background appear to be grounded in the mistaken belief that RNA intrinsically needs the help of proteins to catalyse interesting reactions. In fact, many chemical mechanisms for RNA-catalysed reactions are just as plausible as analogous mechanisms for protein catalysis, even considering the shortage of functional groups in the four common RNA bases[17]. Further, if transfer RNA and ribosomal RNA are presumed to be vestiges of the RNA world, them it seems natural to view the modified bases in tRNA and rRNA as vestigial also. Given these modified bases, RNA catalysts have essentially the same range of functional groups as proteins, and appear, at least at first glance, to have a catalytic potential comparable to that of proteins.

Second, the assumption that metabolic complexity preceeded the invention of translation is required by the logic of the model. If the 'ribo-structures' of ribocofactors are to be explained as vestiges of the RNA world, then the RNA world most plausibly contained RNA enzymes that catalysed reactions using these cofactors, including methyl transfers, phosphorylations and aldol and Claisen condensations. This suggests metabolic complexity. But if metabolic complexity is presumed to post-date translation, the problem of explaining why these metabolically important cofactors all contain fragments of RNA is left unsolved.

Further, biological intuition is contradicted by many recent models, especially those based on a view of RNA viruses as 'living fossils' of early forms of life. Viruses are known to adapt at tremendous rates to survive in specific hosts[18] making it unlikely that RNA viruses living in modern hosts contain many non-functional vestiges of an RNA world that vanished 2,000 million years ago. Conversely, if we interpret the biochemistry of modern viruses as vestiges of an RNA world, we must radically alter our view of the adaptability of viruses.

Thus, if we believe in an 'RNA world', we must believe that translation originated in a 'breakthrough organism' with many riboenzymes catalysing many metabolic reactions. Models for the metabolism of this breakthrough organism can be suggested by modern biochemical data, and the origin of traslation is best viewed in the context of such models. Thus, rather than constructing models for the origin of translation in a primitive metabolic background (a difficult task at best), models for the origin of translation may assume that translation arose in an organism where aminoacylated RNAs were already used metabolically. Some metabolic roles for such RNAs may have survived. A glutamate-RNA ester is the first intermediate in the biosynthesis of chlorophyll[19,20]. A glycine-RNA ester is functionally important in cell wall biosynthesis[21].

Three speculative but interesting suggestions follow from this picture. First a metabolically complex ribo-organism would be expected to evolve divergently to produce many species of ribo-organisms. Most would become extinct after the breakthrough[17]. This presumed extinction implies a limit to our ability to extrapolate from the biochemistry of modern organisms back to the biochemisty of the first life form. To model the biochemistry of an ancient organism, one must normally compare the biochemistries of many of its descendants; examination of a single descendant does not provide sufficient information to distinguish between primitive traits (those present in the ancient organism) and derived traits (those that evolved subsequently). If the picture presented is correct therefore, the breakthrough organism is the most ancient organism that we can hope to reconstruct purely by examining the biochemistry of modern organisms.

Even here, model construction is difficult. But efforts to model the breakthrough organism themselves may be interesting. For example, in one model, the role for RNA in chlorophyll biosynthesis is interpreted as a vestige of a photosynthetic breakthrough organism. The origin of photosynthesis can be approximately dated, and organisms that lived earlier than this date are believed to have left fossils[22]. A conclusion drawn from this model worthy of examination is that these ancient fossils are of ribo-organisms[17].

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Amino-acid sequence similarities

SIR—In a recent News and Views article[1], Lindsay Sawyer proposed that several proteins, including β-lactoglobulin and plasma retinol-binding protein, have common features of amino-acid sequence. He suggests that these features are common to proteins that bind small conjugated molecules that are either sparingly soluble, labile or both and have an associated receptor. This view may be of great importance in the elucidation of the function of the human uterine endometrium during early pregnancy and the molecular interaction between the endometrium and the implanting embryo.

Quantitatively, the main protein product synthesized and secreted *in vitro* in the endometrium from the mid-luteal phase of the menstrual cycle and during the first trimester of pregnancy, is a dimeric glycoprotein with a subunit of relative molecular mass 25,000 (refs 2,3). This protein is a major product of the secretory glandular epithelium. It has been termed endometrial protein 15, pregnancy-associated endometrial α_2-globulin, progestagen-dependent endometrial protein or placental protein 14, and it has been detected in intraluminal uterine fluid and amniotic fluid (see ref. 4 for review). Recent partial sequence analysis reveals strong similarity with the β-lactoglobulin family[5,6] and a 38-residue amino-terminal sequence contains the sequence -Lys-Leu-Ala-Gly-Lys-Trp-His- which conforms to the common sequence proposed by Sawyer[1]: -U-X-X-Gly-X-Trp-Y-(where U is basic, Y aromatic and X any amino acid).

This similarity, and Sawyer's proposals, imply that this endometrial protein may be involved in transport of a ligand and that a receptor system exists. Further sequence and structural analysis may elucidate the function of this protein and the endometrial glandular epithelium in early placental development.

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