

AXON Neuroscience SE

AXON Neuroscience is a biotech company devoted to developing of disease modifying immunotherapy for Alzheimer's disease and related tauopathies.

In 1988, Michal Novak, Claude Wischik, Cesar Milstein and Aron Klug from the Laboratory of Molecular Biology, MRC, Cambridge, UK, discovered that tau protein is the main component of neurofibrillary tangles, the major correlates of cognitive decline in Alzheimer's disease (AD).

In 1991, Michal Novák found that some incorrectly truncated forms of tau protein acquire pathological properties leading to degeneration of nerve cells. Using a plethora of specific antibodies, he demonstrated the existence of uniquely truncated forms of tau protein formed only in the course of Alzheimer's disease and other tauopathies. Michal Novak anticipated that these forms, which he named tauons, could contribute to the development of the disease.

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 an immunotherapy, active vaccine AADvac1 and passive vaccine AADvac2, which were tested on rat and mouse models. The vaccines had a significant therapeutic effect and prevented neurons from degeneration, resulting in an improvement in the health of the animals. Importantly, the active 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 Neuroscience has a world leading position in development of tau active and passive immunotherapeutics for treatment of Alzheimer's disease and related tauopathies.

In 1999, Michal Novak co-founded AXON Neuroscience. Based on the discovery of truncated tau proteins, the company created rat and mouse models that expressed these pathological forms of tau protein in the brain. The animal models developed the neurofibrillary tangles in brains similar to those observed in Alzheimer's diseased brain. 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. The team also found that, as a result of this change, individual truncated tau proteins start to stick

AXON Neuroscience has successfully transformed hypothesis driven research into the first-in-man tau active vaccine for patients suffering from Alzheimer's disease and related tauopathies. The first phase of human clinical trials started in July 2013 and was completed in April 2015. The Phase II Clinical trial is ready to launch in the third quarter of 2015.

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.

AXON Therapy

Kontsekova E, Zilka N, Kovacech B, Skrabana R, Novak M.

Identification of structural determinants on tau protein essential for its pathological function: novel therapeutic target for tau immunotherapy in Alzheimer's disease.

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First-in-man tau vaccine targeting structural determinants essential for pathological tau-tau interaction reduces tau oligomerisation and neurofibrillary degeneration in an Alzheimer's disease model.

Alzheimers Res Ther. 2014 Aug 1;6(4):44.

Zilka N, Kontsekova E, Novak M.

Chaperone-like antibodies targeting misfolded tau protein: new vistas in the immunotherapy of neurodegenerative foldopathies.

J Alzheimers Dis. 2008 Oct;15(2):169-79.

AXON Animal Models

Filipcik P, Cente M, Zilka N, Smolek T, Hanes J, Kucerak J, Opattova A, Kovacech B, Novak M.

Intraneuronal accumulation of misfolded tau protein induces overexpression of Hsp27 in activated astrocytes.

Biochim Biophys Acta. 2015, 1852(7):1219-1229.

Jadhav S, Katina S, Kovac A, Kazmerova Z, Novak M, Zilka N.

Truncated tau deregulates synaptic markers in rat model for human tauopathy.

Front Cell Neurosci. 2015, 23;9:24.

Filipcik P, Zilka N, Bugos O, Kucerak J, Koson P, Novak P, Novak M.

First transgenic rat model developing progressive cortical neurofibrillary tangles.

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AXON Neuroproteomics

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Liquid chromatography-tandem mass spectrometry method for determination of panel of neurotransmitters in cerebrospinal fluid from the rat model for tauopathy.

Talanta. 2014 119:284-90.

Jadhav S, Zilka N, Novak M.

Protein truncation as a common denominator of human neurodegenerative foldopathies.

Mol Neurobiol. 2013 48(3):516-32.

Zilka N, Kovacech B, Barath P, Kontsekova E, Novak M.

The self-perpetuating tau truncation circle.

Biochem Soc Trans. 2012; 40:681-686

Skrabana R, Cehlar O, Flachbartova Z, Kovac A, Sevcik J, Novak M.

Crystallization and preliminary X-ray diffraction analysis of two peptides from Alzheimer PHF in complex with the MN423 antibody Fab fragment.

Acta Crystallogr Sect F Struct Biol Cryst Commun. 2012, 68(Pt 10):1186-90.

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Misfolded Truncated Protein tau Induces Innate Immune Response via MAPK Pathway.

J Immunol. 2011; 187:2732-2739

Kovacech B, Novak M.

Tau Truncation is a Productive Posttranslational Modification of Neurofibrillary Degeneration in Alzheimer's Disease.

Curr Alz Res. 2010; 7: 708-716

Skrabana R, Dvorsky R, Sevcik J, Novak M.

Monoclonal antibody MN423 as a stable mold facilitates structure determination of disordered tau protein.

J Struct Biol. 2010; 171: 74-81

Kovacech B, Zilka N, Novak M.

New age of neuroproteomics in Alzheimer's disease research.

Cell Mol Neurobiol. 2009; 29:799-805

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

2003

AXON Neuroscience developed the first AD transgenic rat model and validated Alzheimer tau as a major cause of AD neurodegeneration. The model was presented in July 2014 in the „Hot Topic Session" at the 9th International Conference on AD (ICAD), Philadelphia

2007

AXON Neuroscience initiated a revolutionary immunotherapy program

2009

AXON Neuroscience discovered the most vulnerable area of Alzheimer tau – the Achilles heel of Alzheimer tau. Based on detailed 3D structure of the Alzheimer tau Achilles heel, AXON produced tau peptide vaccines

2009 – 2011

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

2012

AXON Neuroscience started a GMP vaccine production and finished its GLP (good laboratory practise) toxicology and safety pharmacology studies

2013

AXON Neuroscience presented its therapeutic strategies at the international conference AD/PD 2013 in Florence (March 6-10, 2013)

First-in-man clinical trial with the first active immunotherapy directed against neurofibrillary tau pathology in Alzheimer's disease has started

2014

AXON Neuroscience and MRC Technology announced successful humanization of Anti-Tau Monoclonal Antibody for Alzheimer's disease therapy – AADvac2

2015

AXON Neuroscience successfully finished Phase 1 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 and related human tauopathies.

Main inventions

1.

Misfolded truncated tau protein – major constituent of neurofibrillary degeneration in AD

2.

Truncated tau as an infectious agent spreading cell-to-cell along specific networks

3.

Achilles heel of Alzheimer tau – the most vulnerable region responsible for inducing pathological tau-tau interactions

4.

Active disease-modifying vaccine for AD therapy and other tauopathies

5.

Humanized passive vaccine targeting Achilles heel on tau protein for AD therapy and other tauopathies

Michal Novak



Michal Novak DVM., 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-eight-years of his career to the research of Alzheimer's disease. He published more than 150 research papers which have been cited more than 4500 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 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). He is the coauthor of JPND Strategic Research Agenda that represents a milestone in AD research. He was also principal investigator of the project JUMPAHEAD - Coordination Action in support of the implementation of a Joint Programming Initiative for Combating Neurodegenerative Diseases, in particular Alzheimer's disease (FP7-HEALTH).

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 and other tauopathies.