Corrected: Publisher Correction

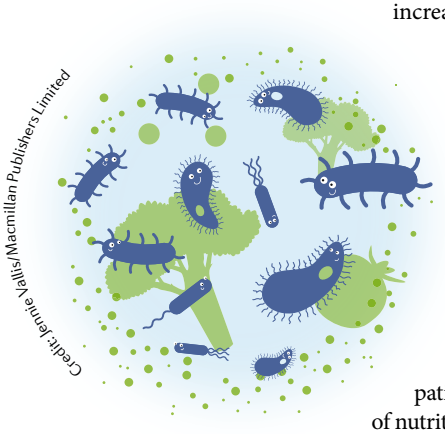
GUT MICROBIOTA

High-fibre diet beneficial for T2DM

The gut microbiota ferments dietary carbohydrates to produce short-chain fatty acids (SCFAs). In patients with type 2 diabetes mellitus (T2DM), there is a decrease in SCFA production and previous studies have shown that a high-fibre diet is beneficial for patients with T2DM. Now, in a new randomized controlled trial, Liping Zhao, Chenhong Zhang, Yongde Peng and colleagues show that in patients with T2DM a high-fibre diet promotes SCFA-producing gut bacteria, which in turn normalizes levels of HbA_{1c} via an increase in the production of glucagon-like peptide 1 (GLP1).

In their study, the researchers assigned 43 patients with T2DM to receive either usual clinical care (patient education and dietary recommendations according to the 2013 Chinese Diabetes Society guidelines for T2DM) or a high-fibre diet based on whole grains, traditional Chinese medicinal foods (such as oats, and white and red beans, which are high in fibre) and prebiotics for 84 days. "We controlled the energy and macronutrient intake between the two groups so that the only dietary difference was the extra amount of diverse fibres in the treatment group," explains Zhang.

Patients receiving the high-fibre diet had greater reductions in levels of HbA_{1c} and body weight, and better lipid profiles than patients in the control group. A higher proportion of the treatment group achieved adequate glycaemic control (HbA_{1c} < 7%) compared with the control group. The high-fibre diet increased the abundance of diverse fermentable carbohydrates in the gut and selected for a specific group of bacteria that produce acetate and butyrate. The increased levels of acetate and butyrate in the gut stimulated the production of GLP1, which in turn promoted insulin secretion. The high abundance of the SCFA-producing bacteria also reduced pro-inflammatory bacterial growth, which reduced inflammation and increased insulin sensitivity.

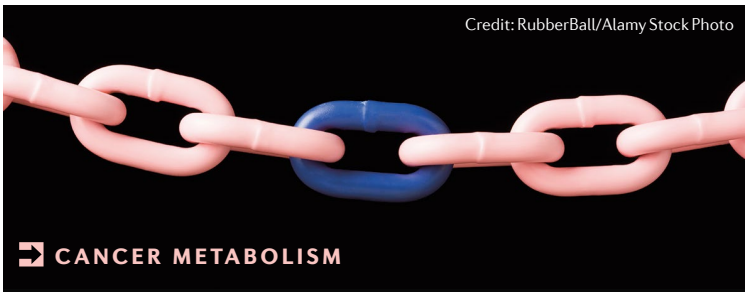


Credit: Jemma Wallis/Macmillan Publishers Limited

"Targeting SCFA-producing gut bacteria with a personalized high-fibre diet would help patients with T2DM normalize HbA_{1c} levels," concludes Zhang. "We now need to conduct more clinical trials to find the best possible benefits for patients from this new form of nutrition therapy."

Ivone Leong

ORIGINAL ARTICLE Zhao, L. et al. Gut bacteria selectively promoted by dietary fibers alleviate type 2 diabetes. *Science* **359**, 1151–1156 (2018)



Credit: RubberBall/Alamy Stock Photo

CANCER METABOLISM

p62 — a new metabolic tumour suppressor

Obesity is a risk factor for cancer; however, the molecular mechanisms linking them are poorly understood. Now, new research by Jorge Moscat, Maria T. Diaz-Meco and colleagues shows that p62 (also known as sequestosome 1; SQSTM1) is a 'metabolic' tumour suppressor in a genetically induced obese mouse model of prostate cancer. The selective loss of p62 from adipose tissue resulted in a more aggressive tumour phenotype by promoting osteopontin-driven fatty acid oxidation and inhibition of tumour-induced nutrient wasting.

Mouse studies investigating the link between obesity and cancer typically induce obesity by feeding high-fat diets or inactivating the leptin pathway. "Both of these strategies lead to increased calorie intake or hormonal pleiotropic disarrangements, which preclude molecular and cellular studies of the crosstalk between adipocytes and tumour cells," explains Moscat. To avoid these problems, the researchers crossed an adipose tissue-specific knockout of p62, which develops obesity without the need of a high-fat diet, with a mouse model of prostate cancer. This novel model provided the ideal background to study the link between obesity and cancer.

The researchers showed that inactivation of p62 in adipocytes results in a more aggressive and invasive tumour phenotype compared with those from mice with active p62. Loss of p62 in adipocytes from the prostate cancer model increased the systemic production and secretion of osteopontin (a cytokine implicated in advancing tumour aggressiveness) and promoted fatty acid oxidation in tumour cells. This effect is important, as fatty acid oxidation is the main bioenergetic pathway for non-glycolytic tumours, such as prostate cancer. "Increased fatty acid oxidation makes the tumour more invasive because it provides the energy necessary for cancer cells to undergo epithelial–mesenchymal transition to metastasize," adds Diaz-Meco.

In Moscat and Diaz-Meco's mouse model, p62 inactivation also prevented tumour-driven energy 'wasting' in adipocytes. Under normal physiological conditions, tumour cells trigger a process in adipocytes termed fat cachexia, in which adipocytes metabolize fatty acids without producing energy. Therefore, during fat cachexia, tumour cells continue to metabolize nutrients, but at the detriment of their energy reserves. The inactivation of p62 in adipocytes, however, prevented this process and therefore increased nutrient availability for tumour cells.

"A critical question that needs to be addressed is how p62 controls the synthesis of osteopontin," concludes Diaz-Meco. "This is important because if we can find a way to inhibit osteopontin synthesis, we will curtail the ability of the tumour to increase fatty acid oxidation, which will lead to its 'starvation' and likely reduce its metastatic potential."

Ivone Leong

ORIGINAL ARTICLE Huang, J. et al. Adipocyte p62/SQSTM1 suppresses tumorigenesis through opposite regulations of metabolism in adipose tissue and tumour. *Cancer Cell* **33**, 770–784 (2018)