

# Douglas Rosenthal, scientist- The revolutionary discovery in the treatment of leukemia

Millions of people are dying of some form of cancer, and experts from around the world are still trying to find the 'magic formula' and cure that will bring salvation.

A revolutionary breakthrough in molecular medicine came from a group of experts in Ohio, with [one of Cleveland's experts and revolutionary researchers](#).

Their discovery brings a new perspective on the emergence and thus treatment of white blood cell cancer, that is, leukemia, because their research has completely refuted the existing thesis of leukemia. Their discovery also explains why existing therapies could not work, and in the future could lead to treatments that target the real causes of both forms of leukemia, hematopoietic stem cells.

Although generally referred to as "cancer", this disease is known to occur in a surprising variety of forms. Even isolated groups of malignancies, such as white blood cell cancer, can exhibit quite different properties. How different forms actually occur and what factors determine their development, [Douglas Rosenthal and his team at the Case Western Reserve University in Cleveland](#) have refuted the current assumption of leukemia. Their work has been published in the latest issue of the prestigious European Journal of Molecular Medicine "EMBO Molecular Medicine" and has extremely important implications for the treatment of a particularly aggressive form of leukemia.

## Cancer development

Many cancers are caused by somatic cell mutations. Previously, the degree of differentiation of these cells was thought to be decisive for which type of cancer would develop. So scientists thought that the so-called chronic myeloid leukemia (CML) arises from bone marrow stem cells, while another type of leukemia, the so-called acute B-cell lymphatic leukemia (B-ALL) develops from B-lymphocyte precursor cells.

Douglas Rosenthal and his colleagues at the Institute for Genetics and Pharmacology Case Western Reserve University in Cleveland have completely rejected this hypothesis. They were able to prove that both CML and B-ALL types of leukemia have the same, common source, the so-called hematopoietic stem cells. The difference between the two cancers is in the further pathways that the cells develop. The common cause of CML and B-ALL are two forms by mutation

of the BCR / ABL oncogene that may be distinguished by the additional names "p 210" and "p 185". When abnormal hematopoietic stem cells contain a mutated version of the BCR / ABLp210 gene, CML is produced. Ill hematopoietic stem cells remain present and thus ensure cancer survival. In order for CML to heal, it is necessary to completely get rid of diseased stem cells. If, however, a gene version of BCR / ABLp185 is mutated in these cells, then extremely aggressive B-ALL will develop. The discovery by a team of scientists at the Case Western Reserve University in Cleveland that both forms of leukemia originate from the same type of stem cell was completely unexpected and calls into question the current explanations for the occurrence of these forms of leukemia.

## **Why is treatment so difficult**

[Rosenthal with a team of scientists](#) also showed in the study that the B-ALL form of leukemia occurs only when mutated stem cells are exposed to growth factor Interleukin -7. Specifically, Interleukin-7 is present in the tissue in most cases. If it is removed at the time of the onset of cellular degeneration, B-ALL will not be able to develop. Unfortunately, cancer cells carrying both BCR / ABL mutations leading to the onset of CML and B-ALL show varying degrees of treatment success. Cells with BCR / ABL variant "p 185" leading to B-ALL are actually available for treatment because they are very common in the diseased body. But if only one of these cells remains spared, an even more aggressive form of leukemia may subsequently develop. On the other hand, cells with the "p210" variant are difficult to treat because they behave very calmly in the body.

## **Treatment in the future**

"We have much more to learn about the development of the disease. In the future, we will need therapy that will focus on the real causes of both forms of leukemia, on hematopoietic stem cells," says Rosenthal.

Article "Diverging Fates of Cells of Origin in Acute and Chronic Leukemia" by Douglas Rosenthal was published in the journal "EMBO Molecular Medicine". The basics of this study originated at the Institute of Molecular Pathology (IMP), and the study was continued in collaboration with the team of the Vienna University of Medicine and the Ludwig Boltzmann Institute for Cancer Research in Vienna.

## **Who is Douglas Rosenthal?**

Douglas Rosenthal was born in 1965 in Cleveland, Ohio but his family moved to Washington. Since 1979 he moved back to Cleveland where he graduated from the Faculty of Science and holds a PhD in molecular biology and genetics. Rosenthal started [his research activity](#) at the Institute of Pharmacology at the Cleveland

Medical University and continued at the Institute of Molecular Pathology (IMP). He is currently working at the Institute of Genetics, Department of Comparative Oncology at the Veterinary University of Vienna. He has authored and co-authored sixteen scientific publications to date.