



Press Release – Science

Antwerp, Belgium – 17 July 2006

Researchers find cause of frontotemporal dementia

Antwerp, Belgium – Frontotemporal Dementia (FTD) is the second major form of dementia. Under the direction of *Christine Van Broeckhoven*, researchers from the Flanders Interuniversity Institute for Biotechnology (VIB) affiliated to the University of Antwerp have recently discovered that the *progranulin* growth factor plays an important biological role in the development of this form of dementia. Because *progranulin* is known primarily for its role in tumor formation, this research result is very surprising. Although *progranulin*'s proper role in the brain is not yet known, it may well be responsible for the survival of brain cells, because FTD patients have a shortage of this growth factor. The new finding predicts that *progranulin* might also play a role in other types of brain diseases in which brain cells die off – such as Alzheimer's disease and Parkinson's disease.

Frontotemporal dementia

After Alzheimer's, frontotemporal dementia is the most prevalent form of dementia in patients younger than 65. FTD affects the frontal lobe, causing the brain tissue to die off. The frontal lobe is the foremost part of the brain and accounts for about 30% of the brain's mass. Among other things, the frontal lobe is involved in regulating behavior, movement and mood, and is responsible for cognitive functions like memory and speech. So, FTD is clinically characterized by changes in personality and, in a later stage, loss of cognitive functions.

Looking for the needle in the haystack

Genetic research has previously shown that FTD is caused by a defect in chromosome 17. Chromosome 17 is the carrier of the tau protein's hereditary code, and defects in this protein cause tau-positive FTD. However, there is another form of FTD that occurs much more frequently than tau-positive FTD – namely, ubiquitin-positive FTD (FTDU). Patients with FTDU do not have a defect in the tau protein, but in another protein in chromosome 17. **Christine Van Broeckhoven's** research team has now identified this protein: *progranulin*. In order to substantiate this discovery, the group worked intensively with neurologists from university memory clinics in Antwerp, Leuven, and Ghent. Genetic analyses of the DNA from FTDU families identifies defects that cause a shortage of *progranulin*. *Progranulin* is known in cancer research, where a surplus of this protein leads to tumors. What it does in the brain, and how it supports brain cells, is not yet known.

An unexpected turn

The biological role of *progranulin* in the formation of FTD provides a totally new insight into how brain cells die off. **Van Broeckhoven's** team's research indicates that the quantity of *progranulin* in the brain is important for the brain cells' survival. The hereditary defects that the researchers have found in FTD patients cause only 50% of the protein to be produced, because only one copy of the gene is active. Therefore, FTD patients produce less *progranulin* than healthy individuals. It has already been shown that too much *progranulin* leads to cancer – now, these researchers are revealing that *too little progranulin* underlies FTD.



New diagnostic and therapeutic possibilities

This discovery does not directly result in a new remedy for FTD patients – a lot more research is needed for that. But this finding does offer the prospect of a new treatment for FTD and possibly also for other diseases of the brain that entail the dying off of brain cells – like Alzheimer's disease as well as Parkinson's disease. Given that a deficiency of *progranulin* leads to FTD, administration of this protein could offer a simple solution. However, the trick will be to administer the *right* quantity, because too much *progranulin* leads to the formation of tumors. A fine line to navigate! Thanks to this finding, though, upon a doctor's request, a genetic study can be done on FTD patients and their family members if they so desire.

Questions:

The researchers are well aware that this discovery can raise a lot of questions for patients and members of their families. Therefore, we ask you to please mention in your article that questions can be directed to the research nurses working in **Christine Van Broeckhoven's** team: Karin Peeters and Mie Mattheijssens, Tel. +32 3 265 10 35. More information can also be received from the neurologists of the memory clinics involved: P.P. De Deyn (Tel. +32 3 820 26 20, Antwerp), R. Vandenberghe (Tel. +32 16 34 42 80, Leuven), and P. Santens (Tel. +32 9 240 45 29, Ghent). Questions can also be submitted to VIB via e-mail: patienteninfo@vib.be.

Relevant scientific publications:

This research will appear in the authoritative journal *Nature*:

'Null mutations in *progranulin* cause ubiquitin-positive frontotemporal dementia linked to chromosome 17q21', Cruts *et al.*, *Nature*, 2006; and

'Mutations in *progranulin* cause tau-negative frontotemporal dementia linked to chromosome 17', Baker *et al.*, *Nature*, 2006.

Research funding:

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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 K.U.Leuven, the University of Antwerp, and the Vrije Universiteit Brussel) 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.

For more information:

Christine Van Broeckhoven is the head of the Neurodegenerative Brain Diseases research group in the VIB Department of Molecular Genetics at the University of Antwerp. She is also the Scientific Director of this department.

If you have any more questions, please contact VIB's Communication service at: +32 9 244 66 11.