Healthcare industry BW

Networker advances fight against Huntington's disease

15 years ago researchers in Boston discovered the Huntington gene on chromosome 4 . Among the successful scientists was the young German neurologist Bernhard Landwehrmeyer, who joined the team three months prior to the discovery and who has maintained his interest in Huntington's disease ever since.

As chairman of the European Huntington's Disease Network, the neurologist from Ulm along with colleagues from all over the world is working hard on the development of therapies for this incurable disease. The intense research and coooperation in a close international network combining science, industry, medicine and Huntington's patients is producing its first fruits: the first drugs will be clinically tested within the next five years. The researchers are hoping that the drugs might also be used in far more common neurodegenerative diseases such as Alzheimer's and Parkinson's.

A bigger picture of the human brain

Huntington researcher Prof. Dr. G. Bernhard Landwehrmeyer (Photo: University of Ulm)

Having been part of this magic scientific moment in the Boston laboratory must have been like a calling. Landwehrmeyer, who did his doctorate under Richard Jung in Freiburg, was interested in higher brain functions, but the descriptive science of his initial academic years was not enough for him. "I wanted a bigger picture of the human brain," said the neurologist who has held a C3 professorship in neurology at Ulm University since 2000.

Soon after the discovery, the young German neurologist started to look for the messenger RNA of the gene in somatic cells and the brain. The weeks following the discovery were very exciting. For the first time ever, the researchers had come across a genetic defect in which too many basepairs (CAG

in the first of a total of 64 exons) led to the disease. Nowadays, people who listen to Landwehrmeyer talking about the disease, will soon understand that this neurodegenerative disease confirmed his holistic ideas.

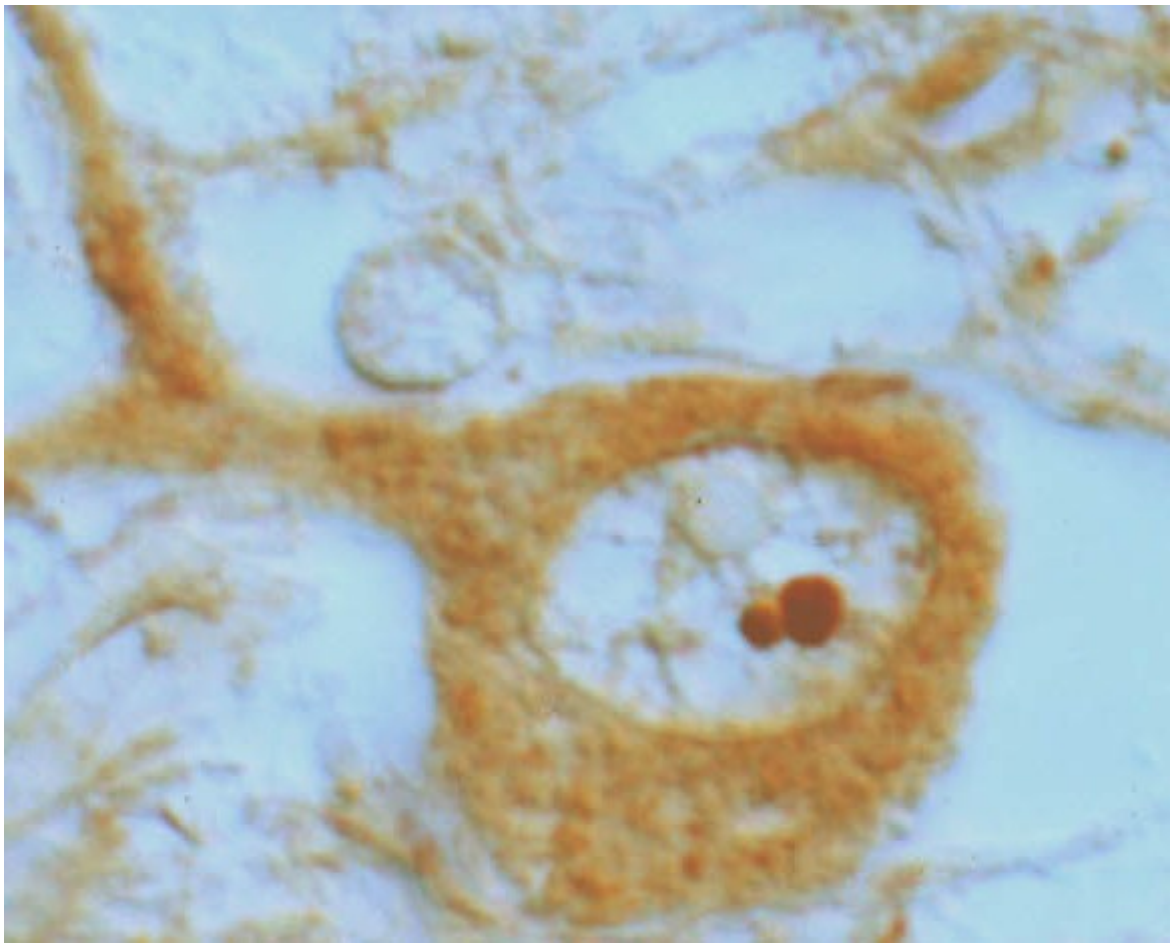
Whole personality required

The fight against this relatively rare inherited disease (10,000 sufferers and 50,000 risk carriers in Germany) involves the commitment of the whole personality – the researcher, doctor, scientific manager and human in Landwehrmeyer. Statisticians may regard the disease as rare, however the extrapolation of the German data soon reaches six-digit numbers: 45,000 Huntington's sufferers in Europe, three times as many risk carriers, and the families of the sufferers.

"This is very moving"

Huntington's disease (HD) affects the whole family ("This is also very moving"), because every child of a person with HD has a fifty per cent risk of contracting the disease. A genetic test can confirm or exclude the risk. Actually, HD goes far beyond the field of medicine and brings together human geneticists, neurologists, psychologists and psychiatrists because the disease quickly leads to severe physical impairments and mental disorders, mental decay and eventually to death.

Treatment of the disease in the symptom-free phase



Nerve cell with inclusion (Photo: European Huntington's Disease Network)

The next goal of the Huntington researcher is to be able to treat the disease at a very early phase before any symptoms are observed because the brain is still able to effectively compensate for the disorder.

Landwehrmeyer hopes that early treatment will prolong quality of life for a longer period. European researchers are working with American and Canadian centres with the aim of identifying neurobiological predictors. In order to test drugs that might delay the breakout of the disease for their effectiveness, it is necessary to find ways and instruments to effectively determine the beginning of HD. For Landwehrmeyer, this type of prevention is also of importance for other neurodegenerative diseases because it would be possible to interfere early enough to prevent damage.

Drug development makes progress

For a long time, the disease reduced the patient to involuntary, dance-like movements. The picture shows St. Veit. Nowadays the term Huntington’s chorea is no longer used. (Photo: European Huntington's Disease Network)

The chances of treating symptom-free Huntington's sufferers are excellent. Since the discovery of the genetic defect, the researchers have found several starting points for treating the disease. On the preclinical level, there are excellent models and reagents, and Landwehrmeyer believes that the conditions for carrying out clinical studies have improved considerably. The specific development of pharmaceuticals is also making progress. The tools of the HD researchers are being improved and refined to the extent that the researchers will no longer have to restrict their research to patients who actually exhibit HD symptoms.

Within the European Huntington's Disease Network, Landwehrmeyer is hoping to carry out reliable

high-quality clinical studies in close connection with basic research, involving for example biomarkers, sophisticated cognitive function tests, quantitative motor tests and imaging methods. Robust and reproducible results are the highest priority.

Current research is also focusing on the development of completely new drugs. It is assumed that these drugs will enter clinical tests within the next five years, and "most probably" not only be used for the treatment of Huntington patients but also for patients suffering from Parkinson's and Alzheimer's. The last two diseases are also caused by deposited and wrongly folded proteins. According to Landwehrmeyer, three of five HD targets can be used for these diseases. Landwehrmeyer also expects progress through a virtual pharmaceutical company that finances an American foundation where academics and scientists from the pharmaceutical industry are working on the selection of clinical test candidates.

USA funds European Huntington's Disease Network

The Ulm neurologist now hopes to accelerate the process of the systematic evaluation of pharmacological targets. This is done in close cooperation with a private, not-for-profit American foundation that has been funding the European Huntington's Disease Network since 2004 and will continue the funding for a total of 10 years. The network is purely result oriented, Landwehrmeyer is pleased to add.

The network now comprises 16 countries and a total of around 130 centres. It is currently working out standards for clinical evaluations and training in close cooperation with HD researchers from the USA and Canada, and it ensures that information is exchanged effectively and rapidly. Language coordinators also guarantee that the results are adequately expressed in the respective languages. The medium-term goal is to establish excellence centres in each country, when for example the drugs currently under development become part of standard care.

When will Europe and Germany catch up?

Landwehrmeyer is hoping that Europe will have increased its research funding in the meantime. At least the US foundation understood the need for a European network. The Ulm researcher is hoping that HD will also find the place it deserves in the new German Dementia Centre in Bonn.

Benefit for general brain research

Brain research also benefits considerably from HD research. For example, through insights gained into the role of basal ganglia (in the frontal brain) for cognitive processes. HD and other age-related diseases have common "final phases", which means that HD drugs can also be used for the treatment of these diseases. According to Landwehrmeyer, HD has, as a prime example of the ethical implications of genetic tests, been a decisive driver in the debate on basic principles.

The neurologist is further concentrating on two objectives: delaying the onset of the disease in terms of a person's age, and continuing the cooperation between basic researchers, industry and clinicians through the European network in order to transfer results to other areas of neurology.

The physician and researcher Landwehrmeyer has found a "happy and satisfying combination" in his intense research into Huntington's disease. The researcher finds his motivation for laboratory work from his contact with patients: "This gives something back to the clinical researcher."

Walter Pytlik, 15th May 2008

Article

01-May-2008
BioRegionUlm

More information