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Gut bugs linked to obesity

For those unable to shed unwanted pounds, the problem may be more than bad genes or lack of willpower: a new study that compares the intestinal flora of lean and obese mice says bacteria may be derailing your diet.

Firmicutes and Bacteroidetes are the predominant bacterial groups that colonize the guts of both humans and mice. Obese humans have been shown to have a higher proportion of Firmicutes compared to their lean counterparts. This, too, is the case in mice, according to work by Jeffrey I. Gordon and coworkers at Washington University in St. Louis, MO. Their work, published in the 21/28 December 2006 issue of *Nature*, demonstrates that not only do obese leptin-deficient mice have a higher proportion of Firmicutes in their gut than their 'fit' littermates, but that the intestinal bacteria of those overweight mice express more genes coding for enzymes that break down otherwise indigestible polysaccharides. Breaking down more polysaccharides means extracting more calories from food.

Gordon's team found that obesity could be transmitted via intestinal bacteria. Microbe-free mice colonized with the intestinal bacteria from obese mice gained significantly more weight than those receiving bacteria from lean mice, suggesting that altering the bacterial makeup of the gut could help people gain or lose weight.

Ethanol alleviates arthritis in mice

Moderate alcohol consumption may help stave off the debilitating effects of rheumatoid arthritis, a chronic autoimmune disease characterized by inflammation of the joints and other tissues. The disease usually leads to some degree of joint destruction within two years of onset.

Knowing that ethanol consumption causes immune system depression, Andrej Tarkowski of Göteborg University (Göteborg, Sweden) tested the effects of moderate ethanol consumption on rheumatoid arthritis development in a mouse model. Male mice immunized with collagen type II and adjuvant to induce autoimmune arthritis were given 10% ethanol in drinking water or water alone. The onset of arthritis was much slower in ethanol drinkers than abstainers, and the ensuing disease much less severe (*Proc. Natl. Acad. Sci. USA*, 2 January). Animals given water spiked with acetaldehyde, the major metabolite of ethanol, also developed less severe arthritis.

While this level of ethanol consumption did not affect liver function, it was associated with increased production of testosterone. That the anti-arthritis effects of ethanol were eliminated in orchidectomized mice suggests that testosterone is the link mediating the anti-inflammatory effects of ethanol consumption. Whether ethanol consumption has similar effects in humans, or how much would need to be consumed to prevent rheumatoid arthritis, remains to be determined.

Cancer drug stops cycle of PKD

A drug being investigated for its efficacy at treating leukemia and other cancers may also correct a common and incurable kidney disease, reports a new study in mice.

Polycystic kidney disease (PKD) is an inherited progressive disorder affecting ~0.1% of Americans. PKD's characteristic renal cysts impair kidney function, ultimately leading to end-stage kidney disease. With no effective treatments available, patients must rely on dialysis or kidney transplantation to survive.

Based on previous studies, Oxana Ibraghimov-Beskrovny and colleagues at Genzyme Corporation (Framingham, MA) hypothesized that a dysregulated cell cycle might be the cause of cyst formation in PKD kidneys and sought to determine whether arresting the cell cycle with (*R*)-roscovitine, a potent cyclin-dependent kinase inhibitor, would slow disease progression in two mouse models. PKD mice treated with roscovitine showed significant decreases in cystic volume, kidney weight to body weight ratios, and blood urea nitrogen levels, the latter indicating improved kidney function (*Nature*, 14 December 2006).

Roscovitine treatment in mice was not associated with any overt signs of toxicity. Moreover, daily administration was not necessary to keep murine PKD at bay; instead, pulse treatment provided long-lasting effects—good news for people who would require life-long treatment.