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Novel Inhibitor Targets both p53-Dependent Apoptotic and Autophagy Pathways as a Pancreatic Cancer Therapeutic

San Diego, Calif., April 24, 2018 – Researchers at the Human BioMolecular Research Institute, UC San Diego Moores Cancer Center and ChemRegen, Inc. have created a small molecule that potently inhibits pancreatic cancer. Presenting April 24, at the *American Society for Experimental Pharmacology (ASPET)* meeting (**Poster C 197**), the team describes how they tested **1**, a man-made, drug-like chemical that can be used to inhibit pancreatic cancer.

"Because pancreatic cancer is the third leading cause of cancer death in this country, and will soon be the second leading cause of cancer death, we need to develop effective new medications for pancreatic cancer," said John Cashman, Ph.D., President of Human BioMolecular Research Institute (HBRI) and co-author of the study. "Using a non-toxic small molecule to stop pancreatic cancer either by itself or in combination with standard of care is very appealing."

Medicinal chemistry affords anti-cancer drug

A team of medicinal chemists at the Human BioMolecular Research Institute, led by John Cashman, Ph.D., using dynamic medicinal chemistry developed the lead compound HBRI-**1**. They also used sophisticated advanced chemical synthesis to make analogs of HBRI-**1**. When added to pancreatic cancer cells, HBRI-**1** potently stimulated inhibition of pancreatic cancer cell proliferation.

"At some point, this molecule could become the basis for a new therapeutic drug for pancreatic cancer," explained Jiongjia Cheng, Ph.D., a researcher in Cashman's lab and lead author of the paper.

Cashman and Cheng in collaboration with Professor Andrew Lowy at UC San Diego 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 disease is important because it is currently the third leading cause of cancer. By 2030, pancreatic cancer will be the second leading cause of cancer in the United States. Currently, it is one of the few cancers that is increasing in abundance in the United States. For pancreatic cancer, the difficult part is figuring out the cellular signals that direct cancer growth and how these pathways can be interrupted.

HBRI-**1** works by blocking two cellular processes known as apoptosis and autophagy (**Figure 1**). Both are involved in cancer proliferation. Apoptosis is a process that tells the cell when to stop dividing and it influences other cell behaviors, such as proliferation and differentiation. With apoptosis signaling turned on, cancer cells are set on a course toward destruction and removal. HBRI-**1** activated an apoptosis protein in mitochondria and chokes cell proliferation, ultimately altering cellular behavior—in this case decreasing cancer cell growth.

HBRI-**1** also triggers the inhibition of cancer cell autophagy, a process that also helps degrade cancer cells, thus inhibiting the whole cancer cell proliferation process. HBRI-**1** is the first inducer of apoptosis and selective inhibitor of autophagy meaning that it works in two main pathways to combat cancer at the same time. HBRI-**1** might also have applications in other cancers controlled by these pathways.

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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.

This research was funded by the California Institute for Regenerative Medicine (DISC1-10583), the National Cancer Institute of the U.S. National Institutes of Health (grant STTR R41CA176931), the Human BioMolecular Research Institute, the Shurl and Kay Curci Foundation.

The study was co-authored by Dong-Hoon Lee, Human BioMolecular Research Institute and ChemRegen Inc.; Karl Okolotowicz, Human BioMolecular Research Institute and ChemRegen Inc; Andrew Lowy, UC San Diego and John Cashman, Human BioMolecular Research Institute and ChemRegen Inc.

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 Moores Cancer Center

Moores Cancer Center at UC San Diego Health is home to nearly 350 medical and radiation oncologists, cancer surgeons, and researchers. It is one of only 45 National Cancer Institute-designated comprehensive cancer centers in the country, a rare honor distinguishing exceptionally high achievement in research, clinical care, education and community outreach and partnerships. For more information, visit cancer.ucsd.edu.

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 human embryonic stem cells to cure major human diseases including heart disease, cancer and other diseases. For more information, visit www.ChemRegen.com.

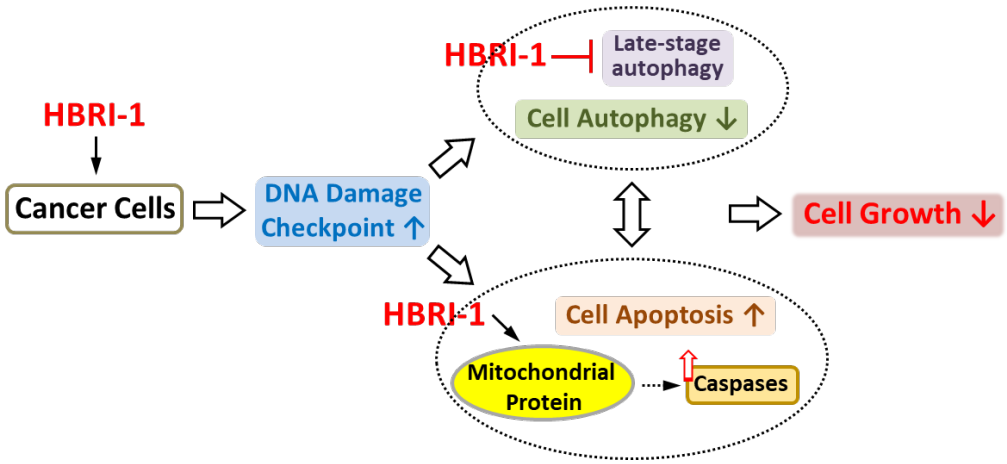

Figure 1. General scheme for the anti-cancer action of HBRI-**1.** HBRI-**1** is a small molecule that works via DNA damage checkpoint modulation to increase apoptosis and decrease autophagy to stop pancreatic cancer cell growth.