

## **DCA research on brain cancer**

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Medical Researchers at the University of Alberta reported today evidence that the orphan generic drug Dichloroacetate (DCA) may hold promise as potential therapy for perhaps the deadliest of all human cancers: a form of brain cancer called glioblastoma. The report is published at the journal *Science Translational Medicine*, a journal of the American Association of the Advancement of Science.

In 2007 the U of A team led by Dr. Evangelos Michelakis, published evidence that DCA reverses <u>cancer growth</u> in non-human models and test tubes. The team showed then that DCA achieves these antitumor effects by altering the <u>metabolism</u> of cancer. By altering the way cancer handles its nutrient fuels, specifically the sugars, DCA was able to take away cancer's most important strength, the resistance to death. Since then, several independent groups across the world have confirmed the Alberta team's findings. In December 2009, the editors of "Science" predicted that cancer metabolism is one of only 5 areas across all scientific disciplines, to "watch for major breakthroughs" in 2010.

The U of A team set out to show that the way that DCA works in actual patients is the same with the way it works in the lab. In addition, researchers wanted to show whether DCA is safe and possibly effective in very sick patients with brain cancer.

By extracting glioblastomas from 49 patients over a period of 2 years and studying them within minutes of removal in the operating room, the team showed that tumors respond to DCA by changing their metabolism. Then, the team treated 5 patients with advanced <u>glioblastoma</u> and



secured <u>tumor</u> tissues before and after the DCA therapy. By comparing the two, the team showed that DCA works in these tumors exactly as was predicted by test tube experiments. This is very important because often the results in non-human models tested in the lab do not agree with the results in patients. In addition, the team showed that DCA has anticancer effects by altering the metabolism of glioblastoma cancer stem cells, the cells thought responsible for the recurrences of cancer.

In the 5 patients tested, the drug took 3 months to reach blood levels high enough to alter the tumor's metabolism. At those levels, there were no significant adverse effects. However, at some of the higher doses tested, DCA caused nerve malfunction, i.e. numbing of toes and fingers. Importantly, in some patients there was also evidence for clinical benefit, with the tumors either regressing in size or not growing further during the 18 month study.

No conclusions can be made on whether the drug is safe or effective in patients with this form of brain cancer, due to the limited number of patients tested by the study's leads Drs Michelakis and Petruk. Researchers emphasize that use of DCA by patients or physicians, supplied from for-profit sources or without close clinical observation by experienced medical teams in the setting of research trials, is not only inappropriate but may also be dangerous. The U of A results are encouraging and support the need for larger clinical trials with DCA. This work is also one of the first in humans to support the emerging idea that altering the metabolism of tumors is a new direction in the treatment of cancer, Michelakis and Petruk said.

The research team hopes to secure additional funding to continue the ongoing trials with DCA at the University of Alberta. Further studies would include more patients with <u>brain cancer</u>, and test the combination of DCA and standard chemotherapies, eventually including patients from other academic health sciences centres.



One of the intriguing features of this work was that it was funded largely by public donations, including philanthropic foundations and individuals. In addition, it received strong support by Alberta public institutions, both the University of Alberta and Alberta Health Sciences. The multidisciplinary team that performed this challenging translational research included members of the Departments of Medicine, Diagnostic Imaging and Biomedical Engineering, Oncology and Neurosurgery. Clinicians, scientists, nurses and graduate students worked together for 2 years and express their gratitude to the people of Alberta, philanthropists, the patients and their families.

**More information:** The report appears today at the journal's web site <u>http://www.sciencemag.org/</u>

Provided by University of Alberta

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