OBESITY

Medicinal mushroom reduces obesity by modulating microbiota

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Ganoderma lucidum—a medicinal mushroom used in traditional Chinese medicine—has been reported to have antidiabetic properties. Now, a new study shows that this mushroom also has antiobesity properties, which are mediated by modulating the composition of the gut microbiota. The findings raise hope that in the future, this mushroom could be used as a prebiotic to combat obesity and obesity-related metabolic disorders.

The researchers prepared a water extract of *Ganoderma lucidum* mycelium (WEGL), which was isolated and cultured using an advanced biofermentation process, and administered it to high-fat diet (HFD)-fed mice daily for 2 months by oral gavage. Supplementation with WEGL dose-dependently reduced weight gain and both epididymal and subcutaneous fat accumulation in HFD-fed mice compared with untreated controls. In contrast to the untreated control mice, those treated with WEGL had reduced inflammation and insulin resistance.

As obesity alters the composition of the gut microbiota in both people and HFD-fed mice, the researchers examined whether WEGL treatment could modulate the gut microbiota. Bacterial 16S RNA sequencing of faecal samples revealed that WEGL treatment reduced the ratio of Firmicutes to Bacteroidetes and levels of Proteobacteria (characteristics of obesity-associated intestinal dysbiosis) in HFD-fed mice. Moreover, transplantation of faeces from WEGL-treated mice to untreated HFD-fed mice recapitulated the antiobesity and microbiota-modulating effects in recipient mice. Finally, the researchers fractionated the mycelium extract to identify the active ingredient in WEGL. The fraction containing high-molecular-weight polysaccharides (>300 kDa) produced similar antiobesity and microbiota-modulating effects as unfractionated WEGL.

"Although the link between obesity and the gut microbiota is well established, our work is among the first to show that a traditional Chinese medicine can be used as a prebiotic to lose weight," comments lead investigator John Young.

David Holmes

Original article Chang, C.-J. *et al*. *Ganoderma lucidum* reduces obesity in mice by modulating the composition of the gut microbiota. *Nat. Commun.* doi:101038/ncomms8489

EPIGENTICS

Obesity-induced hypermethylation of adiponectin gene

The mechanisms underlying obesity-induced dysregulation of the gene that encodes adiponectin have been revealed in a new paper published in *Nature Communications*.

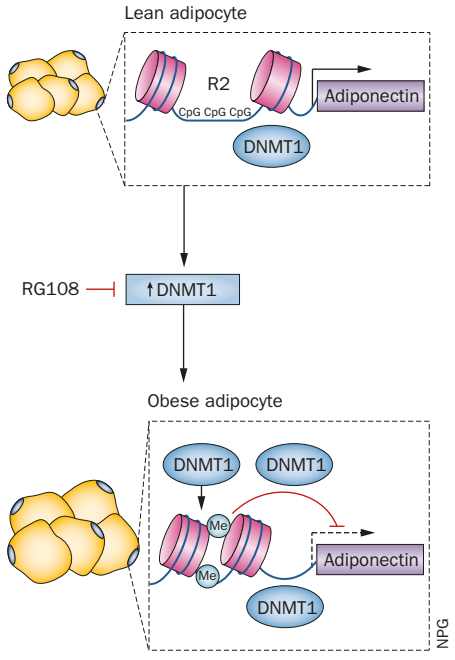
Adiponectin controls the metabolism of glucose and insulin and its expression is decreased in obesity. However, how the expression of this gene is altered in obesity has been unclear. Jae Bum Kim and colleagues speculated that epigenetic changes could be involved in the suppression of adiponectin gene expression in obesity.

The researchers used bisulphite sequencing to analyse levels of DNA methylation of the adiponectin promoter in adipocytes isolated from mice fed either a normal chow diet or a high-fat diet (HFD). HFD obese mice had more DNA methylation at the R2 region of the promoter than did the normal mice. Furthermore, the amount of methylation in the R2 region was inversely correlated with levels of adiponectin mRNA.

Kim and colleagues were also able to demonstrate that levels of DNA methyltransferase 1 (DNMT1) were higher in the HFD mice than in the normal mice. DNMT1 selectively methylated the R2 region, and also caused chromatin remodelling of the adiponectin promoter. Treating obese mice with a DNMT1 inhibitor (RG108) reduced methylation levels at the R2 region and increased levels of adiponectin.

"We have shown that adiponectin gene expression is dynamically regulated by epigenetic modulations, including DNA hypermethylation and chromatin remodelling at the adiponectin promoter, which could explain decreased adiponectin expression in obese adipocytes," says Kim. The researchers hope that future studies examining the molecular mechanisms that control the selectivity of DNMT1 for its target site could aid development of therapies for obesity and its complications.

Claire Greenhill



Original article Kim, A. Y. *et al.* Obesity-induced DNA hypermethylation of the adiponectin gene mediates insulin resistance. *Nat. Commun.* doi:10.1038/ncomms8585