gastric pH. Zinc carnosine produced results similar to those of epidermal growth factor (a potent cytoprotective agent). They admit that their study is limited by the indirect assessment of gastrointestinal injury through measurement of gut permeability, and call for further studies into the effects of zinc carnosine. Rigorous scientific review of the safety and efficacy of similar health-food supplements is warranted.

Original article Mahmood A *et al.* (2007) Zinc carnosine, a health food supplement that stabilises small bowel integrity and stimulates gut repair processes. *Gut* **56:** 168–175

TGF-β insensitivity promotes proliferation and invasion in esophageal adenocarcinoma

Inactivating mutations in the gene encoding transforming growth factor β (TGF-β), or components of its signal-transduction pathway, are known to enhance tumor proliferation and invasiveness, but it has not been determined whether loss of TGF-β activity has this effect in esophageal adenocarcinoma. Onwuegbusi and colleagues, therefore, investigated the effects of alterations in TGF-β signaling on cell proliferation and phenotypic indicators of invasiveness in five esophageal carcinoma cell lines.

Only one cell line (OE33) demonstrated cell-cycle arrest and induction of SMAD-dependent gene transcription in response to TGF-β stimulation. The lack of an antiproliferative response to TGF-β in the other cell lines might, therefore, be caused by impaired SMAD-dependent regulation of transcription, although it is possible that other mechanisms are involved. In all cell lines except one (BIC), TGF-β activated mitogen-activated protein kinase and phosphatidylinositol-3-kinase pathways that upregulate the transcription of genes associated with degradation of the extracellular matrix and basement membrane, angiogenesis, and cell migration. The authors also demonstrated that cells in which these kinase pathways were inhibited had less-invasive characteristics; these findings imply that TGF-β stimulation has an important role in development of the invasive phenotype.

The authors conclude that esophageal adenocarcinoma cells can exhibit a loss of the antiproliferative response to TGF-β, while remaining responsive to TGF-β-mediated activation of kinase signaling pathways. TGF-β could, therefore, be independently involved in both the initiation and progression of esophageal adenocarcinoma.

Original article Onwuegbusi BA *et al.* (2007) Selective loss of TGFβ Smad-dependent signalling prevents cell cycle arrest and promotes invasion in oesophageal adenocarcinoma cell lines. *PLoS ONE* **2:** e177

Pten deficiency causes intestinal polyposis in mutant mice

Intestinal polyposis (a benign precursor of intestinal cancer) is caused by an abnormal increase in crypt number and a concomitant reduction in the differentiation of epithelial cells that arise from crypt intestinal stem cells (ISCs); however, the processes by which mutations in ISCs result in primary tumor initiation are poorly understood. He and colleagues have conducted a study in mice that clarifies some of the molecular events involved in hamartomatous polyp formation. They found that deletion of the tumor-suppressor gene *Pten* (phosphatase and tensin homolog) increases the proliferation and alters the distribution of ISCs in intestinal crypts.

A conditional inactivation mouse model was used, which allows the inactivation of a chosen gene through site-specific recombination only in response to a triggering event; test mice were homozygous for inactive *Pten* ($Pten^{-/-}$). These mice developed multiple polyps 1 month after *Pten* inactivation, but control mice ($Pten^{+/-}$, or mice without the conditional inactivation capacity) did not. Significantly increased proliferation of ISCs was observed in *Pten*-deficient mice compared with control mice (proliferative index 19.4% vs 53.2%, $P<0.01$), and polyp formation was found to originate from such cells.

The authors conclude that a therapy that targets cancer stem cells (but not normal stem cells) is desirable to prevent regeneration of intestinal tumors, although improved knowledge of the differences between these stem-cell populations is required. This study has identified possible signaling pathways that are negatively regulated by Pten, which could have a key role in the development of successful therapies.

Original article He XC *et al.* (2007) PTEN-deficient intestinal stem cells initiate intestinal polyposis. *Nat Genet* **39:** 189–198