

DIABETES

Systemic effects of metformin revealed

Metformin is widely prescribed to treat patients with type 2 diabetes mellitus, but the whole-body systemic responses to the drug remain unclear. Now, new research conducted by Michaela Reagan and colleagues reveals the effects of metformin in lean and obese mice on bone, bone marrow adipose tissue and the gut microbiome.

“Our work demonstrates fundamental differences in how mice respond to metformin depending on their nutritional status, their metabolic state and their microbiome,” explains Reagan. “We also showed that in a mouse model of diet-induced obesity, metformin prevents a decline in bone mass, correlating with a reduction in bone marrow adipose tissue.”

To determine the systemic responses to metformin, the authors treated control mice and mice fed a high-fat diet with metformin. By sequencing the faecal microbiome of the treated and untreated obese and lean mice, Reagan and colleagues were able to identify differences in the gut microbiome. The

authors found that the diversity and type of microbes in the gut changed in response to diet or obesity and treatment with metformin.

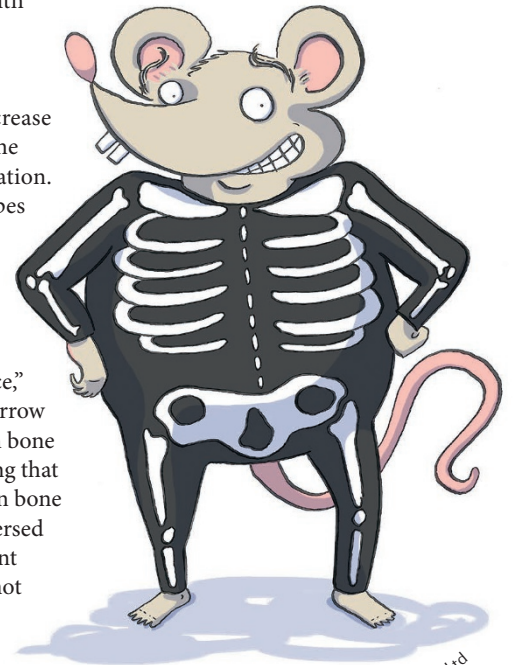
The team then assessed bone health using microCT and immunohistochemistry, and implemented a novel osmium tetroxide microCT method to analyse bone marrow adipose tissue. Compared with the control diet, the high-fat diet was associated with a reduction in ‘bone-building’ osteoblast activity but an increase in osteoclast activity and bone marrow adipose tissue formation. Interestingly, these phenotypes were reversed following treatment with metformin.

“Our work provides the first big-picture analysis of changes induced by metformin in obese and lean mice,” concludes Reagan. “Bone marrow adipose tissue correlates with bone disease. Therefore, our finding that the obesity-related increase in bone marrow adipose tissue is reversed by metformin raises important questions about whether or not

metformin should be used in the clinic to treat patients with metabolic disease and elevated bone marrow adiposity.”

Alan Morris

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