to acquire needed fatty acids for the production of edible oils as well as oleochemicals is greatly improved.

However, there is a dark side to this picture. A number of third-world countries depend on the export of oils produced by their plantations for funds to support their budgets. In the Philippines, coconut oil is a major source of lauric acid for the detergent industries. In Malaysia, now considered a developed country, the very important palm oil industry also supplies lauric acid from the palm kernel oils. Perhaps the marketplace will determine the final outcome of the oils supplied by these countries and those produced by transgenic plants. The immediate impact at present is negligible, but 10 years from now production of oils from the new plants developed by molecular biology may have a severe economic effect on those countries that depend on the sale of their agronomic products for their income.

Paul K. Stumpf
Department of Biochemistry and Biophysics,
Section of Molecular and Cellular Biology,
Division of Biological Sciences,
University of California,
Davis, CA 95616–8535, USA

Familial Polycythemia

Wade Roush, in his Research News article "An 'off switch' for red blood cells" (7 Apr., p. 27), discusses a recent *Cell* paper from Harvey Lodish's group (*1*) that elaborated on the erythropoietin receptor (EPO-R) signal transduction pathway through Jak2 and hematopoietic phosphatase originally reported by James Ihle's group (*2*) and its possible implication regarding the human disease familial polycythemia. Readers may conclude, we believe incorrectly, that the disease referred to as familial erythrocytosis, originally described as autosomal dominant polycythemia or primary familial and congenital polycythemia (PFCP) (*3*, *4*), is something desirable for the human body and its athletic performance. The observation that a Finnish cross-country skier affected with this disorder won three Olympic gold medals should be tempered by cautious reflection about the pathophysiology of this entity, as such speculation may encourage the practice of "blood doping" (hypertransfusion or parenteral administration of recombinant erythropoietin), which is done by some high-performance athletes.

We originally anticipated that this genetic disease was benign, but more than 18 years of clinical and laboratory follow-up of 10 large families and several sporadic cases of PFCP have indicated that this may not have been correct. The propositus from the original family suffered several cardiac vascular and valvular-acquired problems and died in his 50s of a stroke. His affected son had a myocardial infarction at age 40. Another PFCP propositus suffered an intracranial hemorrhage at the age of 29 (*4*), without having any known risk factors. We are aware of a large Swedish family in which all affected polycythemic patients fare generally poorly and are hypertensive even in childhood. Several affected subjects in the large Finnish family with primary familial polycythemia died at a young age. The quoted example of the Olympic gold medal winner may therefore be a testimony to his superior athletic ability in spite of his primary polycythemia.

Circulation of blood through the organs and tissue oxygen delivery are tightly regulated processes with many feedback controls. At a certain point, elevated red cell mass increases whole blood viscosity with resulting decreased oxygen tissue delivery. Although, by "blood doping," athletes may benefit from an absolute increase in red cell mass, the high hemat-

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.

Josef T. Prchal
University of Alabama, Birmingham, AL 35294–0006, USA
Gregg L. Semenza
Johns Hopkins University School of Medicine, Baltimore, MD 21287–3914, USA
Jaroslav Prchal
McGill University, Montreal, Canada H3T 1MS
Lubomir Sokol
University of Alabama, Birmingham, AL 35294–0006, USA

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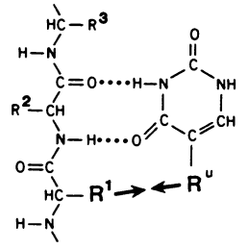
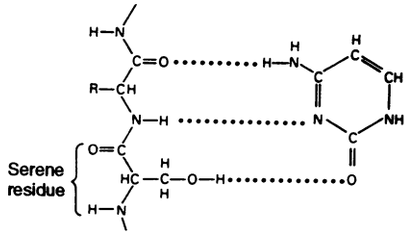
Prebiotic 5-Substituted Uracils and a Primitive Genetic Code

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.

Simon Black
National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892, USA

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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.

Michael P. Robertson
Stanley L. Miller
Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA 92093, USA

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