MedicalXpress

Small molecule offers big hope against cancer

January 16 2007

DCA is an odourless, colourless, inexpensive, relatively non-toxic, small molecule. And researchers at the University of Alberta believe it may soon be used as an effective treatment for many forms of cancer.

Dr. Evangelos Michelakis, a professor at the U of A Department of Medicine, has shown that dichloroacetate (DCA) causes regression in several cancers, including lung, breast, and brain tumors.

Michelakis and his colleagues, including post-doctoral fellow Dr. Sebastian Bonnet, have published the results of their research in the journal Cancer Cell.

Scientists and doctors have used DCA for decades to treat children with inborn errors of metabolism due to mitochondrial diseases. Mitochondria, the energy producing units in cells, have been connected with cancer since the 1930s, when researchers first noticed that these organelles dysfunction when cancer is present.

Until recently, researchers believed that cancer-affected mitochondria are permanently damaged and that this damage is the result, not the cause, of the cancer. But Michelakis questioned this belief and began testing DCA, which activates a critical mitochondrial enzyme, as a way to "revive" cancer-affected mitochondria.

The results astounded him.

Michelakis and his colleagues found that DCA normalized the

mitochondrial function in many cancers, showing that their function was actively suppressed by the cancer but was not permanently damaged by it.

More importantly, they found that the normalization of mitochondrial function resulted in a significant decrease in tumor growth both in test tubes and in animal models. Also, they noted that DCA, unlike most currently used chemotherapies, did not have any effects on normal, non-cancerous tissues.

"I think DCA can be selective for cancer because it attacks a fundamental process in cancer development that is unique to cancer cells," Michelakis said. "Cancer cells actively suppress their mitochondria, which alters their metabolism, and this appears to offer cancer cells a significant advantage in growth compared to normal cells, as well as protection from many standard chemotherapies. Because mitochondria regulate cell death--or apoptosis--cancer cells can thus achieve resistance to apoptosis, and this appears to be reversed by DCA."

"One of the really exciting things about this compound is that it might be able to treat many different forms of cancer, because all forms of cancer suppress mitochondrial function; in fact, this is why most cancers can be detected by tests like PET (positron emission tomography), which detects the unique metabolic profile of cancer compared to normal cells," added Michelakis, the Canada Research Chair in Pulmonary Hypertension.

Another encouraging thing about DCA is that, being so small, it is easily absorbed in the body, and, after oral intake, it can reach areas in the body that other drugs cannot, making it possible to treat brain cancers, for example.

Also, because DCA has been used in both healthy people and sick patients with mitochondrial diseases, researchers already know that it is a relatively non-toxic molecule that can be immediately tested in patients with cancer.

Furthermore, the DCA compound is not patented and not owned by any pharmaceutical company, and, therefore, would likely be an inexpensive drug to administer, Michelakis added.

However, as DCA is not patented, Michelakis is concerned that it may be difficult to find funding from private investors to test DCA in clinical trials. He is grateful for the support he has already received from publicly funded agencies, such as the Canadian Institutes for Health Research (CIHR), and he is hopeful such support will continue and allow him to conduct clinical trials of DCA on cancer patients.

"This preliminary research is encouraging and offers hope to thousands of Canadians and all those around the world who are afflicted by cancer, as it accelerates our understanding of and action around targeted cancer treatments," said Dr. Philip Branton, Scientic Director of the CIHR Institute of Cancer.

Source: University of Alberta