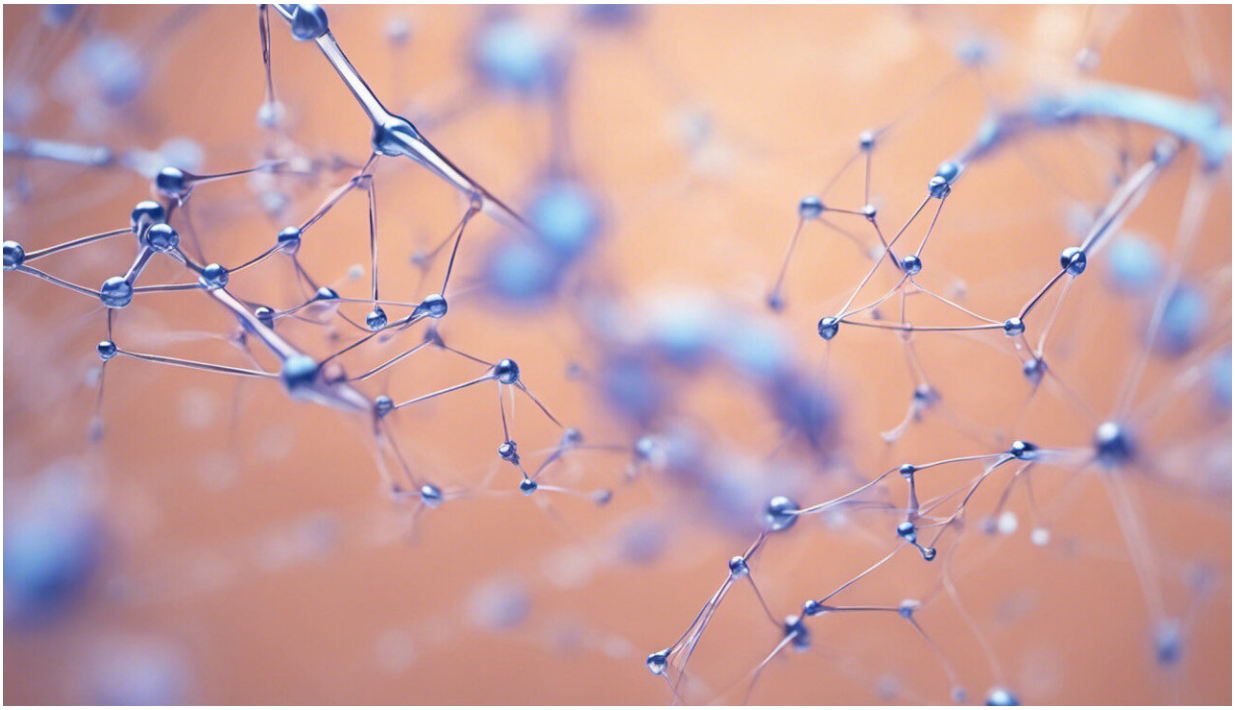
Protein research key for improved metabolism

July 7 2014, by Chris Thomas



Credit: AI-generated image (disclaimer)

Unlocking the mysteries of a certain type of protein could help reduce diet-induced obesity and type 2 diabetes by limiting weight gain, insulin resistance and glucose intolerance.

In WA, nearly 38 per cent of adults are overweight and one in four are

obese—both are major risk factors for type-2 diabetes.

Researchers at the Harry Perkins Institute of Medical Research are focussing on the circulating protein TNFSF14 which, in earlier studies, has shown to be important in metabolism.

TNFSF14 levels were shown to be increased in morbidly obese humans and this observation raised the question as to whether upregulated levels of TNSF14 during obesity were working in a pro or anti-obesogenic manner.

Lead researcher UWA Associate Professor Vance Matthews says TNFSF14 has shown potential because it is a promiscuous ligand (ion that bonds with a central atom).

"It may bind two receptors, which include the lymphotoxin-beta receptor and herpes virus entry mediator, and this increases the number of metabolic cell types that may bind TNFSF14," he says.

"Major metabolic cell types including adipocytes, skeletal muscle cells and hepatocytes express receptors for TNFSF14 and are therefore targets for the protein.

"Obesity and insulin resistance are hallmarks of the metabolic syndrome and we have already shown that TNFSF14 may promote insulin sensitivity in skeletal muscle cells."

Further to this, within skeletal muscle cells, TNFSF14 could actually reduce insulin resistance.

In small animal studies, the presence of TNFSF14 has also been shown to decrease high-fat, diet-induced obesity and insulin resistance.

"Our experiments are the first to utilise a TNFSF14 knockout mouse in high-fat, diet-induced obesity studies," A/Prof Matthews says, referring to a genetically engineered mouse where an existing gene has been replaced or disrupted with an artificial piece of DNA.

"We are fortunate to be collaborating with Dr Bernadette Saunders at Sydney's Centenary Institute.

"With funding assistance from Diabetes Research WA, our group is now determining whether TNFSF14 expression in bone marrow-derived cells reduces diet-induced obesity and type 2 diabetes.

"We are conducting more extensive proteomic analyses to see whether proteins involved in lipid metabolism are also influenced by TNFSF14 signalling."

Other proteins such as leptin and ciliary neurotrophic factor originally also showed great promise, however they failed in clinical trials.

"This was due to upregulation of negative regulators or neutralising antibodies," A/Prof Matthews says.

"The discovery of novel anti-obesogenic proteins are of great need."

But he says his team is excited about the potential of TNFSF14.

Provided by Science Network WA