artificial deletions tested in gene transfer experiments, would remove this putative silencer thereby liberating the promoter and allowing it to operate in an enhancer-independent manner, whereas in the natural situation or in Ig genes used in gene transfer experiments, the silencer is retained and the promoter is dependent upon an enhancer to suppress the silencer.

At present, it is premature to propose any detailed model of the control circuits that might be involved in Ig gene regulation. However, it appears that the Ig enhancer is equally active in cells representing various stages of B cell development[2,3] whereas the Ig promoter is more active in plasma cells than pre-B and B cells[4]. Thus, it would seem that the promoter and its associated element 'sense' the differentiation state of the cell and direct the appropriate level of gene expression. A role for the enhancer (and the putative silencer) is harder to formulate although it is possible that the enhancer responds to other inductive signals, such as those B cell differentiation factors which appear to induce a high rate of Ig secretion[11]. In this context, the putative silencer might act to reduce the expression as soon as the inductive signal ceases.

Note added in proof

Recently Grosschedl and Baltimore (*Cell* 41, 885–897, 1985) have also demonstrated that the tissue-specificity of Ig gene expression is not solely regulated by the enhancer but also the promoter. These workers have also identified an intragenic sequence implicated in this control.

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Archaebacteria coming of age

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In 1977, Carl Woese and George Fox published a proposal concerning cellular evolution which, because of its radical nature, has only recently gained general understanding and acceptance among microbiologists, geneticists and molecular biologists[1,2]. That proposal was, in part, that prokaryotes comprise two distinct phylogenetic lineages of extraordinarily ancient divergence – the *archaebacteria* (all of the methanogens and extremely halophilic bacteria and some sulfur-dependent thermophiles) and the *eubacteria* (everything else in Bergey's manual).

Initially, this distinction was based on extensive comparisons of the sequences of oligonucleotides released by T1 ribonuclease digestion of 16S ribosomal RNAs. The molecular phylogenetic database has now been expanded, to include the complete sequences of several dozen archaebacterial, eubacterial and eukaryotic 16S (18S) rRNAs. The list of additional basic molecular or biochemical characters which define the archaebacteria as a coherent group, no more akin to eubacteria than to eukaryotes, has grown impressively. It includes: (1) 5S rRNAs and tRNAs unique in primary and secondary structure and patterns of modifications; (2) group-specific ribosome morphologies and ribosomal proteins whose sequences are neither eubacterial nor eukaryotic, but sometimes reminiscent of both; (3) sensitivity, *in vitro*, to diphtheria toxin – heretofore thought to ADP-ribosylate only eukaryotic EF-2; (4) large, multi-subunit RNA polymerases which seem in structure and antigenic properties slightly more like their eukaryotic than their eubacterial homologues; (5) the otherwise unknown presence of reverse gyrases, which positively supercoil the DNA of thermophilic strains; (6) intervening sequences in genes for tRNA, rRNA and possibly proteins – see below; (7) cell surface structures and walls of many types, none containing peptidoglycan; (8) membrane lipids containing branched (not straight) side chains in ether (not ester) linkage to glycerol; and (9) a bewildering variety of other metabolic, physiological or ultrastructural curiosities[3,4].

So the archaebacteria deserve molecular genetic attention on their own merits. More than that, even, they deserve attention because in understanding the as yet confusing mixture of eubacteria-like, eukaryotic-like and truly unique molecular characters the archaebacteria exhibit, we will come to understand the last common ancestor of all three 'primary kingdoms', an entity that Woese and Fox, in the second part of their 1977 proposal[1,2], called the *progenote*. The fact that differences between kingdoms involve some fairly basic features of genetic information transfer means, almost certainly, that the process of information transfer itself (mechanisms of replication, transcription and translation) was still undergoing rapid adaptive evolution (towards greater efficiency, accuracy and speed) in the progenote.

These concepts were clear in general from the first international gathering of archaebacterial molecular biologists, in Munich, in 1981 (Ref. 3). The second meeting of this now much larger group was held again in Munich, late this June*. The concepts have grown richer and deeper because of the accumulated molecular details, of which I can describe only a few.

In an opening lecture, Woese presented a new phylogenetic analysis of available 16S (and 18S) rRNA gene sequences. Many phylogenetic divergences within the archaebacteria are very deep; the deepest seems to be that which separates sulfur-dependent thermophilic strains such as *Sulfolobus*, *Thermoproteus* and *Pyrodictium* from the extensively characterized methanogens. (Perhaps surprisingly, given their quite different biochemistry, the halophilic bacteria and the wall-less thermophile *Thermoplasma* appear to have arisen from within the methanogenic group.) Data from ribosomal protein sequencing (Matheson) electron microscopy of ribosomal particles (Stöffler, Lake), antibiotic sensitivity (Böck, Amils) and functional and structural analyses of translation elongation factors (Klink), 5S rRNA (DeWachter, Fox) and

* EMBO Workshop on the Molecular Genetics of Archaebacteria, organized by A. Böck, D. Oesterhelt and W. Zillig.

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