain disorders, cardiovascular disorders and cancer,” Cacabelos elaborates. This revolutionary innovation promises to improve the specificity, and therefore efficacy, of treatments given to a patient while simultaneously reducing their risk of side effects.

THE EB101 VACCINE
One of the most promising areas of research for halting Alzheimer’s disease progression is in vaccine development, and Cacabelos is an international innovator in this field. Patients accumulate senile plaques, deposits of fibrous amyloid beta peptides in the brain that prevent normal neuronal activity. In 2005, Cacabelos’ team began to produce a vaccine capable of preventing amyloid beta peptide deposit build up and reversing neuronal damage in the early stages of disease progression. As a result, the EB101 vaccine was developed – a new immunogen enhanced with neurotrophins for regulating neuron cell survival that is administered through liposomes. "EB101 was tested in transgenic animals carrying the mutant genes responsible for familial Alzheimer’s disease in humans, and this novel immunotherapy was able to avoid the onset of the disease with no side effects such as meningoencephalitis or brain micro-haemorrhages," Cacabelos explains. Registered at the US Patent Office in 2011, EB101 is now heading for clinical trials. If successful, this novel vaccine may prevent the development of Alzheimer’s in the more than 70 million at-risk people within the next 25 years.

THE FUTURE OF MEDICINE
Cacabelos and his team at EuroEspes have spent decades discovering the genetic variations that underpin the development of disease and individual responses to therapeutics. A notable example of this is EuroEspes’ World Guide for Drug Use and Pharmacogenomics (WGPGx), the first ever global guide to pharmacogenomics. Vital information outlined in the WGPGx has already been used to create individual pharmacogenomic profiles and personalised treatment plans that maximise efficacy and minimise side effects for a wide range of diseases, an innovative approach that promises to revolutionise the future of medicine.

THE PHARMACOGENOMICS OF BRAIN DISORDERS AND DEMENTIA
OBJECTIVES
- To research ageing, neurodegenerative disorders and dementia
- To develop biomarkers and new drugs for central nervous system disorders

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