



Press Release – Science

Leuven – 19 March 2009

Progress toward an Alzheimer's drug that saves brain cells

Leuven – VIB scientists connected to the K.U.Leuven have identified a molecule that can form the basis for a new therapy for Alzheimer's disease. This is the first step toward a medicine that could actually stop the progress of Alzheimer's. Existing medicines can at best limit the loss of memory during the first phases of the disease. The authoritative journal *Science* is publishing the results of this research. A first step, however, is still a long way from an approved drug – even if everything goes well, it will be another 15 years before the medicine becomes available.

Alzheimer's disease

Alzheimer's disease is the most prevalent form of dementia in the Western world. The disease's harmful effects on memory and mental functioning make it one of the most terrifying syndromes. It is estimated that, by 2010, our country will have more than 150,000 Alzheimer's patients. At present, this disease is still incurable. Today's medicines for Alzheimer's patients sustain the memory functions for a short time, but they do not stop the brain's cells from dying off.

Plaques and the γ -secretase complex

A typical characteristic of the brains of Alzheimer's patients is the presence of amyloid plaques, which are abnormal accumulations of the β -amyloid protein between the neurons. The sticky β -amyloid arises when the amyloid precursor protein is cut into pieces incorrectly.

The γ -secretase complex – which cuts proteins at a specific place – plays a major role in the creation of these plaques. However, this complex (group of proteins that work together) is also involved in the regulation of a series of other essential proteins such as Notch, which plays a crucial role in the development of an embryo. This is why many of the medicines in development that act on the whole γ -secretase complex run up against toxic side effects.

Aph1B

Under the direction of **Bart De Strooper**, and in collaboration with researchers in other countries, **Lutgarde Serneels, Jérôme Van Biervliet** and their colleagues have been studying the γ -secretase complex in a variety of tissues. They have now been able to demonstrate that the complex assumes a different shape and function according to the tissue in which the secretase is active. For their research on Alzheimer's disease, the researchers have used mouse models. They have found that deactivating the variant, **Aph1B** γ -secretase, in Alzheimer mice leads to reduced formation of the plaques, without any harmful side effects.

Importance of the research

With this discovery, the researchers are once again opening a way toward the development of medicines that deactivate γ -secretase. By concentrating on a variant of the complex that cuts proteins specifically in the brain – the **Aph1B** γ -secretase complex – the formation of the plaques can be prevented, while the other functions of γ -secretase are not affected. This raises hopes for a drug that, for the first time, will succeed in stopping Alzheimer's disease. Furthermore, because the toxic side effects have been cut away, it could also be administered preventively to persons with a risk of Alzheimer's. However, such a medicine will still require at least a good 15 years of further research and development.

Given the fact that γ -secretase is also involved in the onset of certain cancers, research on the various variants of γ -secretase can lead to new insights into these diseases as well.



Questions

Given that this research can raise a lot of questions, we ask you to please refer questions in your report or article to the e-mail address that VIB makes available for this purpose: patienteninfo@vib.be. Everyone can submit questions concerning this and other medically-oriented research directly to VIB via this address.

Relevant scientific publication

This research is being published in the authoritative journal *Science* (Serneels *et al.*, γ -secretase Heterogeneity in the Aph1 Subunit: Relevance for Alzheimer's Disease).

Funding

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Mention both VIB and the university

When reporting this research, please always mention VIB as well as the university concerned.

Note to the Editor

This research has been conducted by **Lutgarde Serneels, Jérôme Van Biervliet** and their colleagues in VIB's Department of Molecular and Developmental Genetics at the Katholieke Universiteit Leuven, under the direction of **Bart De Strooper**.

(More info at: www.vib.be/Research/EN/Research+Departments/Department+of+Molecular+and+Developmental+Genetics)

VIB

VIB is a non-profit research institute in the life sciences. Some 1100 scientists and technicians conduct strategic basic research on the molecular mechanisms that control the functioning of the human body, plants, and micro-organisms. Through a close partnership with four Flemish universities – Ghent University, the Katholieke Universiteit Leuven, the University of Antwerp, and the Vrije Universiteit Brussel – and a solid investment program, VIB unites the forces of 65 research groups in a single institute. Their research aims at fundamentally extending the frontiers of our knowledge. Through its technology transfer activities, VIB strives to convert the research results into products for the benefit of consumers and patients. VIB also develops and distributes a broad range of scientifically substantiated information about all aspects of biotechnology. More info at: www.vib.be.

K.U.Leuven

The Katholieke Universiteit Leuven, founded in 1425, is one of the oldest universities in Europe. The university offers a wide range of programs of study, in Dutch as well as in English. In addition, the K.U.Leuven is an international management research center, with a good balance between fundamental and applied research in a variety of disciplines. The university has over 33,000 students, a tenth of which come from abroad. Over 17,000 people work at the university, about half of whom are employed by UZ Leuven, the university hospitals. More info at: www.kuleuven.be

For more information

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