Gene regulation

A hit-and-run mechanism for transcriptional activation?

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AT present it is a matter for debate whether enhancer/upstream promoter sequences of mammalian genes and the transcription factors binding to them are required for each round of transcription initiation, or whether they are needed only as a trigger to organize a gene into a stable transcription complex, after which transcription by RNA polymerase II can continue without these DNA sequences and their bound factors. Data compatible with a transient enhancer requirement were first provided[1] by Wabl and Burrows, who showed that immunoglobulin gene transcription persists in a B-cell line in which the enhancer had been removed by spontaneous deletion. The recent experiments of two groups[2,3] on transcription from a viral promoter *in vitro* at first sight seem to suggest an explanation at the molecular level for these and subsequent observations *in vivo*. There are, however, alternative explanations for both sets of phenomena, and it may be necessary to look elsewhere for the molecular basis of cellular memory.

When Wabl and Burrows first discovered the apparently transient need for the immunoglobulin enhancer, they considered the enhancer to be an artefact of transfection. The remarkable tissue specificity of the enhancer, however, made this seem unlikely, and in collaboration with Andreas Radbruch and Sigi Klein, we undertook a more detailed investigation of a cell line that continued to produce immunoglobulin transcripts after spontaneous deletion of the immunoglobulin heavy-chain enhancer. One possible explanation was that the cell had mutated to render the presence of an enhancer dispensable for the efficient expression of the endogenous or a transfected immunoglobulin gene. Alternatively, it was also conceivable that the deletion had, by chance, created a substitute transcription factor binding site(s). But when we cloned the endogenous gene and reintroduced it into the same cell line (after appropriate tagging), it was expressed only when linked to an enhancer[4]. At the same time, essentially the same gene, but devoid of the enhancer, was strongly transcribed in its genomic context. Thus, both the above explanations were excluded. We argued at the time that there are only two reasonable explanations for these findings: first, that there is another, as yet unidentified enhancer that substitutes for the deleted immunoglobulin heavy-chain enhancer; or second, that the enhancer organizes the DNA into a stable transcription complex, after which it is no longer required.

It is this latter possibility that seems to be supported by two recent papers on the initiation of transcription from one of the promoters of adenovirus. For several years, Robert Roeder and his colleagues have been analysing the mechanism of transcriptional initiation by RNA polymerase II. Whereas their earlier work concentrated mainly on the adenovirus major late promoter, they have now, together with the group of Michael Green, looked at the E4 promoter of adenovirus. This promoter is particularly suitable because transcription *in vitro* can be stimulated 1,000-fold by the enhancer/upstream binding factor ATF. This cellular transcription factor binds to multiple sites upstream of the E4 TATA box. In a series of experiments[2,3], Roeder, Green and collaborators show that ATF facilitates formation of an initiation complex by TFIID (TATA box factor), RNA polymerase II, TFIIB and TFIIE. The formation of this complex is revealed by an extended footprint over the TATA box and downstream of it. Removal of ATF, using a large excess of competitor oligonucleotide with an ATF-binding site, does not eliminate the extended TATA box footprint, nor does it prevent subsequent transcription by RNA polymerase. The authors conclude that ATF is required only transiently for the process of transcription initiation. In other words, ATF is required for efficient assembly of the

Oldest known reptile found in Scotland

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Stan Wood/British Museum (Natural History)

THE discovery in Scotland of the earliest known fossil reptile is the most important fossil find in the past 50 years, in the opinion of Timothy Smithson (University of Newcastle-upon-Tyne), who identified it. At 340 million years old, it is the oldest animal of its kind by 40 million years, and is contemporaneous with some of the most ancient faunas containing tetrapods of any kind (see *Nature* 333, 768; 1988). The 8-inch-long articulated skeleton was found in Lower Carboniferous rocks in southern Scotland by professional collector Stan Wood, who announced the find at the British Museum (Natural History) in London on 16 November. The fossil, seen in the figure, will be on display there until 17 January. The inset shows an artist's impression (by Michael Coates) of how the reptile might have looked.

Wood has found many spectacular Lower Carboniferous amphibians, but this is his first reptile, marked out as such by anatomical details of the skull table, vertebral column and feet. The discovery will prompt a radical revision of early amniote phylogeny, says Michael Benton (Queen's University, Belfast); that fully evolved reptiles existed in the Lower Carboniferous throws doubt on the supposedly close phylogenetic links between amniotes and anthracosaurs, a group of fossil amphibians.

Potassium–argon isotope dates of 338–340 million years old for the strata were established before the new fossil was discovered. Lower Carboniferous Scotland lay across the Equator, and the humid, tropical jungle was frequently inundated with volcanic ash. This earliest-known reptile may have been boiled to death in a hot spring and covered with dust, which could account for its excellent preservation. Henry Gee.