“Because humans are good at storing fat during times of plenty, we are also excellent at surviving times of famine. The fat tissues of our body are like batteries, providing us with a steady source of energy when food is scarce. Understanding the storage and burning of fat, literally the ebb and flow of energy throughout our body, is crucial to normal physiology and ultimately the treatment of metabolic diseases such as obesity and diabetes.”

Humans are built to hunger for fat, but when deluged by foods rich in fat and sugar, coupled with a sedentary lifestyle, the modern waistline often far exceeds the need to store energy for lean times. The result has been an epidemic of diabetes, heart disease and other obesity-related problems.

Although exercise and calorie restriction are known to be effective at preventing and treating diabetes, the obesity epidemic continues to grow, and new drugs to treat the problem are desperately needed.

Against this backdrop, Evans’s team identified the missing link in the regulation of metabolism. This linchpin is a protein known as fibroblast growth factor 1 (FGF1), which may open new avenues in the treatment of diabetes. The lab found that FGF1 activity is triggered by a high-fat diet and that mice lacking the protein swiftly develop diabetes. This suggests that FGF1 is crucial to maintaining the body’s sensitivity to insulin and normal levels of sugar in the blood.

The scientists also found that the antidiabetic drug Actos, which is used to increase the body’s sensitivity to insulin, regulates FGF1. But Actos and related drugs, though helpful, have side effects that limit their use. Thus, Evans plans to explore whether FGF1 itself might point to a new way to control diabetes by avoiding the drawbacks of Actos and providing a more natural means of increasing insulin sensitivity.

In addition to dietary regulation, mammalian metabolism is highly circadian, with major hormonal circuits corresponding to our sleep-wake cycles. Sleeping is a fasting period, while the remainder of the day involves periodic eating. Synchronizing rhythms of behavior and metabolic processes is important for cardiovascular health and for preventing metabolic disease. Two receptors found on the nuclei of mouse and human cells, known as REV-ERB-α and REV-ERB-β, are essential for synchronizing normal sleep and metabolic cycles. Evans’s findings describe a powerful link between circadian rhythms and metabolism and suggest a new direction for treating disorders of both systems, including jet lag, sleep disorders, obesity and diabetes.

For more information please visit www.salk.edu/faculty/evans