AXON Neuroscience SE

AXON Neuroscience successfully translates ground-breaking discovery of Achilles heel of tau protein into clinical trials

In 1988, Michal Novak, Claude Wischik, Cesar Milstein and Aron Klug from Laboratory of Molecular Biology, MRC, Cambridge, UK, discovered that tau protein is the main component of neurofibrillary tangles, the hallmark of Alzheimer´s disease (AD). In 1991, Michal Novák found that some incorrectly truncated forms of tau protein acquire pathological properties leading to nerve cell death. Using a wide variety of specific antibodies, he demonstrated the existence of uniquely truncated forms of tau protein formed only in the course of Alzheimer's disease. Michal Novak anticipated that these forms, named them tauons, could contribute to the disease development.

tau proteins start to stick to each other and to normal tau proteins forming large clusters filling the space within nerve cells, eventually leading to their death. These critical sections of tau protein were then used to prepare a vaccine, which was tested on experimental animal models. The vaccine had a significant therapeutic effect and prevented formation of deadly fibers, resulting in an improvement in the health of the animals. Importantly, vaccine was shown to be immunogenic in mice, rats and rabbits. The immune response was TH2 dominated with a high IgG1 to IgG2a ratio suggesting the safe desired humoral response.

AXON therapeutic approaches and strategies are going beyond the treatment of symptoms and **target key disease modifications.**

In 1999, Michal Novak co-founded AXON Neuroscience. Based on the discovery of truncated tau proteins, the company created the first rat model that expressed these pathological forms of tau protein in the brain. The animal model developed the neurofibrillary tangles in the brains similar to those observed in Alzheimer's disease brain.

In a second major breakthrough, the team identified key regions of tau protein – Tau´s Achilles´ heel, that tend to change their spatial arrangement at the moment of tau protein truncation. They found that, as a result of this change, individual truncated

AXON Neuroscience has successfully transformed hypothesis driven research into the first active vaccine for AD patients treating the neurodegeneration caused by accumulation of disease modified tau protein. The first phase of human clinical trials started in July 2013, featuring a three month double blind design followed by a three month open labelled study with administration of up to six doses of AADvac1.

AXON Neuroscience's active vaccine brings a new revolutionary look at AD treatment and highlights the importance of tau protein as a key causative factor of Alzheimer's disease.

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History of AXON Neuroscience

1988

Michal Novak, while working with three Nobel Laureates, Cesar Milstein, Aaron Klug and John Walker at MRC LMB Cambridge, UK, was instrumental for the creation of the monoclonal antibody (MN423) allowing discovery of tau protein as an integral constituent of neurofibrillary tangles – the major hallmark of Alzheimer's disease

1991

Michal Novak discovered tau truncation as the most productive post-translational modification in Alzheimer's disease and simultaneously designated truncated tau as a driving force of the neurofibrillary degeneration in Alzheimer's disease

1994

Michal Novak proposed that truncated tau species display features similar to prions and therefore he designated them as tauons

1999

AXON Neuroscience, a biotech company focusing on Alzheimer's disease therapy, was founded (Michal Novak was a co-founder of the company)

2001

AXON discovered and characterized a particular form of the truncated tau protein with a causal role in AD – Alzheimer tau

2003

AXON developed the first AD transgenic rat model and validated Alzheimer tau as a major cause of AD neurodegeneration. The model was presented in July 2004 in the "Hot Topic Session" at the 9th International Conference on AD (ICAD), Philadelphia

2007

AXON initiated a revolutionary immunotherapy program

2009

AXON discovered the most vulnerable area of Alzheimer tau - the Achilles heel of Alzheimer tau

2009

Using knowledge of the 3D structure of the Alzheimer tau Achilles heel, AXON produced tau peptide vaccines

2009 - 2011

AXON confirmed the in vivo efficacy of the vaccines in preclinical studies using AD transgenic rat models

2012

AXON started a GMP vaccine production and finished its GLP toxicology and safety pharmacology studies

2013

AXON presented its therapeutic strategies at the international conference AD/PD 2013 in Florence

2013

Phase 1 clinical trials has begun in the 2nd quarter of 2013

2013

AXON has started humanisation of the AADvac2 Vaccine

2014

AXON has started the preparation of the study design for Phase 2 clinical trials on AADvac1

Mission

The mission of AXON Neuroscience is to discover and develop disease-modifying immunotherapy for the treatment of Alzheimer's disease thus enhancing health and quality of life of Alzheimer's sufferers.

Main inventions:

1. Misfolded truncated tau protein – major constituent of neurofibrillary degeneration in AD
2. Alzheimer tau – novel drug target for AD therapy
3. Achilles heel of Alzheimer tau – the most vulnerable region responsible for inducing pathological tau-tau interactions
4. Active and passive disease-modifying vaccine for AD therapy

Michal Novak

Michal Novak M.D., Ph.D., is a neuroscientist, immunologist and educator. He is currently a professor and founding director of the Institute of Neuroimmunology at the Slovak Academy of Sciences, Bratislava, Slovakia. He has devoted twenty-six years of his career to the research of Alzheimer's disease. He published more than 135 research papers which have been cited more than 3500 times.

A major part of his work has been performed at the MRC Laboratory of Molecular Biology in Cambridge, UK and at ISAS Trieste, Italy. He was a member of the international research teams led by Nobel Prize laureates Sir Aaron Klug and Cesar Milstein. The group discovered that pathologically modified brain protein tau constitutes one of the major hallmarks of Alzheimer's disease – neurofibrillary tangles.

Prof. Novak was International Scholar of the Howard Hughes Medical Institute, Maryland, USA (1995 – 2000) and received grant awards from Human Frontiers Science Organization, Strasbourg, France, and from Howard Hughes Medical Institute.

Prof. Novak is a Founding President of the Slovak Alzheimer's Society (1998), and a co-founder and President of the Slovak Society for Neuroscience (2008). He is the head of the Centre of Excellence for Brain Research which was established to coordinate the collaborative international programs in the Slovak Republic. He was the member of the Executive Committee of the Federation of European Neuroscience Societies (FENS) and the chairman of the FENS-IBRO summer school program (2008 -2012). Prof. Novak is a member of the board of the EU Joint Programme - Neurodegenerative Disease Research (JPND).

In 1999, Prof. Novak co-founded biotech pharma company AXON Neuroscience. The company aimed at the development of disease modifying immunotherapeutics against pathological forms of tau protein in Alzheimer's disease.

AXON Neuroscience Scientific Record

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