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# Kidney cells engineered to produce insulin when caffeine is present in the body

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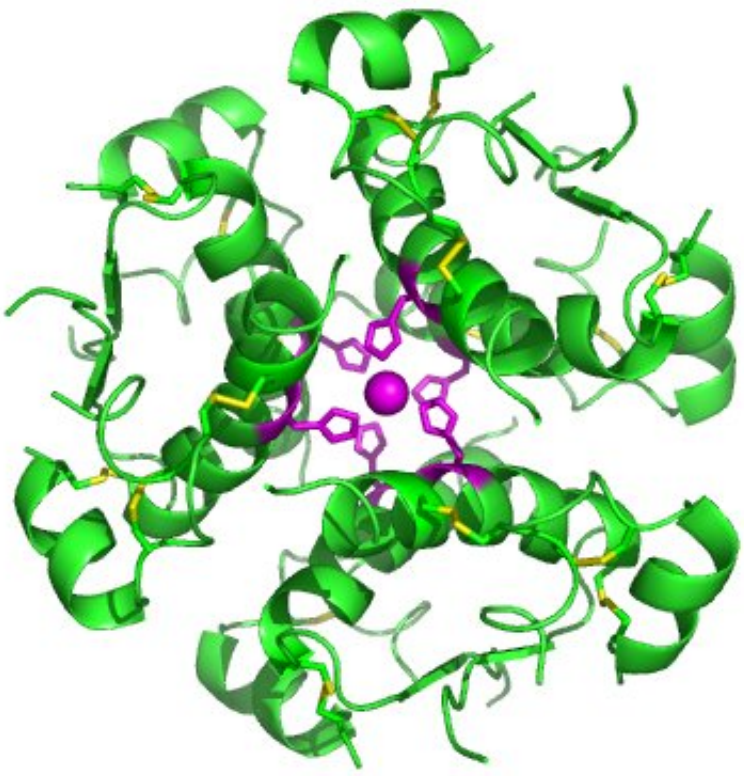

High-resolution model of six insulin molecules assembled in a hexamer. Credit: Isaac Yonemoto/Wikipedia

A team of researchers from ETH Zurich and the University of Basel in Switzerland and Institut Universitaire de Technologie in France has that found that embryonic kidney cells engineered to produce insulin when

exposed to caffeine were able to reduce glucose levels in mouse models. In their paper published in the journal *Nature*, the group describes their efforts and how well it worked in the mouse models.

People with diabetes suffer from higher than normal levels of glucose in the blood, which can lead to a host of health problems. Current treatments include drugs that make cells more sensitive to insulin, or injection of insulin to make more of it available to cells that need it. In this new effort, the researchers have developed a new way to get more insulin into the body when it is needed most.

Instead of adding insulin externally, the researchers engineered embryonic kidney cells to produce it—but only when they were exposed to caffeine. The team chose caffeine because it has been so extensively studied and because the majority of people consume caffeinated beverages, such as coffee and soft drinks. They point out that caffeine is also a substance that appears very rarely in other foods, making its ingestion easy to regulate. The engineered cells were covered with a material that protected them from the immune system and were then put into a device that was implanted into the abdomens of mice that had been engineered to have diabetes. The researchers note that glucose levels tend to spike after people (and mice) eat sugar or food material that the body converts to sucrose. Thus, the optimal time for giving the mice caffeine would be after eating.

The researchers report that they were able to attain relatively stable glucose levels in the mice by varying the amount of caffeine they were given after eating. Putting such a device in human test patients is still a long way off, the researchers acknowledge, but they note their method might also be applicable for treating other ailments.

**More information:** Daniel Bojar et al. Caffeine-inducible gene switches controlling experimental diabetes, *Nature Communications*

(2018). DOI: 10.1038/s41467-018-04744-1

**Abstract**

Programming cellular behavior using trigger-inducible gene switches is integral to synthetic biology. Although significant progress has been achieved in trigger-induced transgene expression, side-effect-free remote control of transgenes continues to challenge cell-based therapies. Here, utilizing a caffeine-binding single-domain antibody we establish a caffeine-inducible protein dimerization system, enabling synthetic transcription factors and cell-surface receptors that enable transgene expression in response to physiologically relevant concentrations of caffeine generated by routine intake of beverages such as tea and coffee. Coffee containing different caffeine concentrations dose-dependently and reversibly controlled transgene expression by designer cells with this caffeine-stimulated advanced regulators (C-STAR) system. Type-2 diabetic mice implanted with microencapsulated, C-STAR-equipped cells for caffeine-sensitive expression of glucagon-like peptide 1 showed substantially improved glucose homeostasis after coffee consumption compared to untreated mice. Biopharmaceutical production control by caffeine, which is non-toxic, inexpensive and only present in specific beverages, is expected to improve patient compliance by integrating therapy with lifestyle.