Fructose powers a vicious circle

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'Walk through any supermarket and take a look at the labels on food products, and you'll see that many of them contain fructose, often in the form of sucrose (table sugar)' -- that's how Wilhelm Krek, professor for cell biology at ETH Zurich's Institute for Molecular Health Sciences, summarizes the problem with today's nutrition. Prepared foods and soft drinks in particular, but even purportedly healthy fruit juices contain fructose as an artificial additive -- often in high quantities. In recent decades fructose spread throughout the food market, due to **a reputation as being less harmful than glucose**. In contrast to glucose, **fructose barely increases blood glucose levels and insulin secretion**. This avoids frequently recurring insulin spikes after any glucose consumption, which are judged harmful. In addition, fructose is sweeter to the taste.

But there's **a downside: the liver converts fructose very efficiently into fat.** People who consume too much high-fructose food can in time become overweight and develop high blood pressure, dyslipidaemia with fatty liver and insulin resistance -- symptoms that doctors group together under the name metabolic syndrome.

Unchecked growth of the heart muscle
A new paper by Krek and his team member Peter Mirtschink describes a further, more troubling side effect of fructose. The researchers have discovered a previously unknown molecular mechanism that points to fructose as a key driver of uncontrolled growth of the heart muscle, a condition that can lead to fatal heart failure. Their study was recently published in *Nature*.

When a person has high blood pressure, the heart has to grow as it is harder to pump the blood through the circulatory system. These growing heart muscle cells require a considerable amount of oxygen. However, since not enough oxygen is available to adequately supply the increased growth, the cells switch to an alternative energy supply. Instead of drawing energy from fatty acids, they rely more on an anaerobic process called **glycolysis** -- literally, the 'splitting of sugars'. **If the heart muscle cells can access fructose in addition to glucose, this can set off a fatal chain reaction.**

Flipping the switch for fructose metabolism
In the study, Krek's research group demonstrates that a lack of oxygen in the heart cells cues the appearance of the HIF molecule. This is a universal molecular switch that flips whenever a pathological growth process is under way, such as cardiac enlargement or cancer. HIF causes the heart muscle cells to produce ketohexokinase-C (KHK-C), the central enzyme in fructose metabolism. KHK-C has a high affinity for fructose and can therefore process it very efficiently. The production of KHK-C also has a reinforcing

effect on glycolysis. Since fructose metabolism doesn't involve any negative feedback regulation, a vicious cycle starts that can lead to heart failure.

Large volumes of fructose are added to many foods, but especially to sweet beverages and soft drinks. This practice drove up per capita consumption of high fructose corn syrup in the USA between 1970 and 1997, from 230 grams per year to over 28 kilograms.