

Compositions and methods for treatment and diagnosis of neurodegenerative diseases - synucleinopathies

Aarhus University

October, 2009

Technical Field

Biotechnology – health, medico-technical

Pathogenesis of α -synucleinopathies, comprising neurodegenerative diseases:

- Parkinson disease
- Dementia with Lewy bodies
- Multiple system atrophy
- Lewy body variant of Parkinson disease.

Business opportunity

- Research collaboration. Early stage invention. Influence on research development and IPR is possible
- Licensing opportunity.

Current state of technology

The invention will require 2 years further development and would follow the following steps:

- Validation of data from gene chip
- Testing functional significance of validated genes
- Testing if functional genes are upregulated in pathological human brain tissue
- Testing in an animal model: block expression and test for protection.

Applications

- Diagnosis equipment
- Treatment
- Drug target identification
- Biomarkers.

Commercial Value

The invention will give opportunity to identify novel neuroprotective targets in the group of neurodegenerative based on identified gene responses and identify novel biomarkers of disease development and progression. In 2006, Parkinson's disease patient population alone accounted for 2m sufferers.

The disorder's prevalence is constantly increasing with a growth rate of 2.8% and an anticipated patient population of 2.4m in 2012. In 2006 the global market sales for the treatment of Parkinson's disease represented \$2.9bn*.

In addition treatment with current available drugs only address the motor symptoms of the patients and not the ongoing underlying nerve cell killing disease process. These treatments only offer temporarily relief and are insufficient on the long term basis.

Accordingly, there is a highly potent market for advanced drug candidates offering neuroprotection, which may slow disease progression and potentially even inhibit development of symptoms if the patients can be identified in the presymptomatic phase.

The Technology

Using this invention an early detection of neurodegenerative disorder or predisposition to neurodegenerative disorder is possible. A regulation of the involved genes will permit to treat, retard, prevent or ameliorate the development of the degenerative process and ensuing symptoms.

The invention consist in investigating genes that are induced early during alpha-synuclein aggregate mediated degeneration. From cellular model, it has been proven that silencing of two of the genes protects the cells against the alpha-synuclein mediated toxicity. The genes being upregulated early during the degenerative process have been patented.

Intellectual Property Rights

A Danish patent application has been filed in April, 2009 and has received the patent number PA 2009 00456. The patent application is unpublished. Aarhus University is the full owner of the all Intellectual Property Rights.

Inventors

Poul Henning Jensen



Professor, dr.med., cand. Med

Poul Henning Jensen is professor and head of the Institute of Medical Biochemistry at the University of Aarhus,

In 1994 he established the Neurodegenerative Group on the Institute of Medical Biochemistry that focuses on Parkinson's disease and related diseases. The group has exploited the strong knowledge generated by clinical genetics and the humane genome project to focus on key molecular players in neurodegenerative processes, in particular the gene products alpha-synuclein and parkin and their up- and downstream pathogenic pathways. This has been done by the use of a broad range of complementary techniques and an extensive network of collaborators. The result has been publications that comprise data ranging from the molecular level to the analysis of human brain tissue within single publications, and which has given a leading role in Denmark within this area. The group is engaged in extensive collaborations, as documented in the list of publications, with numerous national and international groups of complementary scientific skills. The group is partner in the Nordic Center of Excellence in Neurodegeneration established for 5 years from 2005 by the joint committee of the Nordic Medical Research Councils and two EU funded networks.

Poul Henning Jensen has published more than 60 original papers and 10 reviews



Christine Lund Kragh

Ph.D. in Medical Science, Cand. Scient.

Christine Lund Kragh graduated as Ph.D. on Medical science in 2009 at the University of Aarhus, after formerly having received a Master of Science in Biomedicine from University of Southern Denmark.

She joined the Neurodegenerative Group on the institute of Medical biochemistry in 2002.

Christine Lund Kragh has published 3 papers.

References

- Katerina E. Paleologou, Christine L. Kragh, David M. A. Mann, Sultan A. Salem, Rania Al-Shami, David Allsop, Ahmed H. Hassan, Poul H. Jensen, Omar M. A. El-Agnaf. Detection of elevated levels of soluble α -synuclein oligomers in post-mortem brain extracts from patients with dementia with Lewy bodies (2009), *Brain*. 2009 Apr;132(Pt 4):1093-101.
- Kragh, C.L., Jensen, P.H. 2009, "Novel proteins in α -synucleinopathies", in *Focus on Structural Biology*, vol. 7, Springer Science+Business Media B.V., s. 207-224. Review
- Christine L. Kragh, Louise B. Lund, Fabia Febbraro, Hanne D. Hansen, Wei-Ping Gai, Christiane Richter-Landsberg, Poul Henning Jensen. α -synuclein aggregation and Ser129 phosphorylation dependent cell death in oligodendroglial cells (2009), *J Biol Chem*. 2009 Apr 10;284(15):10211-22.
- Kleinnijenhuis, A.J., Hedegaard, C., Lundvig, D.M.S., Sundbye, S., Issinger, O.G., Nørregaard Jensen, O., Jensen, P.H. 2008, "Identification of multiple posttranslational modifications in the porcine brain specific p25 α ", *Journal of Neurochemistry*, vol. 1006, s. 925-933.
- Kirik, D., Gai, W.-P., Jensen, P.H. 2009, "Is alpha-synuclein the culprit of the Parkinsonian neurodegeneration?", *Experimental Neurology*, vol. 209, s. 3-4.
- Power, J.H.T., Asad, S., Chataway, T.K., Chegini, F., Manavis, J., Temlett, J.A., Jensen, P.H., Blumbergs, P.C., Gai, W.P. 2008, "Peroxiredoxin 6 in human brain: Molecular forms, cellular distribution and association with Alzheimer's disease pathology", *Acta Neuropathologica*, vol. 115, s. 611-622.
- Goldbaum, O., Jensen, P.H., Richter-Landsberg, C. 2008, "The expression of tubulin polymerization promoting protein TPPP/p25 α is developmentally regulated in cultured rat brain oligodendrocytes and affected by proteolytic stress", *Glia*, vol. 56, s. 1736-1746.
- Fjorbak, A.W., Varming, K., Jensen, P.H. 2007, "Determination of alpha-synuclein concentration in human plasma using ELISA", *Scandinavian Journal of Clinical and Laboratory Investigation*, vol. 67 nr. 4, s. 431-5.
- Lindersson E, Lundvig D, Petersen C, Madsen P, Nyengaard JR, Højrup P, Moos T, Otzen D, Gai WP, Blumbergs PC, Jensen PH. "P25 α stimulates α -synuclein aggregation and is co-localized with aggregated α -synuclein in α -synucleinopathies". *J Biol Chem*. 2005 Feb 18;280(7):5703-15

* Business Insights Ltd, reports



AARHUS UNIVERSITET

Contactperson:

Kristine Kjer Hansen

University of Aarhus

Phone: + 45 8942 6864

E-mail: kkh@adm.au.dk