demethylation. Genes inactivated by promoter methylation were identified by comparison of microarray data with data from gene sequence and function databases, followed by a confirmatory methylation assay in 14 colon-cancer cell lines, 34 primary colon cancers, and 17 noncancerous colon tissues. Seven of the identified genes had not previously been shown to undergo epigenetic silencing by promoter methylation in colon cancer: *SST*, *TAC1*, *NELL1*, *CAV1*, *AKAP12*, *ENG* and *MAL*. *SST* and *TAC1* are particularly interesting, because their products somatostatin and protachykinin 1 are gastrointestinal peptide hormones with complex autocrine roles in the gastrointestinal tract. Mori and colleagues speculate that inactivation of *SST* inhibits the growth-suppressive effects of somatostatin, and that *TAC1* silencing might promote early-stage carcinogenesis by helping tumor cells to escape immune surveillance and growth-inhibitory signals—mediated by several hormones, of which protachykinin 1 is the precursor.

This study provides novel evidence that somatostatin and protachykinin 1 have roles in preventing colon cancer progression and tumorigenesis.

Original article Mori Y *et al.* (2006) A genome-wide search identifies epigenetic silencing of somatostatin, tachykinin-1 and 5 other genes in colon cancer. *Gastroenterology* **131:** 797–808

Cholesteryl α-glucosides help *H. pylori* evade the immune response

Helicobacter pylori infection persists *in vivo* despite the presence of an ongoing host immune response. A new study by Wunder *et al*. has shown that the balance between persistence of infection and bacterial clearance by the immune response is influenced by *H. pylori*'s glycosylation of cholesterol to cholesteryl α-glucosides—a previously unrecognized mechanism of immune evasion.

The authors showed that *H. pylori* moves along an increasing cholesterol gradient *in vitro*, and extracts cholesterol directly from host cell membranes. *H. pylori* cholesterol α-glucosyltransferase, a newly identified enzyme, converts cholesterol into cholesteryl α-glucosides—these products were found to be essential to *H. pylori*'s evasion of phagocytosis, T-cell activation and bacterial clearance *in vivo*. The authors also demonstrated that the balance between cholesterol and cholesteryl α-glucosides determines whether bacterial clearance or immune evasion occurs: the presence of excess cholesterol in the stomach resulted in reduced *H. pylori* burden and increased gastric inflammation, mediated by an increase in phagocytosis of *H. pylori* by antigen-presenting cells and induction of vigorous, antigen-specific, T-cell activation. Intriguingly, *H. pylori* seems to undergo only limited phagocytosis; Wunder *et al*. speculate that release of cholesteryl α-glucosides within antigen-presenting cells could reduce subsequent phagocytosis of *H. pylori*, or might influence downstream signaling via membrane receptors.

Wunder *et al*. suggest that treatments could be developed that inhibit cholesterol glucosylation and thereby render *H. pylori* accessible to the immune system. Such novel treatments are desperately needed, given the poor compliance and suboptimal eradication rates associated with conventional triple therapy regimens.

Original article Wunder C *et al.* (2006) Cholesterol glucosylation promotes immune evasion by *Helicobacter pylori*. *Nat Med* **12:** 1030–1038

Patients with GERD symptoms despite PPI therapy continue to have reflux

Many patients with symptoms of gastroesophageal reflux disease (GERD) do not undergo pH monitoring unless their symptoms persist despite PPI therapy. Conventional pH monitoring, however, only detects acid reflux. Mainie and colleagues, therefore, used 24 h combined ambulatory multichannel intraluminal impedance and pH (MII-pH) monitoring—which can identify acid and nonacid reflux—to investigate the relationship between reflux and GERD symptoms.

The authors evaluated 168 patients from three centers (mean age 53 years; 103 female), who had been taking a PPI at least twice daily for ≥1 month before undergoing MII-pH monitoring. During testing, 24 patients were asymptomatic; of the 144 symptomatic patients, almost half had a positive symptom index (i.e. ≥50% of their symptoms occurred ≤5 min after a confirmed reflux episode) for at least one symptom. Interestingly, more patients had a positive symptom index after nonacid