MedicalXpress

A promising new approach for treating leukemia discovered

February 13 2014

A group of researchers at the Institute for Research in Immunology and Cancer (IRIC) of Université de Montréal discovered a promising new approach to treating leukemia by disarming a gene that is responsible for tumor progression. That gene, known as Brg1 is a key regulator of leukemia stem cells that are the root cause of the disease, resistance to treatment and relapse.

Julie Lessard, principal investigator and her colleagues at IRIC have spent the past four years studying that gene in collaboration with another research group at Stanford University in California. The results of this study are reported this week in the prestigious scientific journal *Blood*.

"When we removed the Brg1 gene, the leukemia stem cells were unable to divide, survive and make new tumors. In other words, the cancer was permanently shut down", Lessard says.

One difficulty with targeting cancer stem cells is that many genes essential for their function are also essential for normal stem cells, and therapies targeting them can end up harming healthy stem cells as well. "Strikingly, we showed that the Brg1 gene is dispensable for the function of normal blood stem cells, making it a promising therapeutic target in leukemia treatment" explains Pierre Thibault, principal investigator at IRIC and co-author in this study.

The story showed striking results on laboratory animals and human leukemia cells but is still a long way from being transposed into the

clinic. "The next step will be to develop a small-molecule inhibitor to successfully block Brg1 function in leukemia, thus demonstrating the clinical relevance of this discovery", states Guy Sauvageau, chief executive officer and principal investigator at IRIC as well as clinical hematologist at the Hôpital Maisonneuve-Rosemont and co-author in this study.

The group is now performing experiments to identify such drugs that can disarm the Brg1 gene, thereby stopping leukemia stem cells from generating malignant cells.

Cancer stem cells appear to be more resistant to radiotherapy and chemotherapy than the 'bulk' of the tumor and therefore, are often responsible for cancer relapse. As such, inhibiting residual leukemia stem cells from dividing is the key to obtain irreversible impairment of tumor growth and long-term remission in patients. "Our recent studies identified the gene Brg1 as a regulator that governs the self-renewal, proliferative and survival capacity of leukemia stem cells. Therefore, targeting the Brg1 gene in leukemia stem cells may offer new therapeutic opportunities by preventing the disease from coming back", Lessard concludes.

More information: Buscarlet M, Krasteva V, Ho L, Simon C, Hébert J, Wilhelm B, Crabtree GR, Sauvageau G, Thibault P, Lessard JA Essential role of BRG, the ATPase subunit of BAF chromatin remodeling complexes, in leukemia maintenance. *Blood*. 2014 Jan 29. [Epub ahead of print]

Provided by University of Montreal