SciBX
Science-Business eXchange

Releasing the potential of GHRH

By Tim Fulmer, Senior Writer

Researchers at the **University of Miami** and the **Veterans Affairs Medical Center** have designed an agonist of growth hormone releasing hormone that protected rodent hearts following myocardial infarction.[1] They are now seeking a partner to help move the compound into a Phase I trial to treat heart failure.

Growth hormone releasing hormone (GHRH) is a 44-amino-acid peptide produced by the hypothalamus. GHRH is approved to treat growth hormone deficiency in children and works by binding its receptor on the pituitary gland to stimulate production and release of growth hormone.

The receptor for GHRH is also found in tissues outside the brain, including the heart,[2] and in 2009, Italian researchers showed that GHRH has roles beyond growth hormone stimulation. They showed that GHRH increased survival of rat cardiomyocytes and protected against ischemic reperfusion injury *in vitro*.[3]

The University of Miami and Veterans Affairs researchers have now developed a strategy for improving GHRH signaling in animal models of heart failure.

Rather than administer exogenous GHRH, the group used a GHRH agonist, JI-38, which was developed by Andrew Schally, one of the paper's authors. The compound is more potent and stable than native GHRH and thus could have a better pharmacokinetic profile than the naturally occurring hormone.[4]

In rats, JI-38 reduced myocardial infarction–induced left ventricular hypertrophy and improved ejection fraction compared with placebo ($p<0.01$ and $p<0.05$, respectively).

Rats treated with JI-38 also had smaller MI size and less ventricular fibrosis than rats treated with placebo ($p<0.05$ and $p<0.01$, respectively).

Gene expression data confirmed the cardioprotective role of GHRH. In cardiac precursor cells from JI-38-treated rats, compared with those from placebo-treated rats, the antiapoptotic gene *B cell lymphoma 2* (*Bcl-2*; *Bcl2*) was upregulated and the proapoptotic gene *BCL2-associated X protein* (*Bax*) was downregulated.

The findings were published in the *Proceedings of the National Academy of Sciences*. The two lead authors on the paper were Joshua Hare and Schally, both professors of medicine at the Miller School of Medicine at the University of Miami.

Going forward

Hare told *SciBX* the researchers now plan to carry out preclinical studies of the agonist in larger animals. He said they hope to submit an IND for a Phase I trial but would not disclose a timeline.

The trial design for JI-38 could be informed by an ongoing Phase II study of exogenous GHRH to treat congestive heart failure (CHF) in patients over 50. That trial is being run by Kenneth Minaker, chief of geriatric medicine at **Massachusetts General Hospital**, and colleagues at **The Johns Hopkins University**. Minaker did not respond to requests for an interview.

Hare said his group is seeking a licensing partner to help run its Phase I study. JI-38 is covered by issued patents and is available for licensing.

Fulmer, T. *SciBX* 3(6); doi:10.1038/scibx.2010.172
Published online Feb. 11, 2010

REFERENCES

1. Kanashiro-Takeuchi, R. *et al. Proc. Natl. Acad. Sci. USA*; published online Jan. 18, 2010; doi:10.1073/pnas.0914138107
   Contact: Joshua Hare, University of Miami, Miami, Fla.
   e-mail: jhare@med.miami.edu
   Contact: Andrew Schally, Veterans Affairs Medical Center, Miami, Fla.
   e-mail: andrew.schally@va.gov
2. Matsubara, S. *et al. Endocrinology* **136**, 4147–4150 (1995)
3. Granata, R. *et al. Cardiovasc. Res.* **83**, 303–312 (2009)
4. Izdebski, J. *et al. Proc. Natl. Acad. Sci. USA* **92**, 4872–4876 (1995)

COMPANIES AND INSTITUTIONS MENTIONED

The Johns Hopkins University, Baltimore, Md.
Massachusetts General Hospital, Boston, Mass.
University of Miami, Miami, Fla.
Veterans Affairs Medical Center, Miami, Fla.