this process. However, the protective effect was dependent upon gut microbiota because MyD88-null NOD mice born and raised so that they were completely free of microbes, including gut microbiota, had a high incidence of T1DM. Furthermore, exposure of adult, germ-free, MyD88-null NOD mice to either microbiota similar to those normally present in the human gut or to gut microbiota of MyD88-null NOD mice housed under specific-pathogen-free conditions reduced the incidence of T1DM. Specific differences were found in the composition of gut microbiota from normal NOD mice and MyD88-null NOD mice; consequently, the researchers speculate that MyD88 might influence the proliferation of certain gut microbiota and that loss of this mechanism could block T1DM development.

The findings suggest possible future uses for live microbes or microbial products in the prevention and treatment of T1DM.

Original article Wen L *et al.* (2008) Innate immunity and intestinal microbiota in the development of type 1 diabetes. *Nature* **455:** 1109–1113

Hip fracture risk is not increased by 5-α reductase inhibition

The effect of 5-α reductase inhibitors such as finasteride—a first-line therapy for benign prostatic hyperplasia—on long-term bone health is unclear. These agents inhibit conversion of testosterone to dihydrotestosterone, a compound thought to have a role in bone metabolism. Jacobsen *et al.* carried out a case–control study of hip fracture in men in order to evaluate the role of 5-α reductase inhibition in bone metabolism.

Data were collected from Kaiser Permanente Southern California, an integrated managed-care organization. Jacobsen and colleagues assessed medical records from 7,076 men who had a first hip fracture (mean age at diagnosis 77 years) during 1997–2006, and 7,076 control men without hip fracture matched by age and medical center. Benign prostatic hyperplasia was diagnosed in 2,547 (36%) of patients with hip fracture and 2,488 (35%) of controls, respectively. Use of 5-α reductase inhibitors from 1991 onward was identified from electronic data on prescriptions. In total, 109 (1.5%) of patients with hip fracture and 141 (2.0%) of controls had previously used finasteride or dutasteride.

No direct association between 5-α reductase inhibitor therapy and hip fracture was observed. Indeed, Jacobsen and colleagues' findings suggest that 5-α reductase inhibitors might even reduce the risk of hip fracture. The authors attribute the apparent risk reduction to hormonal mechanisms, but recommend further studies to identify the biological mechanisms involved. Such studies could reveal new insights that could be exploited for fracture prevention.

Original article Jacobsen SJ *et al.* (2008) Association between 5-α reductase inhibition and risk of hip fracture. *JAMA* **300:** 1660–1664

Caloric restriction in young, overweight adults does not adversely affect bone health

The ongoing Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy (CALERIE) study aims to assess whether caloric restriction increases longevity. As part of this study, Redman *et al*. have assessed the possible negative effects of caloric restriction on bone health in young individuals.

The researchers randomly assigned 48 overweight but healthy volunteers (mean age 37 ± 1 years) to one of four 6-month programs: a healthy diet (control); 25% caloric restriction from baseline energy requirements; 12.5% caloric restriction plus 12.5% increased energy expenditure by exercise; or a low-calorie diet (890 kcal daily until 15% weight loss, followed by weight maintenance). Vitamin and mineral supplements were not permitted but participants (46 of whom completed the study) received dietary advice and meals for part of the study. In all three caloric-restriction groups, participants' body mass declined by ≥10% as a result of significant losses in fat mass and fat-free mass. However, changes in total body or hip BMD in the three caloric-restriction groups were not significantly different from those in the control group. Nevertheless, some changes from baseline in the levels of bone turnover markers in the caloric-restriction groups suggested subtle changes in bone metabolism.