Toward a more efficient therapy for a specific form of leukemia

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Chronic myeloid leukemia (CML) is a particular form of leukemia or cancer of the bone marrow, which can be treated with targeted imatinib. However, in some cases this medicine has no effect. Researchers at the VIB Vesalius Research Centre, K.U. Leuven, under the direction of Peter Carmeliet, have investigated the role of placental growth factor (PlGF) in mice with CML. Blocking this growth factor increases the life expectancy of these mice, even in those resistant to imatinib.

In our body, white blood cells combat foreign intruders, such as viruses and bacteria. In chronic myeloid leukemia, the formation of granulocytes, a particular type of white blood cells, is disturbed. The cells in the bone marrow which should grow into white blood cells show an uncontrolled increase in numbers as a result of a disruption in the maturing process. This uncontrolled growth may damage various tissues and adversely affect the production of normal blood cells in the bone marrow. A shortage of white blood cells makes patients more susceptible to infection.

Under normal circumstances, our body very accurately regulates the production of white blood cells. This process is triggered by targeted activation of tyrosine kinase. In most forms of CML, a deviant chromosome is present - the Philadelphia chromosome - which gives rise to BCR-ABL1 fusion kinase. This kinase causes the trouble, leading to the increase in CML cells. Existing medicines (imatinib) therefore target this kinase.

While the effect of imatinib in CML patients is usually quite favorable, the use of imatinib is often not sufficient to remove the diseased cells from the body. Sometimes the disease is already too advanced at the start of treatment, or there is resistance.

Researchers from the team headed by Peter Carmeliet have studied the role of placental growth factor (PlGF) in leukemia and the therapeutic potential of PlGF inhibitors. Recent research conducted by Peter Carmeliet had already shown that antibodies against PlGF (antiPlGF) can inhibit the growth of particular tumors.

The present study proves that PlGF also plays a role in CML. The researchers have recorded increased PlGF values in both mice and humans. It appears that PlGF does not only stimulate the division of CML cells but also encourages the formation of blood vessels in bone marrow. Finally, inhibiting PlGF in mice with CML leads to higher life expectancy, even in those mice that are resistant to the current medicine imatinib. All of these findings indicate that the therapeutic potential of PlGF inhibitors in CML needs to be investigated further.

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