An Antidiabetic Medication For Curing Chronic Myeloid Leukemia

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A stunning discovery, published in the prestigious journal Nature, shows that a medication (pioglitazone) currently used to decrease glycaemia in diabetics also succeeded in curing some patients suffering from chronic myeloid leukemia (CML).

Chronic myeloid leukemia is a form of blood cancer caused by a genetic anomaly in the stem cells responsible for the production of white blood cells within the bone marrow. In most cases, this form of leukemia is derived from an exchange of genetic material between chromosomes 9 and 22, which produces a hybrid called the “Philadelphia chromosome” (in honour of its discovery in that city in 1960). This fusion causes problems because it permits the formation of a powerful oncogene, the tyrosine kinase Bcr-Abl, which supports the uncontrolled growth of white blood cells and thus leads to excessive production of these cells in the blood.

While this disease had been very difficult to treat, the struggle against CML underwent a virtual revolution at the beginning of this millennium with the arrival of targeted therapies, able to specifically block the biological activity of the oncogene Bcr-Abl. Consequently, thanks to imatinib mesilate (Gleevec, commercialized in 2001), followed by dasatinib (Sprycel, 2006) and nilotinib (Tasigna, 2008), it is now possible to slow the uncontrolled growth of these cancerous cells and to control the disease for ever longer periods. Using prolonged administration of these medications, patients who respond well to treatment can thus hope to recover a somewhat more normal existence and a good life expectancy.

TARGETING STEM CELLS

In the vast majority of cases, the inhibitors of Bcr-Abl do not, however, provide a cure for CML. In the presence of these medications, the stem cells responsible for the overproduction of white blood cells become inactive, but they are nevertheless not eliminated: they can thus restart the process of uncontrolled growth if the treatment is interrupted. The patients must therefore be treated for the rest of their lives with these medications, which can prove to be difficult due to the presence of several side-effects (cramps, edema, digestive trouble, weight gain). There is also the risk that the cancerous cells may, over time, acquire resistance to these treatments since the continued presence of these medications exerts an evolutionary pressure which favours the emergence of mutants capable of withstanding the effects of these inhibitors. Eliminating the residual stem cells thus represents the ultimate objective in the war against this form of leukemia.

COMPLETE REMISSION

A major advance in this battle was achieved by a group of French and American scientists’. Based on observations showing that the survival of leukemic stem cells requires the presence of the protein STAT5, they had the brilliant idea of testing the impact of medications already known to drastically reduce this protein, i.e. the antidiabetic class of glitazones.

To examine the effect of one of these antidiabetic molecules, pioglitazone, the researchers first recruited patients who suffered from both CML and type 2 diabetes, and who still had leukemic stem cells after five years of treatment with Gleevec. The results they obtained overwhelmingly confirmed their original hypothesis; adding pioglitazone led to the complete elimination of residual stem cells several months after the beginning of treatment! At the time that the article was released, after five years of following these patients post-treatment, they did not present any clinical signs of CML. These very encouraging results were confirmed by a second study on 24 patients, where 57% of the participants who were treated with the two medications were in complete remission.

According to the scientists, it is still too early to talk of a complete cure, since studies have not yet determined whether the observed remissions can be maintained after halting the targeted therapies. The positive results obtained illustrate, however, the immense potential of this approach, and the elimination of the reservoir of cancerous stem cells represents a major advance in the treatment of leukemia. One more victory in our war against cancer.