Antiquity of the plant kingdom and molecular world

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Isotopic fossil and molecular data confirm the origin of primitive life forms up to 3.5 billion years ago. Eukaryotes are more allied to eocytes, the heat-loving and sulphur-metabolizing bacteria, than to the methanogens and halophiles, which evolved much earlier. The spurts in evolution in the Precambrian era were due principally to the endosymbiotic development of chloroplastids, multicellularity and sexual reproduction. The ancient molecule was RNA, possibly of a type similar to transfer RNA. The primitive molecular world was of exons, with homogeneous coding. Possibly, the primitive protein was protamine. In the world of exons, the introns brought about reshuffling and recombination. It is proposed here that the intron sequences have been conserved because of their replication and properties of amplification, mobility and dispersion.

THE origin of eukaryotes, the development of land habit and the ancestry of higher plants are topics which have been extensively debated. The discussions on these issues go back in a large measure to the origin of life itself. Lately, the development of techniques of molecular analysis has provided relevant inputs to the study of phylogeny and evolution. Advances within the past few years have been rather spectacular and new ideas are coming up to explain the origin of life and its diversity of forms.

Origin of eukaryotes

It was deduced earlier that eukaryota is an extremely ancient group like eubacteria and archaeobacteria and these three kingdoms had differentiated independently from a common ancestor[1,2] (Figure 1). Archaeobacteria included the methanogenes and halophiles. Another theory visualized a sort of early dichotomy only between eubacteria and archaeobacteria, the present-day eukaryotes or rather eucarya being related to the latter[1,3] (Figure 2).

With the development of eukaryota, the initial branch of the tree was visualized to include aerotolerant anaerobes living mostly as parasites. They possessed the nucleus and flagella but no mitochondria or chloroplastids, with similarity more to prokaryotes than to eukaryotes. The middle branch, evolving later[2], had mitochondria which had developed through endosymbiosis, but there was no chloroplastid except in some euglenoids. The photosynthetic property was a late acquisition through endosymbiosis with a photosynthetic bacterium. Though aerobic, they could thrive under oxygen-poor

conditions as well[2,4]. Finally, most of the diverse eukaryotes formed a branched crown ranging from plasmodia to animals, fungi, green algae and land plants, including dinoflagellates. This was a period of tremendous spurt in evolution[5,6]. Evidences from molecular
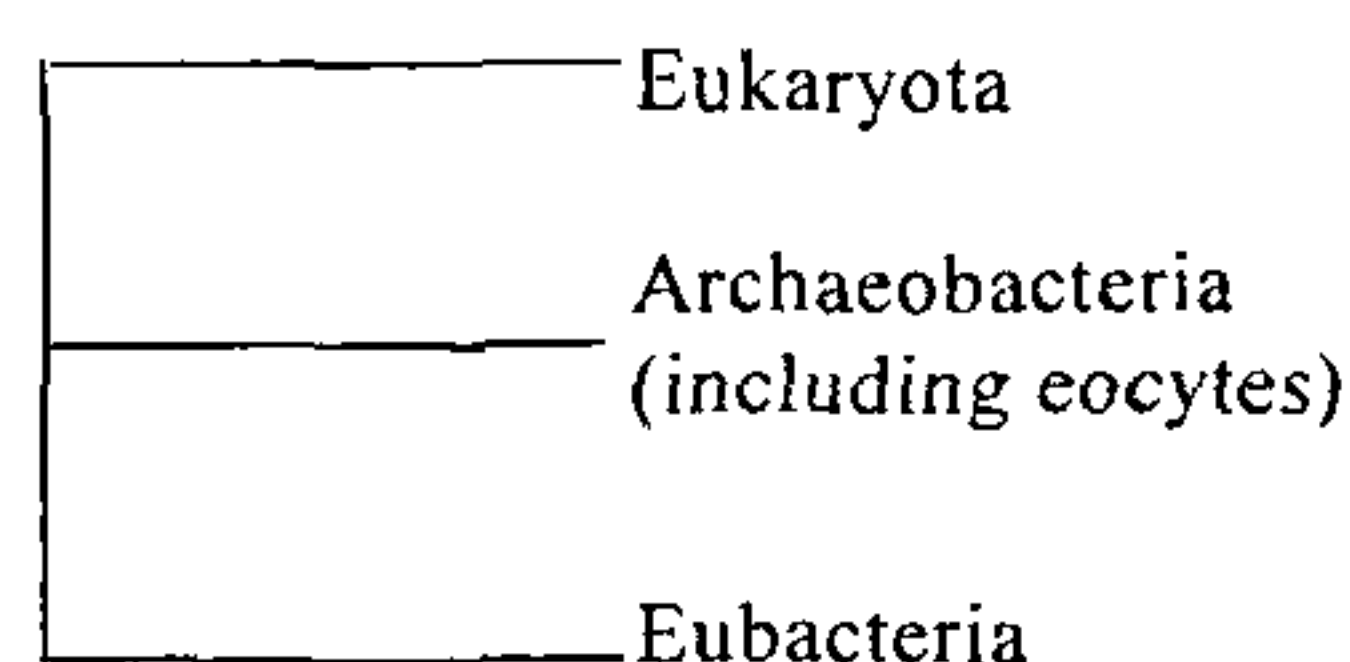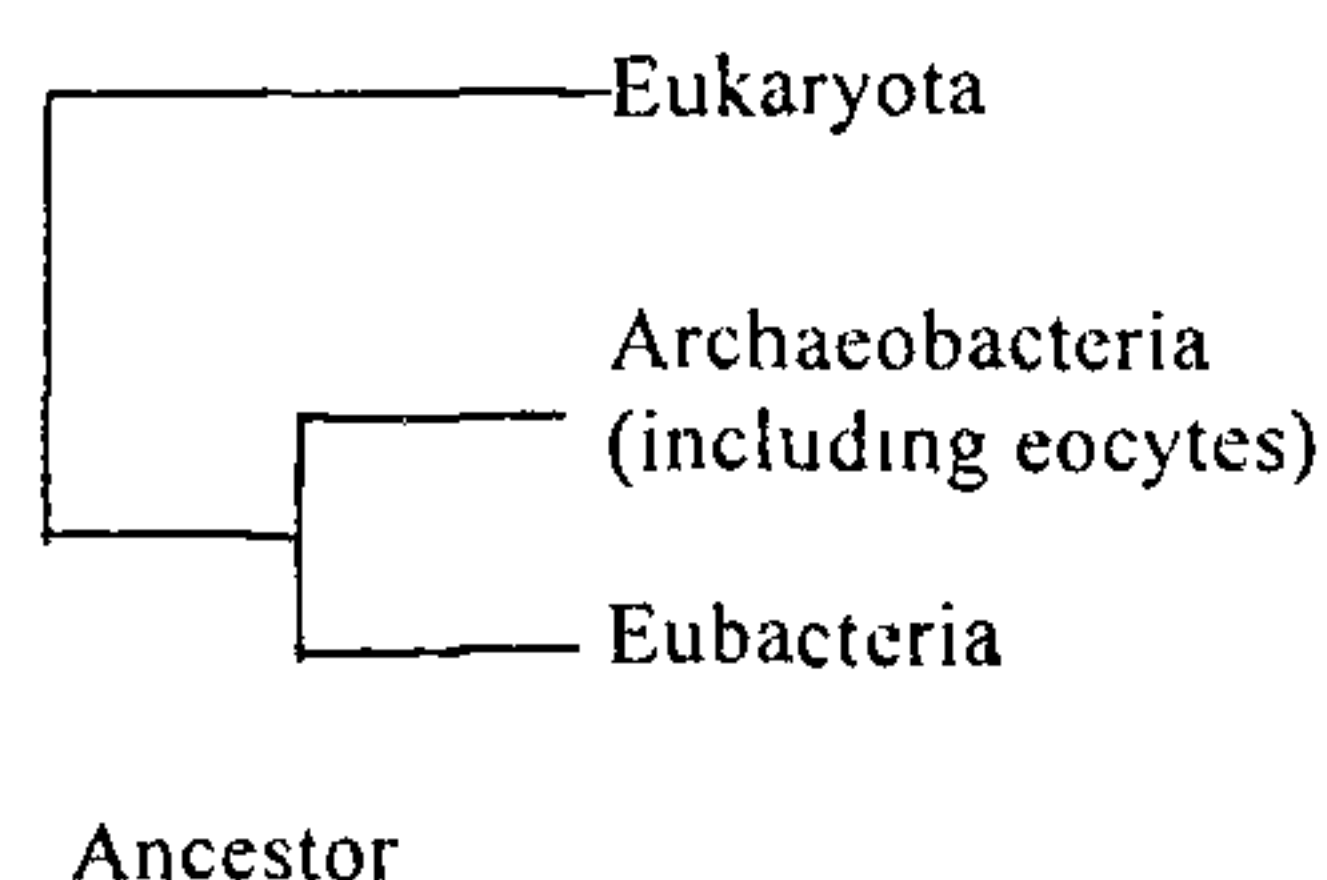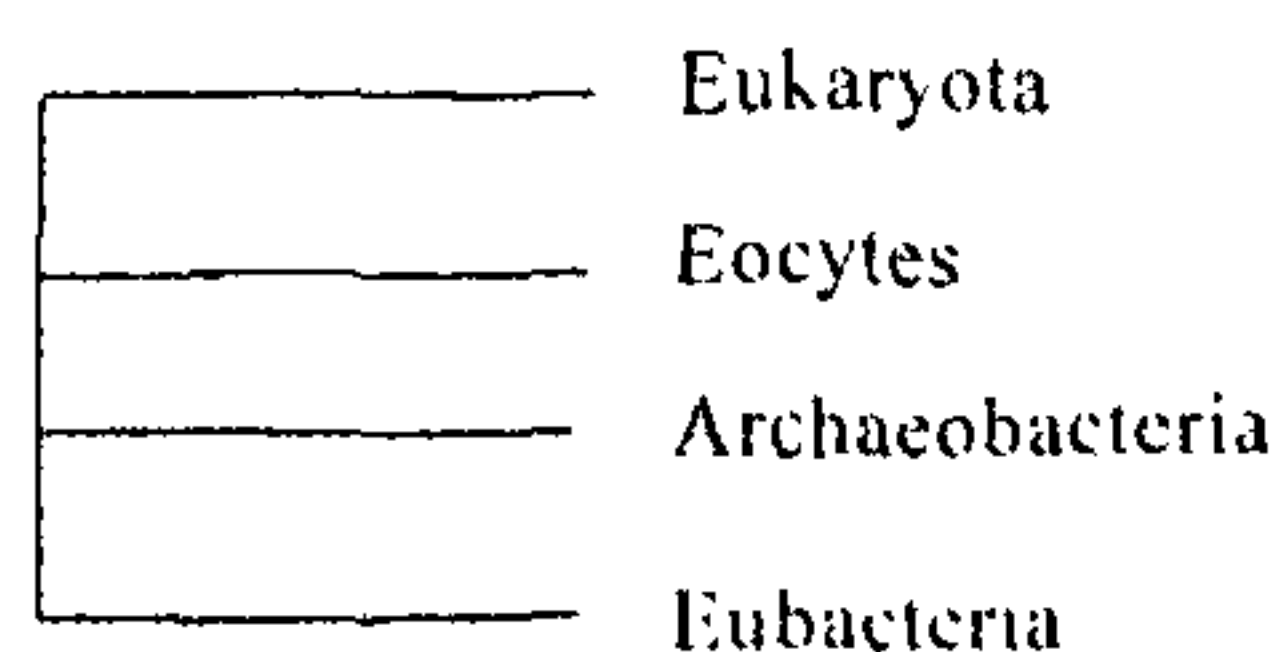
Figure 1.

Figure 2.

Figure 3.

Figures 1–3. Different views of the origin of eukaryota

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analysis suggest a multiple origin of chloroplastids through independent symbiosis leading to brown algae, red algae, cryptophyceae and photosynthetic euglenoids[7]. The sequence of branching within the crown is difficult to ascertain though, in general, photosynthetic types, except for the euglenoids, occupy the upper region. Palaeontological and biogeochemical evidences suggest that eukaryotes belong to 1700–1900 millennia old ecosystems[8]. The oldest multicellular eukaryote which can confidently be assigned to a phylum is a red alga which existed 950–1260 million years ago.

Lately, it has been reported that the unicellular organisms which can grow in extreme heat and metabolize sulphur – the *eocytes* – are the closest surviving bacterial relatives of eukaryotes, a class of cells which evolved more than 2 billion years ago[9] (Figure 3). This theory differs from the one suggested earlier that the eukaryotes share a common ancestry with archaeobacteria, including methanogens, halophiles and eocytes. The present evidences indicate that eukaryotes share ancestry only with eocytes, and the archaeobacteria are more primitive[10].

The earlier evidences were based principally on genes that code for RNA of ribosomes in eukaryotes, archaeobacteria and eubacteria[1], including pathogens like *E. coli*. Current phylogenies of eukaryota depend primarily on small or large subunits of ribosomal RNA (rRNA), although 5s rRNA and a number of protein sequences provide additional proof[3, 11]. The similarity between eukaryotes and archaeobacteria is marked. But more evidences of affinity between eukaryotes and archaeobacteria are noted in their transcription systems. The TATA-binding protein (TBP) being essential for transcription in eukaryotes is considered as an ancient feature. The structural and functional analysis of the protein of *Pirococcus woessii*, an archaeobacteria, shows homology to TBP protein[12]. On the contrary, ribosomes from eocytes are structurally more similar to eukaryotic ribosomes in ultrastructural pattern than they are to other bacterial ribosomes. Moreover, in one of the proteins EF-Tu, which is highly conserved, the sequences of 11 amino acids are almost identical in eocytes and eukaryotes. In other prokaryotes, the sequences are of four amino acids[3, 10] as in EF-G proteins.

Arguments have been raised both for and against these theories. It has been argued that the DNA sequence data may not always present an accurate picture, as often shown by their negative evidences even in cases where phylogenetic relationship is unquestionably well-established from other lines of study. It is claimed that the protein patterns are more reliable than DNA sequencing. An opposite view has been expressed[3] on the basis that inserts often jump in and out of closely related genes, and insertions and deletions are not conservative, and may change the protein pattern. As such, the protein pattern may not give a true picture. In any case, the ar-

chaeobacterial ancestry stood on solid ground till the sequence of amino acids in conserved protein in eocytes was analysed. The eocyte ancestry, as based on ultrastructure and amino acid sequences, has the weight of evidences in its favour.

Evolution of land and seed habits

It has so far been conjectured that land plants are almost 500 million years old. The cyanobacteria in sea could, on the other hand, be traced to 3.5 billion years. The more recent evidences, however, indicate that a cover of green on land might have been present even 1.2 billion years ago[13] and not just 500 million years as presumed earlier.

Indeed, it is paradoxical to visualize a completely barren land 500 million years ago, while the sea was full of flora and fauna much earlier. This presumption has recently been proved to be correct from the data on isotopes, which point to a massive amount of green stuff on the land, though not necessarily embryophytes, almost 1.2 billion years ago[14]. However, the photosynthesizing stuff in the sea could be traced back up to 3.5 billion years[15]. Moreover, it is also claimed that animals and fungi share a unique evolutionary history and that their last common ancestor was a flagellated protist similar to another protist, now extinct, the choanoflagellates[16].

A vast range of new species of higher organisms could be traced in the 100 million years old geological belt. The evolution of life cycle, capable of efficient energy utilization, and highly evolved pollination system, attracting insect pollinators, gave a selective advantage to the flowering plants over the ferns and gymnosperms. It has been presumed that by the last 80 million years, the vascular cryptogams were almost eliminated. But, about 72 million years ago in the Wyoming belt, excellent old fern meadows dotted with palms have been recorded[13]. At that time, angiosperms were no doubt profuse in their diversity, though not necessarily in the number of individuals present in each species.

The first step in the origin of land plants was the greening of land. The vascular plants colonized the terrestrial habitat, providing a soft shaded environment with primary productivity[17]. The next step in evolution was the emergence of the seed, through sexual reproduction, in which a structure like the seed developed to give nourishment to the germinating embryo.

All known seed fossils have a complicated pollen trapping mechanism at the seed apex. Galtier and Rowe[18] had later reported the occurrence of a seed-like body a few million years before the earliest fossil seeds. It had no pollen-trapping structure and there was no evidence of any entry of pollen to the female gametophyte. But the fossil was otherwise markedly different from living gymnosperms. This fossil occupies an intermediate position between *Bensonites* and *Archaeosperma*. It

is not known whether it is a missing link in the formation of seed habit. The mechanism of pollination too could not be worked out. There was the possibility that the seed fell on the soil, to be fertilized by motile sperm, or the pollen were trapped on the outer surface of the seed apex, resembling the deposition on the stigma of flowering plants[17]. In all probability, this discovery may suggest the polyphyletic ancestry of seed habit.

In later years, the pace of evolution in land plants, including angiosperms, was analysed utilizing DNA sequences of both nuclear and chloroplast genome. The rate of nucleotide substitution differs not only among nuclear and plastid genomes but also among different groups of plants. It is assumed that monocots might have diverged approximately 200 million years ago[19, 20].

Spurts in evolution

A glance at the manifestation of evolution reveals an amazing series of events affecting evolutionary pathways in unprecedented ways. One can trace, in general, a systematic progression through accumulated changes, resulting in biologically diverse forms appearing in nature. Such slow gradual changes undoubtedly characterize the normal method of evolutionary progress.

However, certain events often appear which are rather striking and stand as a landmark in the hierarchy of evolution. Such a rare event occurred at the transition from Precambrian to Cambrian, when there was a sudden increase in the type of flora and fauna between 1.2 and 1 billion years. This era was marked by three important biological processes, namely, acquisition of chloroplastids, multicellularity and sexual reproduction, a little later. The sequences, or more precisely regulatory systems, that genetically triggered multicellularity and sexual reproduction are still unknown. From a biological standpoint, such events surpassed in significance, plate movements, drifts in the continents or even periodic ice ages.

While discussing the spurts in evolution, the tropical belt, which is extraordinarily rich in species, assumes importance. This richness has been suggested to be due to the high rate of origin, acting as a *diversity pump*. Simultaneously, the low rate of extinction in the tropics serves as an *intensity accumulator*, leading to a wide range of biota. The combination of the two resulted in the richness of biological diversity in the tropics[21]. As such, the tropics should be regarded both as a cradle as well as a museum of species. In tropical waters, the first appearances of marine orders of the postpalaeozoic era were recorded, further confirming the contention that tropical regions are major sources of evolutionary novelty.

The primitive molecule

One of the outstanding discoveries in the study of evolution has been the unravelling of the property of RNA[9, 22], the primitive molecule. The RNA molecule can act not only as an enzyme by itself, the *ribozyme*, but it can also provide the template mechanism in the same system for replication, as seen in the case of telomeres of chromosomes[23, 24]. Moreover, the recent discoveries of editing the sequences and altering gene expression at the RNA level of the organelle genome have added new dimensions to the RNA world[25]. A significant portion of the mitochondrial genome undergoes RNA editing before translation. The process occurs in a highly regulated fashion through the mediation of guide RNAs[25]. All these evidences indicate that the simple molecules of RNA are capable of autocatalysis and heterocatalysis. The idea is gradually gaining momentum that with the origin of life, three to four billion years ago, the molecule which developed in that anaerobic, dark, hot and inhospitable world was RNA, from which the later forms of life, even DNA, developed. The most crucial issue, however, is: 'When exactly did the RNA world come into existence and how long did it last?' The modality of transition from RNA to DNA is a debated issue.

The ancient RNA molecule was supposed to be stable, symmetrical, 50–100 residues long, rich in guanine and cytosine residues[26]. It possibly had a homogeneous codon pattern with a comma-free read-off[27]. The primitive translational machinery considered likely was a tRNA-like structure, though not so complex[28, 29]. The transfer RNA has the unique and dual property of getting attached to nucleic acids and amino acids, transferring information of the primary sequences of inert nucleic acids to linear structures of functional amino acids. The transfer RNA has thus been assigned a unique role in the pre-protein RNA world[30, 31].

The ancient basic unit and the primitive translational machinery to synthesize protein did not require complex systems of ribosomes, RNA synthetases and protein factors[17]. The RNA molecules with biased codons performed the crucial function of activating amino acids moving along the template RNA, maintaining complementary pairing through 4–5 bases, and finally catalysing the formation of polypeptides by linking amino acids. It is also claimed that protamine is a genetic fossil of the primordial gene products[32]. It is present in the nuclei of the sperm of vertebrates and is a highly DNA-binding basic protein, rich in arginine. The basic unit might ultimately have been a repetition of CGCAGG hexanucleotides, which served as the building block of the primitive gene while duplication and mutation resulted in a sequence similar to the protamine gene. It is suggested that the high GC content of the 120 nucleotide sequences of the protamine gene makes it chemically stable with high fidelity for replication. The basic

codons might encode glycine, alanine, valine, isoleucine, serine, threonine and asparagine[33]. These amino acids are known to be synthesized abundantly by the sparking of a gas mixture which simulates the presumed composition of the ancient atmosphere.

The role of exons and introns in evolution

It is suggested[26,27,34,35] that genes were constructed from a surprisingly small number of genetic building blocks of RNA which existed even 3–3.5 billion years ago[36,37]. Several thousands of these blocks, the exons, underwent shuffling and recombination in new ways during evolution and it is estimated that up to 7000 exons were necessary to construct all the proteins[26]. A reappraisal of this theory has been recently suggested, claiming the absence of any significant correlation between the ancient protein and the exon-encoded modules of structure[55]. The process was, at least at certain early stages, possibly facilitated by *introns*, the so-called nonessential sequences, the role of which has been much debated. The two contrary views can be summed up by stating that *introns* were either derived from transposable or parasitic elements inserted between unsplit genes[38] or they are ancient, as old as the precellular life, and the genes were split from the beginning[39,44]. It has also been suggested that *introns* retained their primitive features and helped recombination of short exons[40]. By separating exons, acceleration of recombination through introns was further demonstrated, permitting the evolution of new genotypes[41].

The antiquity of introns[37] is indicated in the topographical evidence that introns are found in the identical location on the genomes of distantly-related organisms such as corn, chicken and man. This fact is an index that such introns must have been inherited from a common ancestor. The critics of this theory, however, state that the vast majority of hundreds or thousands of introns are found in different positions even within plant genomes and identical locations represent exceptional cases. Moreover, introns are missing from many ancient organisms, including the earliest prokaryotes and some eukaryotes[37]. However, the loss of introns in several groups has been claimed as being due to selective streamlining for more efficient translation. Even in such distantly-related organisms such as corn, fungus, Aspergillus and chicken, the gene triose phosphate isomerase (TPI) has a total of 11 exons and 10 introns, though not in one organism. It is of interest that the ancestral gene was claimed to include all those introns plus one extra intron. This was required to break up one of the exons that was much longer than the others in the genes of modern organisms. It was presumed that the missing intron might have been lost from the organisms studied, though the possibility of its retention in some organisms was suggested. A further report from C. Titti-

ger of Queen's University, Kingston, Ontario[41,42], indicated the presence of an intron in the mosquito genome in precisely the predicted spot. However, an opposing view holds that introns could not have vanished over and over again and they might have been inserted later in a single group of eukaryotes.

The introns have been classified in different categories based on their modality of splicing, a good commentary of which has recently been published[43]. The contradictory views of early or late origin of introns can be reconciled by taking into account the different types of introns and their existence in geological ages. Certain types of introns might have evolved very early in evolution whereas others evolved much later. The self-splicing introns found in leucine transfer RNA in some eubacterial systems[44,45] are undoubtedly very primitive, because of established antiquity of eubacteria. Such self-splicing introns often having mobility[46,47] led later to the development of protein-spliced introns found in the common ancestors of archaeobacteria and eukaryotes, about 1700 million years ago. Further, the complexity of spliceosomal introns common to eukaryotes might have been the even later development through insertion into unsplit proteins. This assumption appears more rational than the other novel ideas[34], which, though possible, bristle with too much speculation.

The intron sequences often have a high degree of repeats. Such sequences have the property of amplification and mobility[47,48]. Their presence in identical sequences in different loci suggests the property of dispersion as well. Evidently, in a number of instances the sequences are repeated, have the property of mobility and are capable of insertion at different loci. In view of the properties of amplification, dispersion and mobility of such repeated sequences and the varying non-specific effects they produce in different organisms, the term dynamic DNA was proposed[49-51]. The varying role of such reiterated sequences, otherwise termed as *dynamic DNA*, is being realized more and more in recent years.

These repeated sequences, which are often called nonessential, are present universally in major segments of chromosomes and are highly conserved. They are located in introns of genes which are considered as entirely non-essential. They occupy a significant portion of the gene, are present in multiple copies and are capable of insertion at different sites. Introns have been found in all major groups of organisms, except in some bacteria.

Though considered as non-essential, these sequences provide valuable clues to the study of evolution. The endosymbiotic concept of the origin of cell organelles visualizes the transformation of engulfed prokaryotes, either a photosynthetic or non-photosynthetic bacterium, into chloroplastids and mitochondria. The evidence of the prokaryotic origin of organelles is borne out by their 70S ribosome, circular DNA and stacking pattern of lamellae[3]. However, subsequent discovery of intron sequences and split gene in chloroplastids and mitochon-

dria posed problems in accepting this concept. Later, such sequences have been located in cyanobacteria[44, 52]. The homology of the introns of this group with those of chloroplastids of the alga *Anabaena* suggests their relationship and presence of a common ancestor which has been maintained in their genome for at least one billion years[45]. This homology provides further support to the endosymbiotic origin of eukaryotic organelles from prokaryotes, the evidence being provided by non-essential sequences of introns.

Further evidences of the role of introns in the analysis of the ancestry of higher organisms are available. It is known that the land plants originated from aquatic ancestors which were the inhabitants of intertidal marks, where sexual reproduction occurred mostly during high tide. Certain forms, in order to escape competition, established themselves on land, where sexual reproduction was possible only during rains or copious dew. Plants had then to develop the alternative method of increase of individuals through sporophytes. Later, the green algal group, the Charophyceae, were considered as the progenitors of land plants[53]. The origin of land plants through algal ancestors, though accepted, suffered from lack of evidence, since the connecting link between the aquatic and land plants could not be found. Lately, intron sequences from chloroplasts of algae like *Coleochaete* and *Chara* have been homologized with those of *Marchantia*[54]. In fact, introns (Group II) were initially found in the chloroplasts of land plants. The later discovery of such introns in green algae brings the two groups together and confirms the lineage. Thus, the long-awaited gap between algae and land plants could be bridged through molecular evidences. Intron sequences of *Magnoliaceous* chloroplastids also provide a clue to their ancestry. Even the human ancestry has been deduced from mitochondrial intron sequences[55].

The highly conserved nature of intron sequences undoubtedly calls for an explanation of their functions[56]. Leaving aside the fact that these sequences are often composed of repeats, the dynamic non-specific property of which has been established, intron sequences *per se* undoubtedly help in bringing about recombination as already recorded. In different organisms, their role in promoting conversion has been proved. This function is in all probability a non-specific one. The specificity or non-specificity can be confirmed through genetic manipulation, both horizontal and vertical.

At any event, their role in recombination along with other properties appears to be established. It is, therefore, not unlikely that in the ancient RNA molecule, the development of introns was favoured in selection, to meet the need of generating genetic diversity through mobility and recombination. This special property of introns, coupled with their capacity of amplification, acquired very early in evolution, has given to such sequences a selective advantage, promoting conservation. Despite the fact that there might have been alterations in their sequences, these two essential properties of replication and promotion of recombination have remained unaltered. Their universal presence even at identical sequences in widely different organisms not merely suggests the great antiquity of certain types, possibly as old as life itself, but also their role in generating diversity.

In the RNA world, the introns, through readjustment of exons, have facilitated evolutionary advance to a marked degree. As a consequence, some of these so-called non-essential sequences have remained unchanged through geological ages and show homology across different groups of organisms. This is because of their selective value despite tremendous diversification of life forms in nature. In addition to such conservation, a significant portion of these sequences has undergone gradual changes in evolution, bringing about genetic diversity and regulating non-specific functions. Their conservation on the one hand and dynamism on the other prove their essential role in evolution

Conclusion

Summarizing the data, it appears that the nearest relation of modern-day eukaryotes might possibly be the eocyte – the heat-loving sulphur-metabolizing bacterium located very early in evolution. The present-day plants can be traced back up to 1.2 billion years. In the Precambrian era, there was a tremendous spurt in evolution, principally due to multicellularity and sexual reproduction, along with the acquisition of chloroplastids later. The primitive molecule of life is presumed to be a transfer-RNA-like structure capable of replication and protein synthesis and the ancient protein the protamine. The ancient molecular world was composed of thousands of exons, mostly GC-rich hexanucleotides. Their reshuffling was facilitated through introns, which might suggest that the latter are equally ancient molecules. The intron sequences are often highly conserved and occur at identical locations in widely different organisms, both primitive and advanced. It is suggested that these introns, having the property of amplification, dispersion and mobility, i.e. the properties of *dynamic DNA*, have been conserved because of their selective value in eukaryota in primarily controlling non-specific functions.

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REVIEW ARTICLE

Androgen receptor and the mechanism of androgen action

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During the past two decades, a great deal of information has accumulated on the structure of androgen receptor (AR) and the mechanism by which it forms a complex with a steroid hormone and then interacts with DNA to regulate gene expression. Steroid hormones enter the cells by passive diffusion and activate their related receptors. The activated receptor binds to specific cis-acting enhancer sequences usually present in the 5'-flanking region of target genes and regulates transcription through interaction of the receptor with DNA, proteins and other transcription factors. Precursor mRNAs are synthesized, processed and translated to produce new proteins. As a result, the cellular function changes. The present review summarizes our current knowledge of the structure of AR and its interaction with DNA to regulate the expression of specific gene(s).