ocrit in association with dehydration during athletic competition has the potential to precipitate catastrophic thrombotic events. We also do not share the opinion that a transgenic polycythemic mouse will be a "Mighty Mouse." Transgenic mice with polycythemia resulting from expression of the human erythropoietin gene (*5*) have reduced life spans, which may be due to complications similar to those identified in patients with polycythemia.

The EPO-R is also expressed in non-erythroid tissues such as endothelial cells (*6*) and brain cells (*7*). The function of EPO-R in non-erythroid tissues is unknown, and the effect of EPO-R mutations in those tissues is even less predictable and may account for some of the pathology we and others have observed. Moreover, if this mutation rendered some advantage to its carriers one would expect the frequency of these mutant EPO-R alleles to increase in the population over time, yet PFCP is an extremely rare disease in which each affected pedigree analyzed has had a different mutation.

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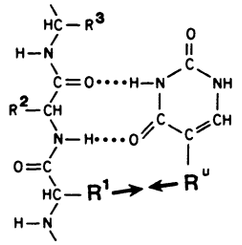
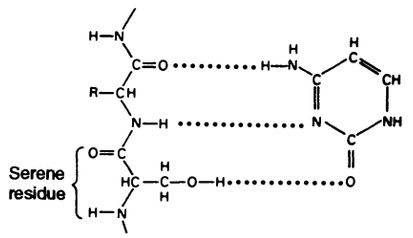
Prebiotic 5-Substituted Uracils and a Primitive Genetic Code

The report "Prebiotic synthesis of 5-substituted uracils: A bridge between the RNA world and the DNA-protein world" by Michael P. Robertson and Stanley L. Miller (5 May, p. 702) provides an empirical basis for our proposal of a primitive prebiotic genetic code (*1*, *2*) in which a 5′-uracil substituent recognizes the side chain of a peptide-bound amino acid.



Peptide ••• uracil-R

The plausibility of such a code is enhanced by an analogous recognition of serine or threonine residues through strong binding to cytosine (*2*),



Peptide •••••••••• cytosine

noteworthy because most of the present codons for these amino acids are cytosine-centered.

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Response: Interactions between 5-substituted uracils and peptide chains may well have been important in the pre-RNA world. This would be particularly important if the backbone of the earliest genetic material was peptide-linked rather than ribose-phosphate–linked, for example, the peptide nucleic acid of Nielsen (*1*). If the interaction between the pyrimidines and the peptide are selective enough, then the origin of protein synthesis may have been easier than previously thought, and the RNA world may have lasted a shorter time than is usually assumed.

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