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Inhibition of invasive pancreatic cancer: Restoring cell apoptosis by activating mitochondrial p53

Small molecule potently decreases pancreatic cancer, featured in *American Journal of Cancer Research.*

San Diego, Calif., February 15, 2019 – Researchers at the Human BioMolecular Research Institute, University of California San Diego School of Medicine and ChemRegen, Inc., have reported on a small molecule that potently inhibits pancreatic cancer. Writing January 18, 2019 in the journal *American Journal of Cancer Research*, the team describes how they tested HBRI-**1**, a synthetic, drug-like compound that can be used to decrease pancreatic cancer.

“In the United States, pancreatic cancer is the third leading cause of cancer-related fatalities and will result in an estimated 44,330 deaths during 2018. It has been projected that pancreatic cancer will become the second most prevalent cause of cancer-related death by 2030,” said Jiongjia Cheng, Ph.D., lead author of the study. “Using a non-toxic small molecule to decrease pancreatic cancer is very attractive.”

Medicinal chemistry leads to safe anti-cancer drug

In earlier studies, the team reported on the small molecule that was useful against breast and colon cancer and that might one day become a drug therapy to treat other cancers. Now, a team of medicinal chemists at the Human BioMolecular Research Institute, led by John Cashman, Ph.D., using dynamic medicinal chemistry showed a molecule called HBRI-**1** is useful against pancreatic cancer. When added to pancreatic cancer cells, HBRI-**1** potently inhibited pancreatic cancer cell proliferation. When HBRI-**1** was added to pancreatic cancer cells with gemcitabine and paclitaxel, a standard of care combination therapy, HBRI-**1** made gemcitabine and paclitaxel much more

effective. HBRI-**1** was effective at decreasing pancreatic cancer in an in vivo tumor model.

“In the future, this molecule could be used alone or with other chemotherapy albeit at lower doses, as a new therapeutic drug to combat pancreatic cancer. This may lead to much less toxicity to the patient,” explained, Cheng, Ph.D., a researcher in Cashman’s lab.

Cheng, Cashman and Andrew M. Lowy, MD, FACS, chief of the Division of Surgical Oncology at UC San Diego Moores Cancer Center and professor of surgery, are now working with San Diego biotech company ChemRegen, Inc., to further develop HBRI-**1** into a therapeutic drug.

How HBRI-1 works

Developing new medications for pancreatic cancer and other cancers is important. Pancreatic ductal adenocarcinoma (PDAC) is the most common form of pancreatic cancer. Despite its prevalence, therapeutic options for PDAC are limited to surgery and/or combination of chemotherapy and radiotherapy. Due to drug resistance and drug-induced side effects, first-line chemotherapy (i.e., gemcitabine, 5-fluorouracil or FOLFIRINOX, etc.) have made minimal impact on PDAC treatment.

For pancreatic cancer, like other cancers, the challenging part is figuring out the cellular pathways that direct cancer growth and how these pathways can be interrupted and halted. A non-toxic chemical that inhibits key cancer-promoting pathways is a very promising strategy.

In pancreatic cancer, HBRI-**1** works by affecting a cellular process known as apoptosis. Apoptosis is involved in cancer cell proliferation. Apoptosis is a process that tells the cell when to stop dividing and it influences other cell behaviors, such as proliferation and differentiation. When apoptosis signaling is turned on, cancer cells are set on a course toward destruction and removal. HBRI-**1** activates an apoptosis protein in mitochondria and chokes cancer cell proliferation, ultimately altering cellular behavior - in this case decreasing cancer cell growth.

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Media contacts: To arrange on-site, phone, or Skype interviews with the researchers involved in this study, please contact John Cashman at (858) 458-9305 / JCashman@hbri.org.

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The study was co-authored by Jiongjia Cheng, Human BioMolecular Research Institute and ChemRegen Inc.; Karl Okolotowicz, Human BioMolecular Research Institute and ChemRegen Inc.; Daniel Ryan, Human BioMolecular Research Institute; Evangeline Mose, University of California San Diego; Andrew Lowy, University of California San Diego and John Cashman, Human BioMolecular Research Institute.

About Human BioMolecular Research Institute

The Human BioMolecular Research Institute is a non-profit research institute conducting basic research focused on unlocking biological and chemical principles related to diseases of the human brain, cardiovascular disease and cancer. The Institute conducts fundamental studies of central nervous system disorders, heart disease and cancer including stem cell approaches and translates findings into new drug development to address human illness. In addition, the Institute promotes scientific learning through community service and public access by disseminating information and sharing research with collaborators, colleagues and the public. For more information, visit us at www.HBRI.org.

About ChemRegen Inc.

ChemRegen is a for-profit company doing research directed at identifying small molecules of use for addressing human diseases. The approach is to develop regenerative medicines to work in conjunction with stem cells to cure major human diseases including heart disease, cancer and other diseases. For more information, visit www.ChemRegen.com.