Novel Drug Cocktail May Improve Clinical Treatment for Pancreatic Cancer

In mice, standard chemo drug plus a new one may be a potent one-two punch

SAN DIEGO (April 27, 2014) – Pancreatic cancer is the fourth leading cause of cancer deaths in the U.S. and has the lowest overall survival rate of all major cancers (~6%). With current treatment options being met with limited success it is anticipated that pancreatic cancer will move up to the second leading cause of cancer deaths by as early as 2015. Surgical removal of the tumor presents the best chance of survival, however only 15% of patients are eligible due to the late stage of diagnosis common with this disease. With very limited improvements in patient outcome over the last two decades there remains an enormous need for new therapies and treatment options.

David Durrant, a Ph.D. student in the laboratory of Dr. Rakesh Kukreja from the Pauley Heart Center at Virginia Commonwealth University’s School of Medicine, is studying a novel combination therapy for the treatment of pancreatic cancer. The traditional chemotherapy drug, doxorubicin (DOX), has long been used in the treatment of several cancers. However, patients commonly acquire resistance to DOX because of increased activation of specific survival proteins or through increased expression of drug transporters which reduce cellular levels of the drug. This is especially true for pancreatic cancer, which does not respond to multiple treatment strategies, including those that contain DOX. The current research focuses on targeting these resistance mechanisms, which could possibly re-sensitize cancer cells to DOX, giving patients with pancreatic cancer another option in their fight against this devastating disease.

In the current study, Mr. Durrant used pancreatic cancer cells to assess the efficacy of combining DOX with a drug that inhibits the survival proteins involved in DOX resistance called BEZ235 (BEZ). The results showed that treatment with the combination of DOX and BEZ had significantly lower rate of surviving pancreatic cancer cells than the cells with single drug treatment. This correlated with the increase in DNA damage and apoptosis (programmed cell death). More interestingly, combining BEZ with DOX caused significantly higher accumulation of DOX in the cancer cells. These results demonstrate a dual function for BEZ i.e., its primary function of inhibiting survival proteins implicated in drug resistance and, a novel function of inhibiting drug export, thereby retaining DOX in the cancer cells. Furthermore, the in vitro effect of combining BEZ and DOX in enhanced killing of cancer cells was confirmed in the in vivo model. Treatment with BEZ and DOX in mice bearing pancreatic tumor xenografts resulted in inhibition of tumor growth as compared to BEZ and DOX alone.

These exciting results of combining BEZ with DOX in enhanced killing of pancreatic cancer cells may lead to clinical trials and potentially facilitate the development of a viable treatment option for patients with pancreatic cancer.
Mr. Durrant will present the findings during the Experimental Biology 2014 meeting on Sunday, April 27 from 12:30 –2:30 p.m. at the Cancer Chemotherapy poster session in Exhibit Halls A-D (Poster #B214) of the San Diego Convention Center.

The study was funded by the American Heart Association and a National Institutes of Health MERIT Award.

###

**About Experimental Biology 2014**

Experimental Biology is an annual meeting comprised of more than 14,000 scientists and exhibitors from six sponsoring societies and multiple guest societies. With a mission to share the newest scientific concepts and research findings shaping clinical advances, the meeting offers an unparalleled opportunity for exchange among scientists from across the United States and the world who represent dozens of scientific areas, from laboratory to translational to clinical research. [www.experimentalbiology.org](http://www.experimentalbiology.org)

**About the American Society for Pharmacology and Experimental Therapeutics (ASPET)**

ASPET is a 5,100 member scientific society whose members conduct basic and clinical pharmacological research within the academic, industrial and government sectors. Our members discover and develop new medicines and therapeutic agents that fight existing and emerging diseases, as well as increase our knowledge regarding how therapeutics affects humans. [www.aspet.org](http://www.aspet.org)

###

**MEDIA CONTACT**

Jim Bernstein  
Cell/Text: 301-646-3259  
jbernstein@aspet.org

**ONSITE NEWSROOM**

San Diego Convention Center  
April 26-30, 2014  
Phone: 619-525-6211