Earth science

How do your mountains grow?

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The soaring, jagged peaks of the world's second highest mountain range, the Andes, could owe their stature not to the power of the Earth but to that of the sea. So propose Simon Lamb and Paul Davis in this issue (*Nature* **425,** 792–797; 2003).

Most mountain ranges are created by the collision of two continental plates, such as the grinding action of India against Asia that thrust up the Himalayas. But the Andes are perched on a point where an oceanic plate slips down beneath a continental one. Great mountains aren't usually born of such meetings. Heavy, dense oceanic plates tend to slip underneath continental ones, causing major earthquakes but not world-class mountains. If the push of the mid-Atlantic ridge on tectonic plates were the only factor driving up the Andes, one calculation shows that they would be no more than two kilometres high — half their actual height.

Lamb and Davis argue that the extra push comes from the fact that the forces of the plate collision are focused on a small area — a stretch of the plate boundary where the friction in the trench between the Pacific and South America is particularly high. The cold water current that sweeps up the west coast of Peru and Chile from high southern latitudes encourages little water evaporation, and therefore little rain. That means there are no rivers to dump worn mountain sediment back into the ocean — sediment that could act as lubrication. Instead, the trench off the coast of the Andes is rough and dry. That extra friction, say the authors, helps to prop up the mountains.

There could even be a positive feedback loop in place, causing the mountains to bulk up more and more over time. The higher the mountains grow, the drier the coastline becomes — as any wet air coming in from the Atlantic is blocked by the towering peaks — which in turn further reduces erosion and props the mountains up still more.

Complex relationships between rock, air and sea have been found before, although it's usually mountains that are thought to affect climate, rather than the other way around. The Himalayas, for example, are believed to have changed the air flow enough to spark the formation of the Indian monsoons. And as all that rain weathered away the mountains' rocks, carbon dioxide was taken out of the air and sent down streams as carbonate, to be buried at the bottom of the sea; this extraction of greenhouse gas is thought to have cooled the global climate. But in the Andes, rather than the mountains making the climate, the climate might actually have made the mountains. **Nicola Jones**

mutation. Basal-cell carcinoma of the skin — a common result of exposure to sunlight — is most often triggered by ultraviolet damage to both copies of the *ptc* gene[5,6]. Mutation of *ptc* has also been implicated in certain brain[7] and muscle tumours[8]. Cancer can also result from mutations in *smo* that convert the protein to a permanently activated form[9].

Berman *et al.*[3] and Thayer *et al.*[4] now implicate the Hh pathway in the genesis of cancers of the digestive system. Rather little has been understood about the origins and growth of these often fatal forms of cancer, but the role of Hh in the normal development of these tissues hints that defective Hh signalling might allow growth to explode. Curiously, however, it seems that neither *ptc* nor *smo* is mutated in tumours of the digestive tract. Instead, the cancer cells make too much Hh.

Berman *et al.* surveyed the production of Hh in cultured cells derived from several different types of digestive-system tumour, including those of the oesophagus, stomach, biliary tract, pancreas and colon. They detected Hh expression in all of these cell types, which led them to hypothesize that this signalling molecule might be the trigger for tumour growth. To test this idea they tried to inhibit the growth of cultured tumour cells by using a Hh-blocking antibody. Treatment with the antibody blocked the growth of a wide range of tumour cells, whereas the addition of Hh caused tumour growth to spurt.

Meanwhile, Thayer *et al.* examined Hh production in 20 human pancreatic cancer biopsies and found that the protein was aberrantly expressed in 70% of the specimens. To investigate whether Hh might contribute to the genesis of pancreatic cancer, these authors examined transgenic mice in which Hh had been overproduced in the developing pancreas. All of these mice contained abnormal pancreatic cells that bore similarities to precancerous cells observed in a form of human pancreatic cancer.

Importantly, the link between the Hh pathway and cancer of the digestive tract is accompanied by ideas for treatment. Both Berman *et al.* and Thayer *et al.* inhibited tumour growth in mice with the drug cyclopamine. This chemical is a teratogen — a compound that can cross the placenta and cause defects in a developing fetus. It was first discovered in extracts from the corn lily, a beautiful but treacherous flower often found in alpine meadows. If a pregnant sheep eats the plant, the fetus develops with cyclopic facial features — the same defect that is caused by inadequate Hh activity in people and mice. It turns out that cyclopamine can block the activity of Smo, so this, or other drugs that affect the Hh pathway, have potential as anti-cancer drugs[10].

Both groups used a 'subcutaneous xenograft model' of digestive-tract cancer to test the effect of cyclopamine. In this model, tumour cells are seeded under the skin of immune-deficient mice. Berman *et al.* waited until the tumours had grown to a certain size, before injecting them with cyclopamine each day. Remarkably, the treated tumours regressed completely within 12 days. Meanwhile, Thayer *et al.* found that treatment with cyclopamine reduced the