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Combination of Viagra and Anti-Cancer Drug Shrinks Tumors in Vivo, Researchers Discover

ScienceDaily (Sep. 29, 2010)

Virginia Commonwealth University School of Medicine and VCU Massey Cancer Center researchers have shown that the impotence drug Viagra (sildenafil), in combination with doxorubicin, a powerful anti-cancer drug, enhances its anti-tumor efficacy in prostate cancer while alleviating the damage to the heart at the same time.

For more than four decades the chemotherapeutic agent doxorubicin has been used to treat a number of human cancers, including that of the prostate. Despite doxorubicin's clinical efficacy for cancer treatment, its use is associated with irreversible heart damage, often presenting several years after treatment stops. Researchers have been working over the past 15 years to find an optimal therapeutic intervention for protecting the heart against the cytotoxicity associated with doxorubicin.

In the study published in the Early Edition of the journal Proceedings of the National Academy of Sciences, researchers using a variety of powerful in vitro and in vivo approaches, have shown that a combination of Viagra, generically known as sildenafil, and doxorubcin significantly enhances the generation of reactive oxygen species that trigger cell death, or apoptosis, in prostate cancer cells. They also observed that the combination did not harm the normal, healthy prostate epithelial cells.

"We believe sildenafil could be an excellent candidate for incorporation into cancer treatment protocols -- with the potential of enhancing the anti-tumor efficacy, while protecting the heart against both short term and long term damage from doxorubicin," said principal investigator Rakesh C. Kukreja, Ph.D., scientific director of the VCU Pauley Heart Center and the Eric Lipman professor in cardiology in the VCU School of Medicine, and Anindita Das, Ph.D., assistant professor in the Department of Internal Medicine the VCU School of Medicine.

Kukreja is excited about the potential translational impact of this work. "My team and I are hoping to move the research forward to a clinical trial and plans are under way to do so," he said. The clinical trial would evaluate the effectiveness of the drug combination in cancer patients.

Kukreja's laboratory is one of the first to explore the area of preconditioning. This preconditioning effect was modeled in his lab by "pretreating" mice with doses of sildenafil which also increases therapeutic levels of nitric oxide in the heart.

A preconditioned or pretreated heart has an improved ability to produce nitric oxide and directly improves a patient's outcome following a heart attack. Generally, damage following a heart attack is related to an inability to recover from lack of oxygen.

The work was supported in part by a MERIT Award to Kukreja from the National, Heart, Lung and Blood Institute of the National Institutes of Health.

Kukreja and Das collaborated with Paul Dent, Ph.D., a research member with the VCU Massey Cancer Center. Also contributing to this work were VCU researchers David Durrant, Clint Mitchell, a postdoctoral fellow in Dent's lab, Eric Mayton, a research assistant in Kukreja's lab, Nicholas N. Hoke, a graduate student in Kukreja's lab, Fadi N. Salloum, assistant professor of Internal Medicine and researcher with the VCU Pauley Heart Center, Margaret A. Park, a postdoctoral fellow with Dent's lab, Ian Quershi, a graduate student in Kurkeja's lab, and Ray Lee, former assistant professor of internal medicine.

Story Source:

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