EARTH SCIENCE

# Hot and deep

LORRAINE FIELD

The landscape of Afar in Ethiopia (pictured) is tortured, because underlying tectonic plates are pulling apart from each other. Such rifting can lead to continental break-up, and is often accompanied by voluminous magmatism — the production of large amounts of melt. In this issue, Ferguson *et al*. report the cause of this magmatism in Afar (D. J. Ferguson *et al*. *Nature* **490,** 70–73; 2013).

The authors developed a model of magmatism in the region using geochemical data from lavas that erupted along the rift. They conclude that melting is generated at great depths — 80 kilometres or more — and is driven by an unusually hot region of the mantle.

Using another model, Ferguson and colleagues tracked the development of melting at the rift, and found that thinning of the tectonic plate over the past 30 million years has been much less than expected. This suggests that an abrupt phase of plate thinning during the final stages of break-up would be required for an ocean basin to form in Afar. **Andrew Mitchinson**

CANCER

# An acidic link

**Obese people are at higher risk of multiple types of cancer, but why? One explanation could be that obesity enhances the production of pro-inflammatory, and carcinogenic, bile acids by gut microorganisms.** **SEE LETTER P.97**

SUZANNE DEVKOTA & PETER J. TURNBAUGH

The rise in the global prevalence of obesity has been accompanied by a wide array of other morbidities, including diabetes, cardiovascular disease and cancer. Despite strong epidemiological data that link obesity to a higher risk of developing numerous cancers, the mechanisms underlying this connection remain unclear. A few important clues have been uncovered: that obesity-associated inflammation contributes to liver cancer[1]; that obesity is associated with marked changes to the trillions of microbes found in the gastrointestinal tract[2]; and that obesity-associated bacteria can produce inflammatory metabolites[3]. On page 97 of this issue, Yoshimoto *et al.*[4] present a plausible link by which deoxycholic acid, an obesity-associated by-product of microbial bile-acid metabolism, might contribute to hepatic inflammation and the subsequent progression to cancer in obese mice*.

The authors began by using a strain of mouse in which expression of a gene that induces the senescence-associated secretory phenotype (SASP) can be monitored non-invasively by luminescence. Senescence, or cell-cycle arrest, has conventionally been viewed as a favourable process when trying to correct DNA damage and halt abnormal cell proliferation, but it has more recently been shown that senescent cells are active and can produce pro-inflammatory signalling proteins that promote tumour growth — key hallmarks of SASP[5]. Yoshimoto *et al.* found that tumour initiation with a chemical carcinogen triggered luminescence in the abdomen (indicative of liver cancer) of obese mice fed a high-fat diet, whereas lean mice fed a standard diet were protected from liver cancer. The researchers saw a similar response in mice that were deficient in the appetite-regulating hormone leptin, demonstrating that both dietary and genetically induced obesity can promote liver cancer. *In situ* analysis of gene expression in the livers of these obese mice revealed the expression of multiple components of SASP.

But how exactly does obesity stimulate SASP? The authors' experiments using antibiotics implicate obesity-associated gut microbes. Treatment of the mice with a cocktail of four antibiotics resulted in a marked reduction of liver cancer, as did treatment with another antibiotic, vancomycin, to target bacteria in the Firmicutes phylum, which are found at higher abundance in obese animals[6]. Furthermore, the authors detected high serum levels of deoxycholic acid (DCA) in mice fed a high-fat diet, and observed that these levels were reduced by vancomycin treatment. DCA is a secondary bile acid produced by gut microbes such as *Clostridium sordellii*; it is known to be carcinogenic and has long been implicated in colorectal cancer[7]. When the authors inhibited microbial 7α-dehydroxylation, the biochemical reaction that produces DCA, liver cancer was suppressed in obese mice, whereas when they supplemented antibiotic-treated animals fed a high-fat diet with DCA, carcinogenesis was enhanced.

Together, these results emphasize the key

*This article and the paper under discussion[4] were published online on 26 June 2013.