used to study inductive processes. Animal cap cells can mount a bewildering range of responses to TGF-β proteins. For instance, a member of the bone-morphogenetic-protein subfamily (BMP4) can induce ventral-type mesoderm only, Xnr3 induces neural tissue, and different doses of activin induce at least four different mesodermal cell types. How, then, is signalling by different TGF-β ligands and doses translated into distinct transcriptional responses?

Although different receptor isoforms may confer specificity at the membrane level, it has been unclear how specificity is maintained during signal transduction to the nucleus. In *Xenopus*, mesoderm induction by activin, fibroblast growth factor and BMP4 all depend on Ras function, which doesn't help to further our understanding of specificity.

An important clue towards identifying the downstream effectors of TGF-β-type signals came from a genetic screen of *Drosophila* by Gelbart and colleagues[6], who systematically searched for enhancers of a *dpp* mutant phenotype. They identified *Mothers against dpp* (*Mad*), a gene that turned out to be a member of a family of related genes in *Caenorhabditis elegans*, *Sma2–4* (ref. 7). *Mad* family genes encode proteins of relative molecular mass about 50K. They contain conserved amino- and carboxy-terminal domains separated by a proline-rich linker, but they do not have any protein motif that gives a clue to their function.

With the aid of a database of expressed sequence tags, Liu *et al.*[1] have now cloned *Smad1*, a human homologue of *Mad*. As described in the paper, they used the GAL4-system to find out if the gene encodes a transcription factor: it emerged that the carboxy-terminal domain of Smad1 indeed activates transcription, but the full-length protein does not. When cells are cotransfected with BMP type I and II receptors, however, and then treated with BMP4 ligand, full-length Smad1 becomes transcriptionally active. This implies that Mad proteins have latent transcription-factor activity that is activated by ligand binding to TGF-β receptors. So Mad proteins may provide the link in signal transduction from the cytoplasm to the nucleus in response to TGF-β growth factors.

It remains to be seen whether Mad proteins can bind DNA, but from the new results it seems that they can directly initiate transcriptional responses. Because Smad1 protein enters the cell nucleus in response to BMP4, Mad latency may be due to its retention in the cytoplasm. Regulation of transcription factors by controlling their sojourn in the cytoplasm is a recurring strategy in signal transduction[8], and an attractive hypothesis for Mad control. The main message of one of the *Cell* papers, that by Hoodless *et al.*[2], is that phosphorylation of the protein may be the event that instructs it to enter the nucleus.

This leaves the issue of explaining the specificity of signal transduction by different TGF-β-type growth factors. Enter Graff *et al.*[3], who cloned two *Mad* homologues in *Xenopus*, *Xmad1* and *Xmad2*, and used the animal cap system to show that their protein products mediate distinct TGF-β signalling responses. Like BMP4, Xmad1 induces ventral mesoderm only; and like medium and high doses of activin, Xmad2 induces dorsolateral and dorsal mesoderm in a concentration-dependent manner. Signal transduction by a specific set of Mad proteins may therefore explain the differential response of individual cells to various TGF-β-type growth factors (see figure). Given that Mad proteins elicit such specific responses, they could become a promising pharmaceutical target — not least because the first *Mad* candidate for a tumour-suppressor gene has just surfaced[9].

We are of course left with many questions. How can overexpression of Mad proteins lead to a response when their activity should be latent? Like the transcription factor NF-κB, whose nuclear translocation is inhibited by I-κB, retention of Mad protein in the cytoplasm may involve accessory proteins that may be titrated (see figure), explaining the relatively high doses of exogenous Smad1 and Xmad1 required for induction of ventral mesoderm. If the dose-dependent effects of TGF-β really are transduced by individual, 'smart' Mad proteins, how do they integrate the signal dose? Finally, what are the target genes for Mad and what determines their specificity? We can expect a few of the answers before too long — indeed, some of them are undoubtedly on still-wet autoradiograms in the many laboratories working in this area. □

Christof Niehrs is in the Division of Molecular Embryology, Deutsches Krebsforschungszentrum, INF 280, 69120 Heidelberg, Germany.

1. Liu, F. *et al. Nature* **381,** 620–623 (1996).
2. Hoodless, P. A. *et al. Cell* **85,** 489–500 (1996).
3. Graff, J. M., Bansal, A. & Melton, D. A. *Cell* **85,** 479–487 (1996).
4. Kingsley, D. M. *Genes Dev.* **8,** 133–146 (1994).
5. Smith, J. *Nature* **381,** 367–368 (1996).
6. Sekelsky, J. J., Newfeld, S. J., Raftery, L. A., Chartoff, E. H. & Gelbart, W. M. *Genetics* **139,** 1347–1358 (1995).
7. Savage, C. *et al. Proc. natn. Acad. Sci. U.S.A.* **93,** 790–794 (1996).
8. Vandromme, M., Gauthier-Rouviere, C., Lamb, N. & Fernandez, A. *Trends biochem. Sci.* **21,** 59–64 (1996).
9. Hahn, S. A. *et al. Science* **271,** 350–353 (1996).

Erratum

In the article 'Continents of the core' by Michael E. Wysession, published on 30 May (*Nature* **381,** 373–375; 1996), the last reference was inadvertently left out. It should have read:

7. Kingma, K. J., Cohen, R. E., Hemley, R. J. & Mao, H.-K. *Nature* **374,** 243–245 (1995).

DAEDALUS

Fire from heaven

BENJAMIN FRANKLIN famously proved that lightning was electrical, by flying a kite in a thunderstorm and drawing sparks from the wet string onto his knuckle. He was lucky. The next man to try it was electrocuted. Indeed, the test could easily provoke a lightning strike. The deadliest version of the experiment, says Daedalus, would be to fly the kite on a string impregnated with caesium or its salts. The resulting discharge would follow the string to Earth, boiling off its caesium, whose vaporized ions conduct electricity very readily. The resulting column of hot conducting plasma might act as a sort of extended lightning. All the energy of the thunderstorm would drain to Earth in one long, roaring blaze.

This could be a neat way of short-circuiting a thunderstorm. The farmer seeing a downpour about to wreck his harvest, the sportsmen facing the washing out of their match, the anxious outdoor concert promoter, all might love to short out a gathering storm and get it over with. But what heroic fool would fly the deadly initiating kite? Daedalus has a safer idea. A rocket powered by caesium-rich fuel could be fired into the clouds by remote control. It would leave a hot, conducting trail, similar to the ionized exhaust plume by which he planned last week to power an electrically augmented space rocket. With one deafening blast, the thunderstorm would drain to Earth down the trail of the rocket. The clouds, deprived of their mechanism for electrostatic precipitation, would drift away harmlessly.

But a thunderstorm is not an isolated event. The world's thunderstorms keep the lower ionosphere, 40 km up, charged to over 200 kV. So Daedalus is scaling up his ideas. He is planning a big rocket, powered by a mixture of caesium perchlorate and buckminsterfullerene (both of which form ions very readily), to soar into the ionosphere and short it out.

This stable 'cable' will draw power from the whole conducting ionospheric shell. Its fiery trail to Earth will be a sort of permanent lightning, compacted and stabilized by the magnetic pinch effect of its steady current. With a caesium-rich ground electrode to accept and anchor the discharge, and release ions to keep it going, it will deliver gigawatts of power to the distribution grid. Sadly, the world's thunderstorms will not be arrested, but intensified — to return to the ionosphere the huge current being drawn from it. The column could also usefully serve as a global transmitter. Radio and television signals sent up it would be conducted round the Earth on the ionosphere, and radiated down to receivers everywhere.

David Jones