PRESS RELEASE

**Increased Blood Flow triggers Liver Regeneration**

 **The liver is one of the few human organs that completely regenerates within a few weeks after more than half of the organ has been removed. However, so far the cause of this remarkable feature remains unclear. Within the framework of the Collaborative Research Center 974 and with support from the German Center for Diabetes Research (DZD e.V.), scientists in Professor Eckhard Lammert's research team at the German Diabetes Center (DDZ), the Leibniz Center for Diabetes Research at Heinrich Heine University (HHU) Düsseldorf, in cooperation with colleagues from HHU and Düsseldorf University Hospital (UKD) showed for the first time that increased blood flow through the small blood vessels of the liver triggers the release of signals from cells of these vessels, thus promoting liver growth. The results are published in the current issue of *Nature*.**

**Düsseldorf (DDZ)** – The liver is one of the most important human organs. It is essential for metabolism, blood detoxification and the functioning of the immune system. Moreover, the liver is the only organ which can fully regenerate its cell mass within a few weeks after more than half of the organ has been removed. The researchers led by Professor Eckhard Lammert have discovered that it is due to increased blood flow and subsequent dilation of the liver vasculature that the liver receives signals for growth. The signals come from the cells of the blood vessels that react to the mechanical stimulation. The publication is based on the findings published in 2001 that blood vessels affect organs in their function and growth (Lammert et al., Science 2001).

"In our study of the liver and its blood vessels, we identified an important trigger for organ growth. For the first time, we were able to show that blood flow and vasodilatation release growth-promoting signals from blood vessels," said Professor Eckhard Lammert, director of the Institute for Beta Cell Biology at the German Diabetes Center (DDZ) and head of the Institute for Metabolic Physiology at Heinrich Heine University Düsseldorf. "In the future, these exciting results could also become important for the understanding and treatment of fatty liver disease in obesity and diabetes," added Professor Michael Roden, scientific director and board member of the German Diabetes Center and director of the Department of Endocrinology and Diabetology at Düsseldorf University Hospital.“ The research results are of great importance for understanding the complex processes involved in liver regeneration and its disorders,“ said Professor Dieter Häussinger, director of the Department of Gastroenterology, Hepatology and Infectious Diseases at Düsseldorf University Hospital and spokesperson of the Collaborative Research Center 974.

**Experimental Procedure**

The molecular causes of this organ regeneration are the subject of a study published by Düsseldorf scientists in the journal *Nature* (Lorenz et al., Nature 2018). Specifically, the scientists were able to show that increased blood flow through the liver leads to the release and activation of growth signals from blood vessels. One of these signals is the hepatocyte growth factor (HGF), which is particularly important for the growth and survival of liver cells. The endothelial cells of the blood vessels recognize the increased blood flow through the liver by means of so-called integrins. These are cell surface proteins that connect the extracellular matrix to the cytoskeleton and are able to activate other receptors such as the vascular endothelial growth factor receptor-3 (VEGFR3). The activation of the β1 integrin (a subunit of the integrins) due to the increased blood flow leads in endothelial cells to the activation of VEGFR3 and the activation and release of growth factors such as HGF. The latter induce the growth of the liver. As soon as the liver has grown to its normal size and new blood vessels have formed, a normal amount of blood per endothelial cell flows through the liver again. This normal mechanical stimulation of the endothelial cells could explain why the liver stops growing. The scientists postulate that this molecular mechanism causes the liver to grow as soon as its organ size is reduced and then to stop growing when it is restored.

**Original Publication:
Lorenz L, Axnick J, Buschmann T, Henning C, Urner S, Fang S, Nurmi H, Eichhorst N, Holtmeier R, Bódis K, Hwang JH, Müssig K, Eberhard D, Stypmann J, Kuss O, Roden M, Alitalo K, Häussinger D, Lammert E.** **Mechanosensing by β1 integrin induces angiocrine signals for liver growth and survival.** **Nature. 2018 Sep 26. doi: 10.1038/s41586-018-0522-3. [Epub ahead of print]
Advance Online Publication (AOP) on** <http://www.nature.com/nature>

**Photo Reference:**

1. A video about the study can be found at: <https://figshare.com/s/f7ceb9d5980d10084ad8>

2. An illustration of an artificially stained blood vessel is shown. It is a scanning electron micrograph of a hepatic blood vessel. The image was taken and edited by Dr. Daniel Eberhard (Institute of Metabolic Physiology, HHU) and S. Köhler (Center for Advanced Imaging, HHU).

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The German Diabetes Center (DDZ) serves as the German reference center for diabetes. Its objective is to contribute to the improvement of prevention, early detection, diagnosis and treatment of diabetes mellitus. At the same time, the research center aims at improving the epidemiological data situation in Germany. The DDZ coordinates the multicenter German Diabetes Study and is a point of contact for all players in the health sector. In addition, it prepares scientific information on diabetes mellitus and makes it available to the public. The DDZ is part of the Leibniz Association (Wissenschaftsgemeinschaft Gottfried Wilhelm Leibniz, WGL) and is a partner of the German Center for Diabetes Research (DZD e.V.).

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