conservation of *H19* imprinting between species, and might facilitate the identification of specific 'imprinting control factors' that bind to the 42 bp element. However, the true significance of this sequence conservation will only be identified by deleting the 42 bp element in the mouse germline, which we predict will perturb *H19* and *Igf2* imprinting.

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The G-rich repeat 1.5 kb upstream of mouse *H19* mentioned in the legend to Fig. 1 was recently shown to be present in rats but absent in humans, and is not essential for *H19* imprinting[1].

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Going to extremes

Archaea: Bridging the Gap Between Bacteria and Eukarya (A Keystone Symposia), Taos, NM, USA, 9–14 January 1999

Most visitors to Taos, New Mexico, think of themselves as seekers of the extreme. If any such individuals had attended this meeting about Archaea, they would have realized what living at extremes really means. Within Archaea – the so-called third domain of life – are some of the most 'extremophilic' organisms known. The field of Archaeaology can trace its roots to 1977, when analysis of small-subunit rRNA sequences led to the conclusion that the prokaryote–eukaryote dichotomy was misleading, and that prokaryotes should be split into two groups – the standard bacteria and what became known as Archaebacteria (Fig. 1a)[1]. Subsequent analysis of other data, supported this revolutionary trichotomy of life, and in 1990 the three groups were assigned a new taxonomic status (the Domain) and Archaebacteria were renamed Archaea to emphasize their uniqueness[2]. A second Archaeaological revolution began when analysis of anciently duplicated gene families suggested that Archaea and Eukarya were sister groups[3,4] (Fig. 1b). This rooted tree has dominated Archaeal studies for many years and is, in part, responsible for the 'Archaea as bridge' concept. A third revolution in Archaeaology started with the publication of the complete genome sequence of *Methanococcus jannaschii*[5]. The genomics era is both shaking up the tree of life, and stimulating experimental work on Archaea.

A major topic of discussion at Taos was the need for new concepts of the tree of life. For example, evolutionary trees of rRNA sequences, which many people use as their only map of the relationships among species, might be biased by a variety of reconstruction problems[6]. A more compelling problem is the possibility of gene transfers between species in the past. Recent analyses of complete genome sequences were presented, suggesting that the extent of lateral gene transfers is much greater than previously thought. Thus, while the concept of a phylogenetic tree might work for individual genes, a phylogenetic network might be a more appropriate metaphor for the evolution of genomes (Fig. 1c). Genome analysis also shows that many other events (e.g. gene loss, gene duplication and gene rearrangement) are also very common. This means that ostensibly closely related species could have major genomic differences, which in turn could lead to major biological

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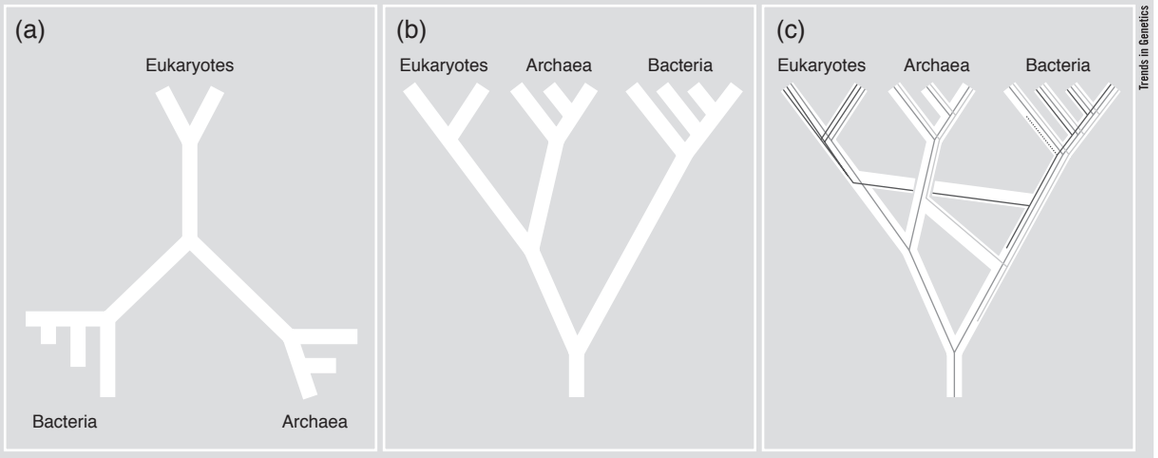
FIGURE 1. The evolution of a phylogeny



Panels show different representations of phylogenetic relationships among organisms. (a) Initial studies of rRNA genes identified Archaea as a third form of life. (b) Studies of duplicated genes allowed the rooting of the tree of life and suggested that Archaea and eukaryotes were more closely related to each other than either was to bacteria. (c) The analysis of complete genome sequences suggests that gene transfer, gene loss, gene duplication and related phenomena have played a major role in evolution. Thick lines represent the evolution of individual genes showing examples of gene loss (thin lines end before thick lines do), gene duplication (thin lines split within a single thick line), and lateral transfer (thin and thick line crossing over). This adds complexity to our view of the history of living organisms.

differences. Such differences between close relatives are, in fact, being found (Karl Stetter, University of Regensburg).

Despite these, and other problems with evolutionary analysis, there was much discussion of practical uses for the rRNA tree of life (e.g. identification and isolation of novel species and testing of evolutionary theories) and for evolutionary analysis in general (e.g. identification of lateral transfers, classification of multigene families and prediction of function for uncharacterized genes)[7].

Whether or not the 'Archaea as a bridge' concept is phylogenetically correct, there was much discussion on the fact that Archaea possess some features similar to those of eukaryotes (e.g. tRNA maturation, histones, chromatin and proteosomes), some features similar to those of bacteria (e.g. restriction enzymes) and some unique features. In addition, Archaea may provide good model systems for studies of eukaryotic biology because many of their eukaryotic features are simpler than those of eukaryotes themselves (e.g. transcription and histones).

While the genome data has clouded the picture of the tree of life, it has served as a great stimulant to studies of Archaeal biology. For example, the contents of a genome were shown to be of great use for understanding genome structure, identifying genes and pathways that might have otherwise not been found, and for identifying redundant pathways. What is missing from a genome sequence is also of use – in particular, when genes for which activities are thought to be essential, or for which activity has been found, cannot be identified (e.g. aa-tRNA synthetases[8]). Despite the power of genome sequence analysis, there was also much discussion of its limitations, including the fact that it does not allow easy identification of novel pathways and that predictions of function are not always correct. Thus, genome sequences should be considered a stepping stone to help design better experiments and not an end in themselves.

Another major topic of discussion was adaptation to extremophily and, in particular, adaptation to extreme temperatures. Approaches to understanding such adaptations included cell biology, biochemistry, crystallography and sequence analysis. Some suggested thermophily adaptations including positive supercoiling to limit DNA unwinding, tungsten replacing molybdenum as a cofactor, ADP instead of ATP, novel intercellular connecting structures, salt bridges, increasing protein packing and reducing thermal expansion. There was also some discussion of extreme radiation resistance, and possible parallels between *Deinococcus radiodurans* (a bacterium) and some Archaea.

Future areas of Archaeaology were also emphasized, including new genome sequences, attempts to develop more genetic tools in thermophilic Archaea and continued studies of the diversity of uncultured Archaea. As one of the meeting organizers said at the start of the meeting, one should study Archaea for some interesting feature that they possess, not simply because they are considered to be Archaea. As Archaea possess many interesting features, the future of Archaeal studies is bright.

Further reading

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