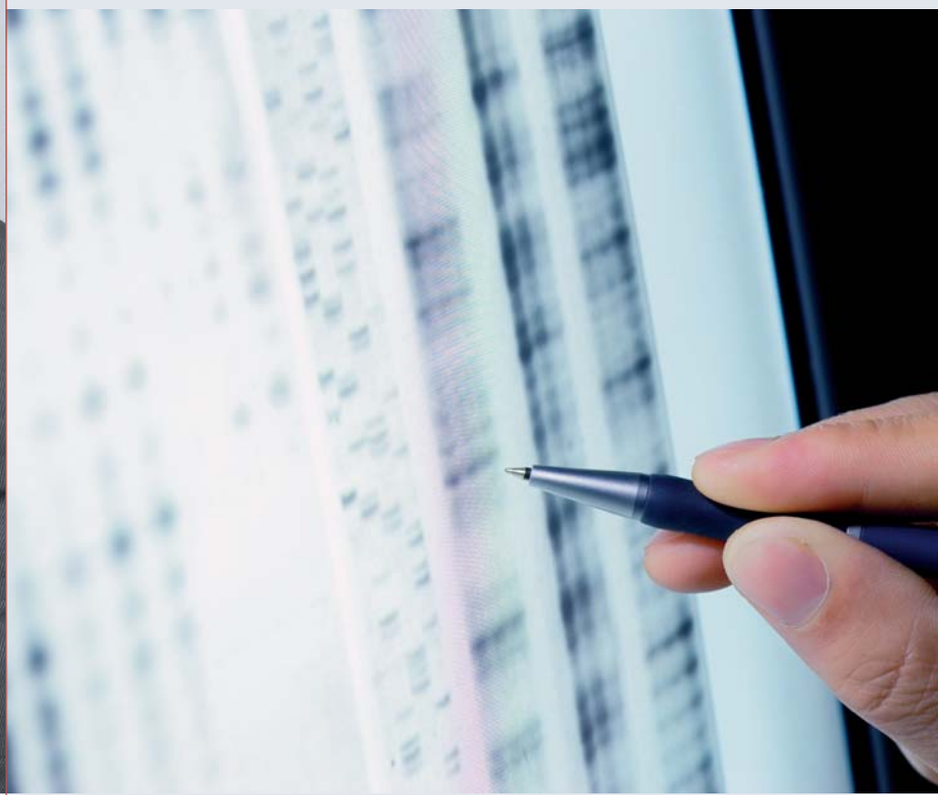
interview to **Dr. Luis Izquierdo**

Researcher and doctor specialized in genetics



Luis Izquierdo López was born in Madrid in 1961.

Following the family tradition, he studied medicine at the Complutense University in Madrid, where he took his doctorate. After this, he moved to Glasgow (UK) to take his Masters in medical genetics.

After returning to Spain, he has worked as a researcher at the Clinical Hospital sponsored by the Health Research Fund (FIS). He has been a professor at the European University of Madrid and since 2000, has been working in his laboratory in the Genetic Research Center (C.I.G.). This center was founded by his father, a doctor specializing in gynecology and genetics in the department headed by Professor Botella, who pioneered the development of cariotypes in Spain during the 1960s (cariotypes are a method of mapping the chromosomes of a cell arranged according to its morphology).

"We still have to learn about the structure of many genes"

Genes are the basic units of heredity. They carry the genetic information needed to synthesize proteins - the chemical compounds whose function is to regulate all the processes in the human body. Researchers have been decoding the information contained in genes over recent decades, enabling them to use genetic tests to assess the likelihood that an individual will contract certain diseases during his or her lifetime. Genetic research is enjoying its heyday, despite the ethical problems that it is generating. Thanks to the decoding of the Human Genome in 2003, there is enormous scope for the future of medical genetics as regards research into diseases and prevention based on the application of personalized solutions.

How would you define medical genetics?
It is the area of medicine that focuses on the diagnosis of hereditary diseases. Victor McKusick, the American professor of medicine who is our doyen, said that just as the kidney is the organ of reference for nephrologists and the heart occupies the same position for cardiologists, the field where medical geneticists "operate" is the Human Genome. McKusick and his collaborators laid the foundations for this specialism in the 1940s and 1950s. McKusick died a short time ago, but it was he who brought together the entire extant body of scientific and medical knowledge on this subject at a certain moment in time.

Since you completed your doctoral studies in medicine in 1986, what changes have you seen in the field of genetics?
Every kind of change. In fact, this has been an excellent period to observe the transformations that have taken place. We have witnessed a total revolution as regards DNA (the English abbreviation for deoxyribonucleic acid, known as ADN in Spanish, which is the primary substance in chromosomes and genes). I was in Barcelona in 1986 when genetic research was already under way into Duchenne (a type of muscular dystrophy). There is also another disease known as fragile X syndrome (FXS), which causes mental retardation. And at the end of the 1980s, in connection with yet another disease -spinal muscular atrophy- I contacted the researcher who had discovered the mutation gene because I had a family to whom I had to give a diagnosis. I have always worked in this ill-defined border area between research and clinical application. Another very interesting event that I experienced was the discovery of the breast cancer gene. There was a geneticist in New York, Marie Claire King, who was studying several families where it was shown that breast cancer was hereditary,

Spanish women have a lower incidence of breast cancer than women in Anglo-Saxon countries due to the influence of diet and environmental conditions

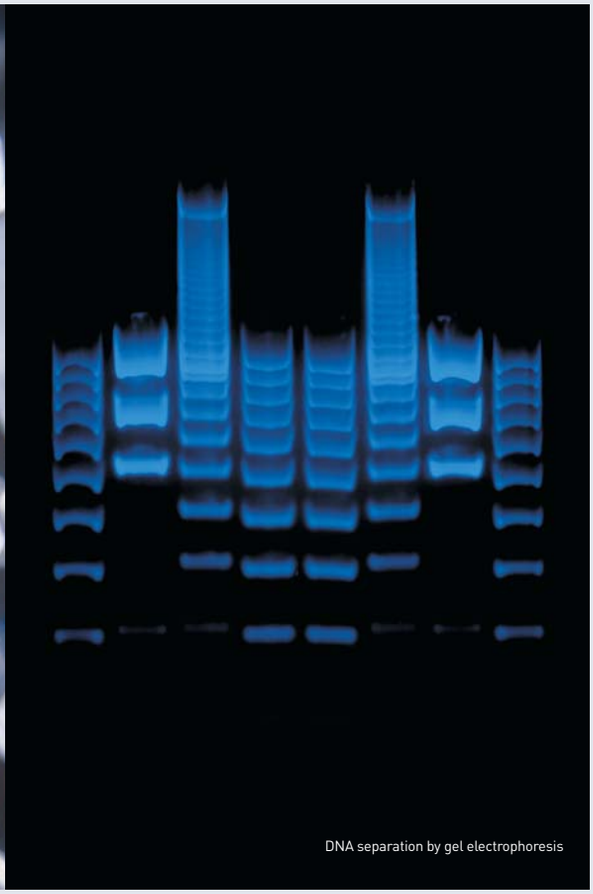
but nobody believed her - until a congress in the 1990s when she managed to prove that it was indeed hereditary, and is in fact one of the most frequent of all hereditary diseases.

In a genetic heredity profile, is the function programmed in a particular gene bound to trigger, or are there external factors that can prevent this from happening?

No, it is not bound to trigger. There are many external influencing factors that are still unknown to us. Take breast cancer, for example. What is strange is that women who carry the same anomaly in one of the genes that are known to produce breast cancer are not certain to get the disease. If such women live to the age of 70, 80 per cent of them will contract breast or ovarian cancer. But that figure is for the population in America, where the incidence of breast cancer is higher. When this research was carried out in Spain, which has a lower incidence of breast cancer than the Anglo-Saxon countries (due to the influence of diet and environmental conditions), women carrying this same mutation proved to be less likely to develop the disease. Instead of 80 per cent, the rate of occurrence drops to 60 or 50 per cent. It's clear that there are other factors which influence the development of the disease.

In 1969, 300 genetic diseases had been described and 6,000 had been identified by the end of 2000. Is the number continuing to increase at this pace?

It is continuing to rise, but more slowly. Let's say that development peaked during those years. There are two important factors in the progress of genetics, or in our knowledge of the genes that are responsible for diseases: one is the technology of DNA, which was essentially revolutionized by the polymerase chain reaction or PCR, a fundamental process in molecular biology. This is a method whereby you can obtain hundreds of thousands of copies from one fragment of genetic material. It is like cloning a fragment of DNA. This has been a key element in the search for genes that transmit diseases, making it possible to sequence and complete the Human Genome, which is the combination of genes that characterizes our species. The other factor is the computer. This research would have been impossible without computers or information technology. Over this period, the advance of computer technology and the develop-



DNA separation by gel electrophoresis

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ment of PCR, which emerged in the mid-1980s, were the factors that made it possible to discover many of the genes that are related to diseases.

What are the applications for medical genetics?
Basically, the diagnosis and prevention of hereditary diseases.

And is it possible to intervene before the symptoms appear?
No. But in terms of prevention, it is sometimes possible to take action so that the patient does not suffer with the disease. For instance, if you make a diagnosis before the appearance of symptoms of hemochromatosis, which is one of the most frequent hereditary diseases, you can prevent the person from suffering the consequences of the disease by administering a simple treatment throughout their lifetime.

Who has an interest in knowing an individual's genetic profile?
First and foremost, other doctors who specialize their own fields. Cardiologists want this information to detect heart rhythm disorders; it helps pediatricians to identify malformation problems; neurologists can utilize it to confirm neurological diseases that they detect, and it is also helpful to oncologists if they suspect the presence of hereditary cancer. All these groups send us patients according to their specialist areas.

What interest does the insurance industry have in this field?
It is a way of diagnosing and preventing diseases. That is the key fact.

Is there any kind of restriction on the use of genetic data or information by insurers?
The new (Spanish) Law on Assisted Reproduction passed in 2006 refers to the confidentiality of genetic data. It states that this data regarding clinical history is confidential, and is the property of the patient; so in that respect, it does not differ greatly from other data. This means that patients can forward this data to an insurance company or to anyone else they like.

Can insurers request a genetic test at a specific time?
That could happen, but such tests are not carried out at present.

Digital illustration of DNA structure

Genetics is a very transparent science and there are no problems to obtain data on the incidence of diseases or their prevalence in certain groups among the population

Genetic science isn't very popular. It can provide information, but maybe it won't produce a specific cure.

This is something that happens quite often: people expect genetics to provide more than it can really deliver at present. Of course, there are some diseases that we can cure or prevent: hemochromatosis is one example. But in fact, society expects far more than what can be delivered in reality. There are some things that we can do, such as taking preventive action - but we cannot reverse the action of a gene in an individual. It is impossible to block the expression of a gene that is causing a disease in someone; once we have achieved that, we shall definitely be able to cure cancer.

The Human Genome -or the total number of chromosomes in the body- was decoded in 2003. What was the significance of that?

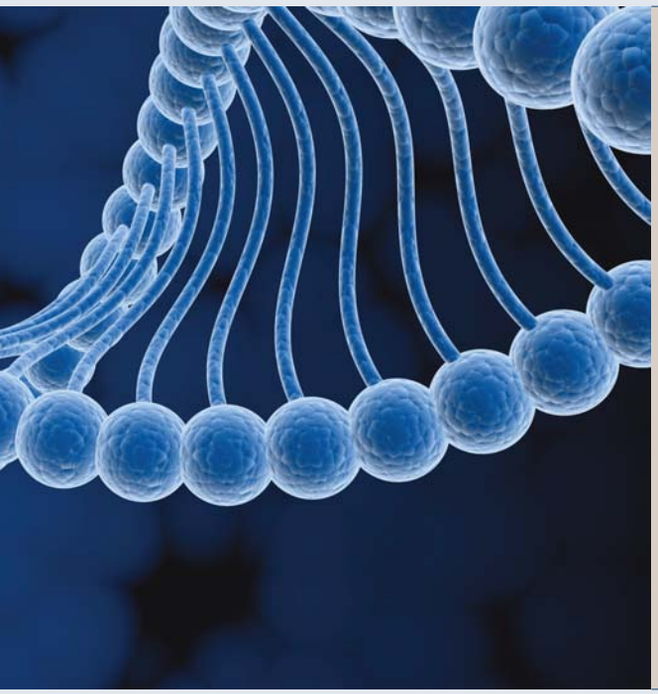
It was a fundamental factor in a very large number of fields relating to the diagnosis of diseases.

What still remains to be done?

We need to learn about the structure of many genes, how they behave, and so on. Many genes act as regulators of other genes. We still need to discover how they are interrelated, and to identify the functions of certain fragments that have already been sequenced. But this work has had some important implications. In the field of pharmacogenetics, for instance, it is known that everyone has their own individual susceptibility to the action of a particular drug, and this will lead to individualized medicine in the near future. There is no reason for one psychiatric patient who is taking an anti-depressive treatment to receive the same dose as another patient with a different genetic profile.

What is the international scope of genetic research as it applies to the insurance sector, given that insurers need information which they can theoretically use to select their clients?

The recent development of medical genetics as a whole, and of the entire body of knowledge regarding genetics, has taken place in the middle of the Internet era. This has made it one of the most transparent branches of science and one whose consequences for the general public are easier to identify. Work on hereditary diseases or genetic features is being published everywhere. For example, there is a venture called "The Code Genetics" which set out to log the genetic variants for the entire population of Iceland. This is supplying a great deal of information about genetic variants that may cause a predisposition for this or that disease. All of this material has been published. I repeat: genetics is a very transparent science in this regard, and there are no problems when it comes to obtaining data on the incidence of diseases or their prevalence in certain groups among the population.



How are these activities regulated in Spain?
There is no specialist field of medical genetics.

Is there a professional association?
Yes, there are various associations, and many people devote their efforts to this aspect, but the problem is that there is no training program. There are various societies such as the Spanish Association of Human Genetics (AEGH), and (within it) the Association of Medical Genetics (AGM). Then there are two associations within the Spanish Pediatric Society (SEP), which also has a medical genetics section. And there is a prenatal diagnostics section within the Spanish Gynecological and Obstetrics Society (SEGO).

Do all the professionals who practice or research here know one another?
Plenty of them do. But the main problem is that Spain has no officially regulated training in medical genetics, whereas studies in this field are recognized by many countries in the European Union. I think that this is the case in virtually all of them, including Portugal.

What advances shall we witness in genetic research over the coming decades?
Essentially, we shall see the development of drugs that aim to control the expression of genes, or to block genes that are causing a disease.

Will it be possible to control the ageing gene? Is it true that we are genetically programmed to live for 120 years?
Firstly, let's hope that we will be able to control more diseases, including leukemia. There is not one single ageing gene - several different ones are involved. And yes, it is true that life expectancy is continuing to increase. Before antibiotics appeared on the scene, the highest mortality rates were for infectious diseases. After the arrival of antibiotics, mortality due to infectious diseases decreased but there was an increase in mortality caused by other diseases which where unknown until then because people had not experienced them sufficiently. It is possible that we are programmed.

Are treatments in connection with medical genetics very expensive? Might they only be available to the elite?
Yes, they are very expensive. In Spain, they are available to everyone thanks to the public health system, but whether this system can afford the treatments is another question. For example, there are drugs specifically designed for genetic anomalies which could cost as much as EUR 60,000 per week.

Is Spain especially prominent in any particular field of genetic research?
The National Center for Oncological Research (CNIO) is giving an enormous boost to genetic research applied to oncology. There have always been universities focusing on this field, geneticists with sufficient interest in it, and good results. More so in Barcelona than Madrid.

Is the USA still the country of reference as regards genetic research?
Yes. That is basically because it allocates far more money from its budget to research than has been possible elsewhere, and this has enabled the USA to make more progress in diagnostic procedure as well as drugs.

Nowadays, with globalization, how long does it take to get a new treatment? A matter of days or hours?
But it does take time. Being treated by the person who has developed a drug is not the same as treatment by someone who has to learn how to do it. For 99 per cent of diseases or tumors, it is not worth the trouble of going to look for a treatment, but it is still worthwhile in 1 per cent of cases; basically because the USA is a country that invests far more in research than the entire European Union. At the end of the day, the results of this are visible. There is a reason why the best researchers and doctors go there.

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