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A Novel Inhibitor Targets Both Wnt Signaling and ATM/p53 in Colorectal Cancer

Novel Inhibitor for colorectal cancer, HBRI-**1**, featured in *Cancer Research*.

San Diego, Calif., July21, 2018 – Researchers at the Human BioMolecular Research Institute, and Stanford University have created a small molecule that potently inhibits colon cancer. Publishing July 21, 2018, in the journal *Cancer Research*, the team describes how they tested HBRI-**1**, a man-made, drug-like chemical that can be used to inhibit colon cancer and other cancers.

"Because colorectal cancer (CRC) is the second leading cause of cancer-related death for men and women in the United States and resulted in an estimated 50,260 deaths during 2017, we need to develop effective new medications for colon 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 colon cancer either by itself or in combination with standard of care chemotherapy is very appealing."

Dynamic 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 colon cancer cells, HBRI-**1** potently stimulated inhibition of colon cancer cell proliferation.

"At some point, this molecule could become the basis for a new therapeutic drug for colon 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 Mark Mercola at Stanford University 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 colon cancer and other cancers is important. Currently, colon cancer is the third most common cancer in the United States. For colon cancer, the difficult part is figuring out the cellular signals that direct cancer growth and how these pathways can be interrupted and halted.

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HBRI-**1** works by affecting two cellular processes known as apoptosis and autophagy (**Figure 1**). Both are 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. 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. The Wnt pathway is potently inhibited by HBRI-**1** in an anti-proliferative mechanism.

HBRI-**1** also triggers the inhibition of cancer cell autophagy, a mechanism that also helps degrade cancer cells, thus inhibiting the whole cancer cell proliferation process. HBRI-**1** is the first potent inducer of apoptosis and selective inhibitor of autophagy meaning that it works in two main pathways to combat cancer at the same time. A key protein that is stabilized and activated by HBRI-**1** is p53. 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.

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The study was co-authored by Jiongjia Cheng, Human BioMolecular Research Institute; Mary Dwyer, Human BioMolecular Research Institute; Karl Okolotowicz, Human BioMolecular Research Institute and ChemRegen Inc; Mark Mercola, Stanford University 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 Stanford University
Stanford University is a leading teaching and research institution. The University is organized around three traditional schools consisting of 40 academic departments at the undergraduate and graduate level and four professional schools that focus on graduate programs in Law, Medicine, Education and Business. 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 med.stanford.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.

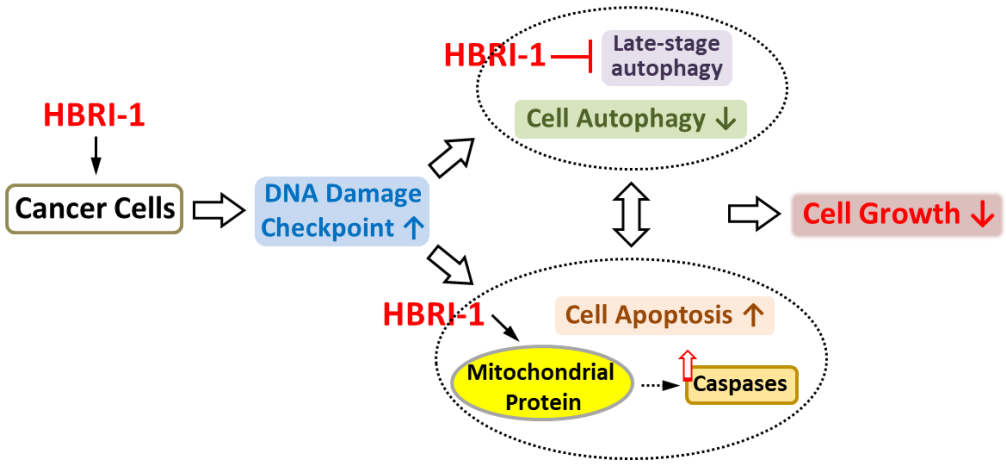

Figure 1. General scheme for the anti-cancer action of HBRI-**1.** HBRI-**1** is a small molecule that works via DNA damage checkpoint modulation to increase apoptosis and decrease autophagy to stop cancer cell growth.