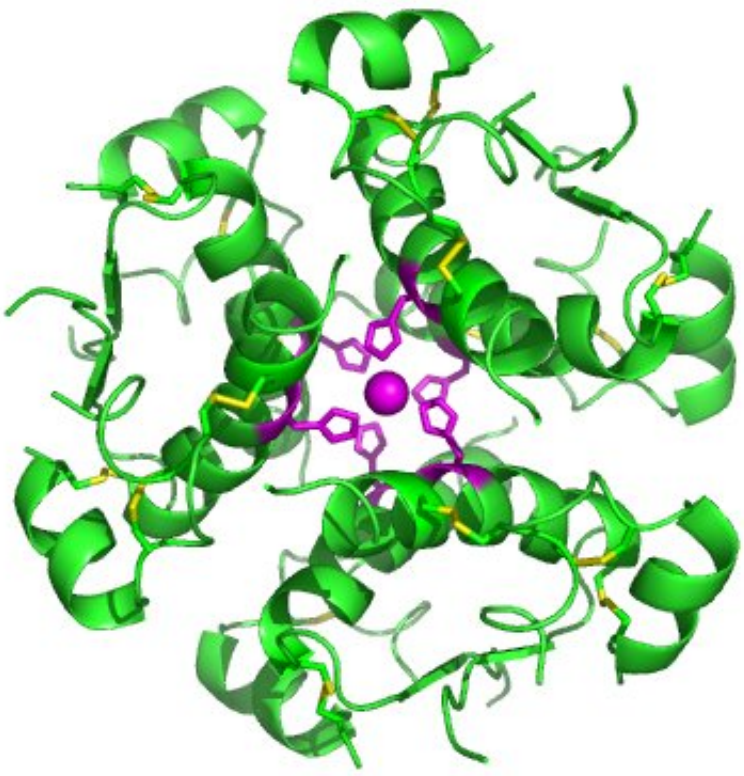
Simple molecule could prevent, alleviate pre-diabetes

February 7 2018



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

Restoring levels of coenzyme Q10 (CoQ), a key molecule in energy production in cells, could overcome insulin resistance or pre-diabetes—a precursor to type 2 diabetes and cardiovascular disease.

Levels of CoQ and the presence of insulin resistance were analysed in a range of experimental laboratory settings, mouse models and samples from humans, as part of an ambitious research collaboration conducted with the University of Sydney, Victor Chang Cardiac Research Institute, Duke University School of Medicine, Garvan Institute of Medical Research, Genentech Inc. and the University of New South Wales.

Concentrations of CoQ were found to be lower in insulin resistant body fat and muscle tissue. When the researchers replenished CoQ, insulin resistance or pre-diabetes was reversed.

Co-author Dr Daniel Fazakerley from the University of Sydney's School of Life and Environmental Science and Charles Perkins Centre said CoQ provides a vital role in converting nutrients like fat and sugar into usable energy.

"CoQ is found in mitochondria, the power plants in the cells of our body, where it is required for the flow of electricity to the cell's 'motor' which is responsible for energy production," he explained.

"Energy production can also generate reactive chemical species - often referred to as 'reactive oxygen species' or 'oxidants' - as by-products, which can be damaging to cells.

"Previous studies have shown that these oxidants can cause insulin resistance. Our study has found that lower mitochondrial CoQ enhanced oxidant formation by mitochondria.

"Importantly, by replenishing CoQ in mitochondria, either in cells or in animals, we were able to restore 'normal' mitochondrial oxidants and reverse insulin resistance."

Published in *eLife* today, the research provides a missing link in our

understanding of how changes in our diet can trigger insulin resistance, said co-lead author Professor David James, Leonard P. Ullmann Chair of Metabolic Systems Biology at the University of Sydney's Charles Perkins Centre.

"Eating a high fat, high sugar diet has long been known to be a major risk factor for obesity and pre-diabetes and our latest work brings us one step closer to understanding how and why," Professor James explained.

Co-lead author Professor Roland Stocker from the Victor Chang Cardiac Research Institute and the University of New South Wales added that the findings provide direction for potential future treatments for insulin resistance and pre-diabetes.

"Replenishing CoQ could prove an invaluable preventive measure for insulin resistance- or pre-diabetes-linked diseases such as type 2 diabetes, cardiovascular disease, cancers and dementia," he said.

"However, oral CoQ supplements may not effectively restore mitochondrial CoQ due to its low absorption," Professor Stocker explained.

"This work has provided an impetus for us to find alternate means of increasing CoQ in mitochondria to treat insulin resistance and pre-diabetes. If not an external supplement, perhaps we can stimulate the body to form more of the coenzyme itself - or find ways to prevent levels from lowering in the first place."

More information: Daniel J Fazakerley et al, Mitochondrial CoQ deficiency is a common driver of mitochondrial oxidants and insulin resistance, *eLife* (2018). DOI: 10.7554/eLife.32111

Provided by University of Sydney