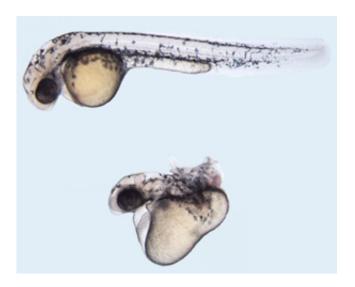


Researchers uncover a hormone that plays a vital role in heart development

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The ELABELA hormone is important for heart development in the early embryo. Zebrafish embryos lacking ELABELA display a range of severe cardiac and other developmental anomalies (bottom) unlike those that express the hormone (top). Credit: Elsevier

Hormones—regulatory biochemicals produced by the body—were first identified over 100 years ago. Since then, improvements in researchers' understanding of the key role that hormones play as chemical messengers in processes such as growth, metabolism and reproduction have enabled some of the most significant medical advances in the twentieth century. The discovery of insulin, for example, led to the first effective treatment for diabetes, and the identification of other



hormones, such as cortisol, estrogen, progesterone and testosterone, has resulted in unprecedented advances in human fertility and healthcare.

Now, a team of researchers from the Human Genetics and Embryology Laboratory at A*STAR's Institute of Medical Biology (IMB) and Institute of Molecular and Cell Biology has uncovered a new <u>hormone</u> that plays an essential role during embryonic heart development. Known as ELABELA, the novel hormone opens up new avenues for the treatment of hypertension, cardiovascular disorders and even HIV infection.

In addition to being a breakthrough for biomedicine, the team's discovery highlights the importance of carefully decrypting sequenced genomes for possible hidden gems. "Although the human genome was completely sequenced and assembled a decade ago, it is bewildering that hitherto unknown hormones are still being discovered," says Bruno Reversade, the senior principal investigator at the IMB who led the research team.

Located on human chromosome 4, the gene ELABELA encodes a small secreted peptide hormone consisting of just 32 amino acids. Reversade and his team determined that in zebrafish lacking the ELABELA hormone, <u>embryonic heart development</u> was significantly impeded or, in some cases, stopped completely (see image)—a finding that has since been replicated by researchers at Harvard University in the United States.

Reversade's team showed that the ELABELA hormone binds to a specific protein found on the surface of cells known as the apelin receptor. Prior to the finding, scientists thought that the apelin receptor could only be activated by the APELIN hormone, which plays multiple roles in the body, influencing, among other essential metabolic functions: myocardial contractility (the intrinsic ability of the heart to



contract); the regulation of blood pressure, water and food intake; the release of hormones from the pituitary gland; and bone development.

So far, the team has demonstrated that ELABELA is present in human embryonic stem cells and is also expressed in the adult human prostate and kidney. The researchers' next step will be to investigate ELABELA's role in a wider range of organs and tissues. If ELABELA is shown to signal through the apelin receptor in adults as well, the newly discovered hormone could have beneficial effects similar to those of APELIN. The hormone may even block HIV entry to the cell since the apelin receptor is one gateway for viral entry into human cells.

"This discovery shows great promise for the development of targeted therapies for heart disease and blood pressure control in the future," notes Birgit Lane, executive director of the IMB. "It is an excellent example of how basic research can lead to surprising and unexpected findings that may change and refine medical practice."

More information: Chng, S. C., Ho, L., Tian, J. & Reversade, B. ELABELA: "A hormone essential for heart development signals via the apelin receptor." *Developmental Cell* 27, 672–680 (2013). dx.doi.org/10.1016/j.devcel.2013.11.002

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