Figure 1 Outline of a developmental pathway based on NF- κ B signalling. **a**, Signalling through NF- κ B in chick limb cells occurs by its release from I- κ B and translocation to the nucleus where it regulates target genes (activation of *Twist* and repression of *Bmp-4*). Gene(s) encoding receptors for fibroblast growth factor (FGF) could lie downstream of *Twist*. These targets in the chick limb bud cells were identified by Kanegae *et al.*¹ and Bushdid *et al.*² by reference to known targets of NF- κ B in *Drosophila*. **b**, In *Drosophila* blastoderm, signalling through Dorsal, a homologue of NF- κ B, occurs by its release from Cactus and translocation to the nucleus, where it activates *Twist* and represses expression of *decapentaplegic* (*dpp*, of which *Bmp-2* and *Bmp-4* are vertebrate homologues). A *Drosophila* homologue of vertebrate FGF receptors (DFR1) appears to lie downstream of *Twist*, at least in the imaginal discs. A human connection comes from the finding³ that mutations in the *Twist* gene cause Saethre–Chotzen syndrome, which is characterized by limb anomalies. For simplicity, NF- κ B activity is represented here as a single entity, although it is known to act as a hetero- or homo-dimeric complex.

develop normally, however, presumably because other NF- κ B family members compensate for its absence⁸.

Further dissection of the NF- κ B signalling pathway in the chick limb was possible

because of the extraordinary parallels between development in *Drosophila* and in vertebrates. NF- κ B is homologous to the product of the *Drosophila* gene *Dorsal* — *Dorsal* signalling occurs by the same mecha-

nism as NF- κ B signalling, with Cactus being the homologue of I- κ B (Fig. 1b)⁹. *Dorsal* is known to activate expression of a gene called *Twist* (encoding a regulatory helix–loop–helix protein), in the region of the insect body where mesoderm will form.

This led Kanegae *et al.*¹ and Bushdid *et al.*² to examine *Twist* expression in the chick limb, and they show that, when NF- κ B signalling is blocked, *Twist* expression is reduced. Interestingly, early limb buds of *Twist*-null mouse embryos, which die about midway through gestation, have been reported to be stunted¹⁰. This then fits very nicely with the limb truncations obtained when NF- κ B signalling is blocked. Another insight from *Drosophila* links *Twist* expression to apical ridge signalling. In *Drosophila*, a gene closely related to the genes encoding receptors for vertebrate fibroblast growth factor appears to be downstream of *Twist*⁵. Apical ridge signalling in the chick limb is known to be mediated by fibroblast growth factors. So *Twist* expression in the limb could be directly connected with the ability of cells in the progress zone to respond to ridge signals.

In *Drosophila*, *Dorsal* not only promotes *Twist* expression but also represses expression of *decapentaplegic* (*dpp*), which encodes a signalling molecule (Fig. 1b). Again, a parallel emerges in the chick limb. Bushdid *et al.*² show that blocking NF- κ B signalling leads to increased expression of a vertebrate homologue of *dpp*, a gene encoding a bone morphogenetic protein, BMP-4. These proteins were originally named because of their ability to induce bone. They now appear to be multifunctional molecules, being implicated not only in skeletal

Extragalactic astronomy

A ring in truth

The orange bullseye is an image of two galaxies. One, at the centre, has stretched the image of the other into a ring — the first complete ‘Einstein ring’ ever seen. This is just one of many gravitational lenses collected in recent years, by a programme that aims to answer fundamental questions about the Universe’s geometry and composition.

Einstein’s theory of General Relativity predicts that light rays are curved by gravitational fields. The first confirmation of this effect came in 1919, when the Hyades star cluster was observed slightly out of place during a solar eclipse — a weak example of gravitational lensing. More interesting lenses occur where one distant galaxy or quasar appears to us in several distorted images, around the position of an intervening galaxy or galaxy cluster. More than 20 are known, including some partial Einstein rings, where the

lensed and the lensing objects are almost perfectly aligned.

Prompted by observations from the MERLIN array of radio telescopes, the Hubble Space Telescope has imaged this

complete Einstein ring (L. J. King *et al.* *Mon. Not. R. Astron. Soc.* 295, L41–L44; 1998). The radio image, shown below Hubble’s infrared image, isn’t a complete ring because the radio-emitting part of the lensed galaxy is a little off-centre.

So how do lenses reveal the geometry of the Universe? It is a matter of statistics. The redshift distribution of lensed objects tells us what proportion of our lines of sight to distant regions are blocked by intervening galaxies. That is a function of the geometry of space-time, which in turn depends on the amount of matter present, and on the energy density of empty space — the ‘cosmological constant’, which Einstein introduced and then abandoned, but which is beginning to come into vogue again. By the end of this year, the team working with MERLIN hope to put the strictest limits yet on the cosmological constant.

Stephen Battersby