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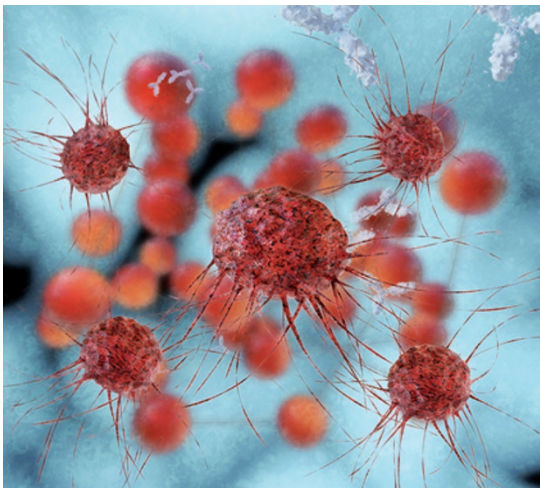
NUTRITION

High-fat diet and dysbiosis accelerate tumorigenesis in mice



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In mice with a predisposition to develop intestinal cancer, dysbiosis as a result of a high-fat diet accelerates the development of intestinal tumours, reports a new study in *Nature*.

"We were interested to see if the caloric input or constituents of a diet could alter the composition of an individual's microbiota," explains researcher Melek Canan Arkan (Technical University Munich, Germany). "If they did, could these changes be associated with disease development in the gut?" The team used a mouse model of intestinal cancer ($Kras^{G12Dint}$) to investigate these points.

After 22 weeks of being fed one of two diets, none of the mice on a normal diet had developed intestinal cancer, compared with 60% of the mice on a high-fat diet. After 40 weeks on a high-fat diet, the tumour cells had metastasized to the liver, pancreas and spleen. Arkan and colleagues then investigated the possible mechanisms underlying this result. The expression of oncogenic *Kras* downmodulated host immunity, by decreasing the Paneth-cell-mediated antimicrobial defense response. In conjunction with the expression of oncogenic *Kras*, the alterations in the gut microbiota caused by the high-fat diet changed the host immune response to the development of a tumour. In combination, these factors increased susceptibility to intestinal cancer.

To determine whether the relationship between dysbiosis and tumour progression was causal, the researchers transferred faecal samples from $Kras^{G12Dint}$ mice that had intestinal tumours and were fed a high-fat diet to healthy $Kras^{G12Dint}$ mice that had been treated with antibiotics for the preceding week and were on a normal diet. The colonized mice developed intestinal tumours, which suggests that the relationship is causal. Furthermore, treatment with antibiotics completely prevented tumour formation in $Kras^{G12Dint}$ mice.

"If this relationship holds true for humans as well, then personalized dietary interventions might enable us to modulate an individual's microbiota to promote health," says Arkan.

The researchers are now planning to define the metabolic alterations that occur in microbial communities when the diet is changed. They will then investigate which changes in microbial gene expression might be associated with health and disease.

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Original article Schulz, M. D. *et al.* High-fat-diet-mediated dysbiosis promotes intestinal carcinogenesis independently of obesity. *Nature* doi:10.1038/nature13398