

Press Release – Science

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New treatment for specific type of leukemia

Leuven, Belgium – Leukemia – or cancer of the bone marrow – strikes some 700 Belgians each year. Chronic Eosinophilic Leukemia (CEL), a specific form of leukemia, is currently treated with Glivec. However, recent research has shown that prolonged usage can cause resistance to Glivec, rendering this chronic form of leukemia untreatable. Researchers from the Flanders Interuniversity Institute for Biotechnology (VIB) connected to the Catholic University of Leuven have now discovered that another drug, Sorafenib (Nexavar), works on patients that have developed this resistance. This finding is not only important for CEL patients, but it also provides a new approach for treating specific forms of leukemia. It is clear from this research that a combination of targeted drugs provides a greater chance of lifelong effective treatment.

Chronic Eosinophilic Leukemia (CEL)

Our body's white blood cells combat foreign intruders (such as viruses and bacteria). However, in **chronic leukemia**, the cells in the bone marrow that should develop into white blood cells multiply uncontrollably. These blood cells do not function properly, jeopardizing the production of normal blood cells. Among other consequences, this makes patients more susceptible to infections. Chronic leukemia appears in several forms – in CEL, a rare form of leukemia, the excessive increase of eosinophils (a certain type of white blood cell) can cause tissue damage in the heart, the skin, and the central nervous system.

The mechanism behind the cause

Under normal circumstances, our body regulates the production of white blood cells very precisely by means of a targeted activation of tyrosine kinases, which start this production. But sometimes defects in the DNA cause these tyrosine kinases to be active continuously, giving rise to diseases like leukemia. In 2003, **Jan Cools** and his colleagues under the direction of **Peter Marynen**, along with colleagues **Elizabeth Stover** and **Gary Gilliland** from Boston, discovered that CEL is caused by this kind of defective activation of the tyrosine kinase FIP1L1-PDGFR α . Now, with additional research, they have uncovered the molecular mechanism behind the abnormal activation of FIP1L1-PDGFR α . This new research is being published this week on the website of the scientific journal *PNAS*.

Resistance to the remedy

In the fight against CEL (and other forms of leukemia), scientists use substances that inhibit the tyrosine kinases. Glivec is such an inhibitor and is effective against CEL because it specifically inhibits the activity of FIP1L1-PDGFR α . However, CEL patients must take Glivec every day for the rest of their lives – and recent research shows that, over time, alterations in the DNA can arise, causing resistance to Glivec. The longer Glivec is taken, the greater the chance resistance will develop. At that point, treatment with Glivec is no longer effective.

On the path to a long-lasting effective treatment

This problem prompted VIB researchers **Els Lierman** and **Jan Cools** to look for alternatives. They have found that Sorafenib, another inhibitor, works effectively in treating the resistant form of CEL. Sorafenib is already on the market in the US as a remedy for kidney tumors. This new research indicates that, to be able to treat certain forms of leukemia (like CEL) effectively over a long period of time, several inhibitors must be used, either together or successively. The scientists emphasize the importance of testing known inhibitors for their effectiveness against CEL and other forms of leukemia. This research has recently appeared in the scientific journal *Blood*.



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. Everyone can submit questions concerning this and other medically-oriented research directly to VIB via this address.

Relevant scientific publications

The results of the research reported here appear in the authoritative journals *PNAS* (*Stover et al.*, Activation of FIPL1-PDGFR α requires disruption of the juxtamembrane domain of PDGFR α and is FIP1L1-independent, *PNAS*, 2006) and *Blood* (Lierman *et al.*, Sorafenib (BAY43-9006) is a potent inhibitor of FIPL1-PDGFR α and the imatinib resistant FIP1L1-PDGFR α T674I mutant; *Blood*, 2006).

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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 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.

For more information

Please contact VIB's Communication service

VIB Communication: +32 9 244 66 11

Peter Marynen leads the Applied Human Genomics group in the Department of Human Genetics under the direction of **Guido David** (for more info, see: www.vib.be/Research/EN/Research+Departments/Department+of+Human+Genetics/Peter+Marynen)