

## Press Release – Science

Antwerp, Belgium – 19 April 2006

### ***Researchers discover a new genetic cause of Alzheimer's disease***

**Antwerp, Belgium – Researchers from the Flanders Interuniversity Institute for Biotechnology (VIB) connected to the University of Antwerp are the first to show that changes in the promoter region of the amyloid protein lead to a higher production of this protein. This is a major risk factor for Alzheimer's disease. Amyloid protein has already been known to be the primary component of the senile plaques in the brains of patients. The new discovery demonstrates that the greater the quantity of the protein that is produced, the younger the dementia patient is.**

#### **Alzheimer's disease**

Alzheimer's disease is a memory disorder that affects up to 70% of all dementia patients. In Belgium, about 100,000 people suffer from this disease. The disease gradually destroys brain cells in the deep areas of the brain that are responsible for memory and knowledge. Ever since the disease was first reported by Alois Alzheimer – 100 years ago now – scientists have been searching diligently for ways to treat it.

#### **Amyloid plaque formation plays a key role**

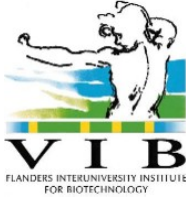
Genetic research has previously shown a direct connection between amyloid protein and the development of senile plaques and loss of cells. Amyloid protein originates when it is cut by enzymes from a larger precursor protein. In very rare cases (fewer than 1 in 1000 patients), mutations appear in that amyloid precursor protein, causing it to change shape and be cut differently. The amyloid protein that is formed now has different characteristics, causing it to begin to stick together and precipitate as amyloid plaques. The development of amyloid plaques in the brain tissue of Alzheimer patients is a central factor in the search for a therapy for Alzheimer's disease.

#### **A lot or not much of the amyloid precursor protein is a risk factor**

The fact that patients with Down syndrome get Alzheimer's disease shows that the quantity of the amyloid precursor protein contributes to the disease: in fact, patients with Down syndrome have 3 copies of the gene (or hereditary code) for the amyloid precursor protein and therefore produce 150% instead of 100% of the protein.

So, **Jessie Theuns** and her colleagues, under the direction of **Christine Van Broeckhoven**, hypothesized that the quantity of amyloid precursor protein might also play a role in Alzheimer's disease. The geneticists from Antwerp systematically studied the hereditary code that is responsible for controlling the expression of the gene (= promoter). Biological processes in our body are strictly regulated, primarily by closely controlling the amount of each protein that is produced. The promoter of a gene has the most important control function in this process.

In younger Belgian and Dutch Alzheimer's patients (younger than 70), the researchers found genetic variations in the promoter that increased the gene expression and thus the formation of the amyloid precursor protein. These variations in the promoter that increase expression occur up to 20 times more frequently (2 per 100 patients) than the mutations in the precursor protein that change the shape. Furthermore, there is a connection with the age at which the symptoms are first detected: the higher the expression (up to 150% as in Down syndrome), the younger the patient (starting between 50 and 60 years of age). Thus, the amount of amyloid precursor protein is a genetic risk factor for Alzheimer's disease in the ageing process.



### **Prospects for tests and treatments**

These new findings lead to a new understanding: namely, that the quantity of the amyloid precursor protein, and thus of the amyloid protein, in brain cells contributes significantly to the risk of contracting Alzheimer's. This discovery will have to be taken into account in diagnostic tests and in the search for new medicines.

### **Relevant scientific publication**

The research results of Christine Van Broeckhoven's group will appear in June in the authoritative scientific journal *The American Journal of Human Genetics* ("Promoter Mutations that Increase Amyloid Precursor-Protein Expression are Associated with Alzheimer's Disease"; Theuns *et al.*, *The American Journal of Human Genetics*, 2006). An electronic version of the publication is available via the journal's website.

### **Funding**

This research is being funded by VIB and the private research funds of the University of Antwerp, as well as via external national and international funding from IWT, FWO, the Alzheimer Research Foundation, the European Commission, and the Alzheimer Association (USA).

### **Note to the Editor:**

VIB, the Flanders Interuniversity Institute for Biotechnology, is a research institute where 850 scientists conduct gene technological research in a number of life-science domains, such as human health care and plant systems biology. Through a joint venture with four Flemish universities (Ghent University, the Catholic University of Leuven, the University of Antwerp, and the Free University of Brussels) and a solid funding program for strategic basic research, VIB unites the forces of nine university science departments in a single institute. Through its technology transfer activities, VIB strives to convert the research results into products for the benefit of consumers and patients. VIB also distributes scientifically substantiated information about all aspects of biotechnology to a broad public.

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

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(For more info, see:

[www.vib.be/Research/EN/Research+Departments/Department+of+Molecular+Genetics/Christine+Van+Broeckhoven](http://www.vib.be/Research/EN/Research+Departments/Department+of+Molecular+Genetics/Christine+Van+Broeckhoven))