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THE RELATIVE REACTIVITY OF DEOXYRIBOSE AND RIBOSE: DID DNA COME BEFORE RNA?

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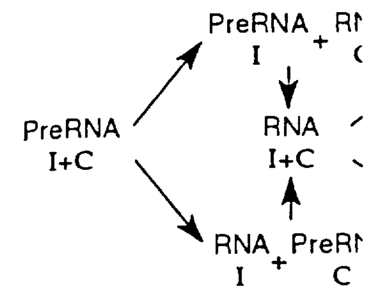
If it is assumed that there was a precursor to the ribose-phosphate backbone of RNA in the preRNA world (such as peptide nucleic acid), then the entry of various sugars into the genetic material may be related to the stability and non-enzymatic reactivity of the aldose. The rate of decomposition of 2-deoxyribose has been determined to be 1/3 that of ribose (Larralde *et al.*, 1995). In addition we have measured the amount of free aldehyde by ^{1}H and ^{13}C NMR and find that it has approximately 0.15% free aldehyde compared to 0.05% for ribose at 25°C (Angyal, 1986). This suggests that deoxyribose would be significantly more reactive with early bases in the absence of enzymes. This is confirmed by urazole and deoxyribose reacting to form the deoxynucleoside 45 times faster at 25°C than urazole reacts with ribose to form the ribonucleoside. Urazole is a potential precursor of uracil and is a plausible prebiotic compound which reacts with aldoses to form nucleosides (Kolb *et al.*, 1994). Thus the non-enzymatic reactivity of deoxyribose would favor its early use over ribose until enzymes could change the relative reactivities.

Most of the reasons that RNA is presumed to have come before DNA are extrapolations back from contemporary metabolism (e.g. the abundance of ribose based coenzymes, the biosynthesis of histidine, deoxyribonucleotides are synthesized from ribonucleotides, etc.) (Joyce, 1989). It is very difficult to reconstruct biochemical pathways much before the last common ancestor, and it is even more difficult to do more than guess at the biochemistry of very early self-replicating systems. Thus we believe that these reasons are not compelling and that the non-enzymatic chemistry may be more important than enzymatic pathways for constructing the earliest of biochemical pathways.

While the RNA world has been discussed at great length, there has not been an exploration of the transition out of the RNA world. We have constructed many possible schemes of genetic takeover events from preRNA to the modern DNA, RNA, and protein system which could generate the RNA metabolic fossils we see today. Figure 1 shows a few plausible schemes in which RNA came before DNA with several possible pathways of how DNA, RNA, and protein could have taken over the functions of preRNA. It is less likely that RNA or DNA could have taken over both informational and catalytic functions simultaneously, so the one-step takeover of RNA from preRNA is not shown.



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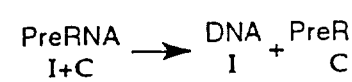

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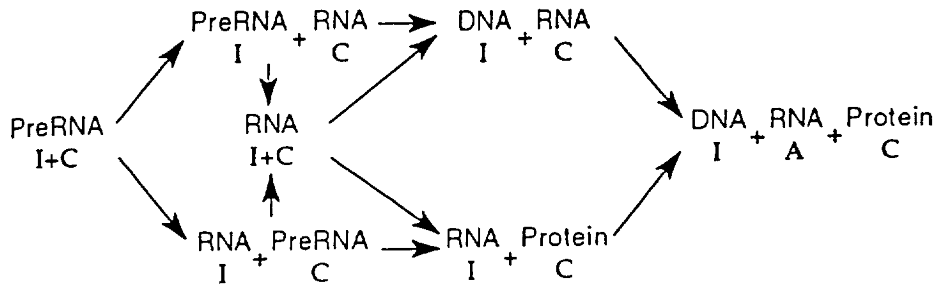

Fig. 1. A possible scheme of the pathway of genetic takeover events in which RNA came before DNA. Arrows indicate genetic takeover. I represents informational molecules, C indicates catalytic molecules, and A indicates auxiliary functions.

Figure 2 shows two schemes in which DNA is the first informational molecule after preRNA. It can be seen that the scheme of replacements is as feasible as in the RNA-first of Figure 1.

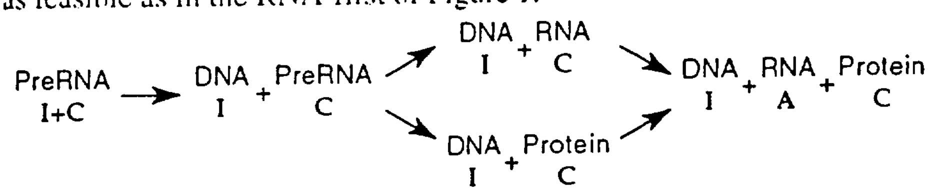

Fig. 2. A second possible scheme of the pathway of genetic takeover events in which DNA came before RNA. Arrows indicate genetic takeover. I represents informational molecules, C indicates catalytic molecules, and A indicates auxiliary functions.

These considerations suggest that, assuming there was a preRNA world, the DNA before RNA scheme is at least as likely as RNA before DNA. The metabolic arguments may favor the latter, but the stability and reactivity of deoxyribose favor the former. Other advantages include one less chiral center, the absence of 2'-5' and 3'-5' ambiguity, and greater stability of DNA at the pH of the current ocean (8.2). Thus the DNA before RNA proposal needs to be seriously considered.

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