has metastasized to the liver—although (as noted by Marshall) scores of patients at the University of California, San Francisco and Cornell University have received adenovirus-mediated gene therapy for other indications, with no fatalities and only two serious incidents of toxicity.

While a treatment is still unproven and unfamiliar—the stage at which gene therapy is now—therapeutic success may be elusive. In the 1970s, for example, bone marrow transplantation was highly experimental. It was being performed at only a handful of medical centers in the United States, and success rates were abysmal. But clinical research has refined the technique and identified diseases for which the technique is useful: in thalassemia major, for example, a genetically determined disease of red blood cells, more than 80% of the patients are now cured.

In the Gelsinger case, the FDA has thrown its weight around inappropriately and prematurely. The result has been the intimidation of gene therapy researchers throughout the country and, possibly, costs to future generations of Jesse Gelsingers.

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Sickle Cell Anemia Therapy: Progress Since Pauling

In his Perspective on the importance of the 1949 paper on sickle cell anemia by Linus Pauling and his associates ("Sickle cell anemia, a molecular disease," *Science*'s Compass, 19 Nov., p. 1488), Bruno J. Strasser repeats a theme that we believe is outdated. Strasser says that "extremely detailed understanding of the molecular etiology of sickle cell anemia...has contributed only modestly to improvements in therapy." This view is perhaps also an implicit criticism of the reductionist approach of the current era of molecular medicine that resulted from Pauling's work.

Research during the last three decades on how deoxygenated sickle hemoglobin polymerizes inside the cell, and on the specific inhibition of this polymerization by fetal hemoglobin, has led to the discovery of ways to increase the production of fetal hemoglobin pharmacologically in patients (*1*). Among the useful agents that have been studied are 5-azacytidine, hydroxyurea, recombinant erythropoietin, and butyrate analogs, all of which augment fetal hemoglobin production in patients, with minimal short-term toxicity (*2*). Indeed, hydroxyurea was found to afford significant clinical benefit to adult patients (*3*) and has been approved for this use by the U.S. Food and Drug Administration.

Obviously, cure of sickle cell anemia by gene replacement is the ultimate, yet still distant, goal for this "first" molecular disease. However, rapidly improving methods of hematopoietic stem cell transplantation have effectively done this for many patients by allowing the permanent replacement of the abnormal cell population with normal genotype cells.

The transition from identification of an abnormal gene to an effective therapy for patients with inherited diseases is rarely simple or rapid. We should not, however, lose sight of the fact that molecular medicine is advancing in small but significant incremental steps, on the basis of the continuous feedback between basic and clinical research, beyond diagnoses toward effective treatments. We suggest that this is another historical message that one should ponder on this 50th anniversary of Pauling's work, as we near the completion of the DNA sequence of the human genome and the "postgenome" era of medical research.

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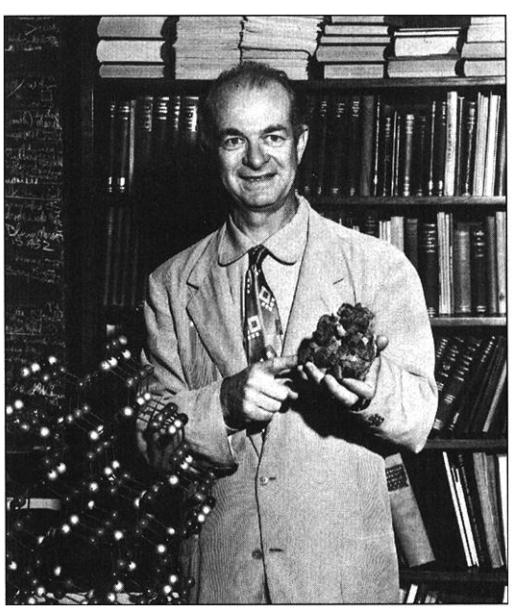

Linus Pauling (1901–1994), one of the pioneers in the field of molecular medicine.

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Response

Schechter and Rodgers shed a welcome light on recent advances in the field of sickle cell anemia therapy. However, in my Perspective article, I focused on a historical argument.

Therapies and cures depend on much more than an experimental breakthrough or a promising clinical trial (*1, 2*). The therapeutically "useful agents" Schechter and Rodgers mention remain at a preliminary stage, even according to the review they cite. The review notes "conflicting results" for recombinant erythropoietin, "conflicting data" for butyrate, "limited clinical trials" for 5-azacytidine, and "appropriate concern about the possible induction of tumors" for long-term hydroxyurea treatment (*3*). Apart from hydroxyurea, none of these "useful agents" has gone beyond the stage of "experimental therapy" (*4*) and thus is not yet a social reality for sickle cell anemia patients.

My historical perspective does not deny the progress achieved by medical researchers—including Schechter and Rodgers—in the treatment of sickle cell anemia. My claim was in regard to the origin of such progress, not its very existence. Even the development of hydroxyurea treatment, with its undeniable therapeutic benefits, was not a simple outcome of our understanding of the disease's molecular etiology. Indeed, the initial insights for this therapy were largely of a clinical and epidemiological nature (*5–7*). It would not make sense to address "an implicit criticism of the reductionist approach of the current era of molecular medicine." What deserves our criticism is the overly optimistic promises, made by Pauling and many after him, that knowledge of molecular processes alone would quickly and easily yield effective therapies at the molecular level. The story of sickle cell anemia, along with that of many other diseases, highlights the fact that the development of new therapies has come about not just through basic research reaching the clinic, but rather through "continuous feedback between basic and clinical research," as Schechter and Rodgers have nicely put it—restating the basic point of my Perspective.

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Room-Temperature Hydrogen Storage in Nanotubes

In the reports "Hydrogen storage in single-walled carbon nanotubes at room temperature" by C. Lui *et al.* (5 Nov., p. 1127) and "High H_2 uptake by alkali-doped carbon nanotubes under ambient pressure and moderate temperatures" by P. Chen *et al.* (2 July, p. 91), the authors make the same error in referencing our work on hydrogen storage in carbon single-wall nanotubes (*1*). There is apparently some confusion on the matter, which we wish to clarify here, referring to Liu *et al.*'s report for illustrative purposes.

Liu *et al.* say that we investigated hydrogen adsorption on single-wall nanotubes at 133 kelvin. This is not correct. This was simply the temperature we cooled the sample to in the presence of hydrogen at a pressure of 300 torr. The hydrogen gas was evacuated from the chamber after the sample was cooled, and temperature-programmed desorption spectroscopy was then performed to assess H_2 adsorption onto the nanotubes. As the temperature was raised at 1 kelvin per second, hydrogen was evolved from the sample. Hydrogen was stable on the surface of the nanotubes to temperatures well in excess of 133 kelvin, and the rate of hydrogen evolution peaked between 275 and 300 kelvin (room temperature). To a first approximation (in the absence of mass transport limitations), the shape of the temperature-programmed desorption spectrum is a map of the density of hydrogen on the sample as a function of stability temperature. The fact that the spectrum peaked around room temperature indicated that some hydrogen was stabilized to this temperature by the single-wall nanotubes. This observation was the point of our *Nature* publication and was appreciated and referenced correctly in an earlier paper from this group (*2*).

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References and Notes

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Response

Our misunderstanding of Dillon *et al.*'s work (*1*), which we cited in our report (5 Nov., p. 1127), came from the following