

## Gene therapy for cholesterol disorder

Researchers report partial success in the first test of gene therapy as an experimental treatment for a rare, inherited form of high blood cholesterol.

James M. Wilson of the University of Michigan Medical Center in Ann Arbor announced last week that an injection of genetically engineered liver cells lowered the soaring concentration of low-density lipoprotein (LDL) cholesterol in the blood of a 29-year-old Canadian woman with familial hypercholesterolemia. This disorder, which strikes only about 100 individuals in the United States, results from mutations in the gene that codes for the cellular receptors that filter LDL cholesterol — the so-called “bad” cholesterol — from the bloodstream.

Wilson and his colleagues received approval last year from the National Institutes of Health's Recombinant DNA Advisory Committee (RAC) to administer liver cells containing added LDL receptor genes to three patients with familial hypercholesterolemia (SN: 10/12/91, p.230). Such patients have up to 10 times the normal amount of blood LDL cholesterol and usually suffer repeated heart attacks, beginning in childhood.

Wilson told a meeting of the RAC last week that his group's first patient — the 29-year-old woman — had an LDL cholesterol concentration of roughly 500 milligrams per deciliter (mg/dl) when she received gene therapy five months ago. Since then, he said, her LDL cholesterol has dropped as low as 325 mg/dl — still more than twice the healthy amount.

Wilson says he and his colleagues hope to reduce the woman's LDL cholesterol concentration further by treating her with cholesterol-lowering drugs. Because such drugs work by stimulating the activity of LDL cholesterol receptors, she was

not able to respond to them before the gene therapy.

Based on the Michigan group's partial success with the Canadian woman, the RAC voted last week to extend the total number of patients the team may treat to five. Wilson and his colleagues plan next to administer the gene therapy to a 7-year-old Colombian girl, two boys from Cyprus, and a second female patient from Canada.

## Breast implants and autoimmune disease

A new study strengthens the link between silicone gel breast implants and autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, and a skin-hardening disorder known as scleroderma.

Scientists led by Eng M. Tan of Scripps Research Institute in La Jolla, Calif., have found so-called antinuclear antibodies in the blood of 23 women who developed autoimmune disease after receiving breast implants made of silicone gel. Tan and his colleagues report in the Nov. 28 LANCET that those women with the highest levels of such antibodies had the worst symptoms. Moreover, women whose implants had ruptured or leaked silicone experienced symptoms more than five years sooner than women whose implants had remained intact, they say.

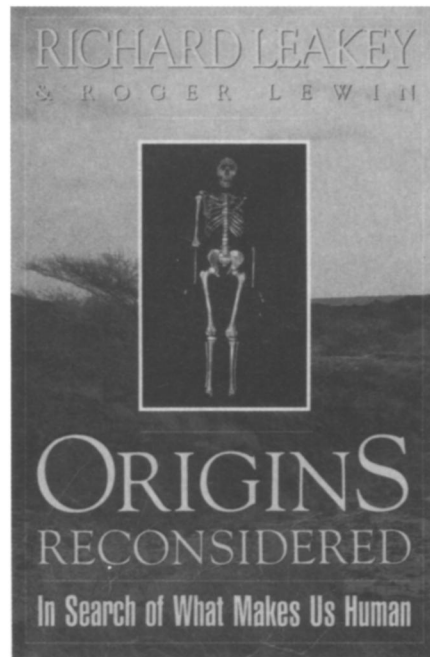
Physicians currently use elevated levels of specific antinuclear antibodies — so named because they attack proteins within cell nuclei — to diagnose various autoimmune disorders. Tan and his colleagues suggest that exposure to silicone can cause autoimmune diseases. However, they caution that their data do not allow them to rule out the possibility that such exposure simply hastens the onset of symptoms among women already developing an autoimmune disease.

In *Origins Reconsidered*, Richard Leakey, one of the most respected and influential scientists of our time, takes us on a brilliant and provocative journey through human history. For Leakey the most compelling question is no longer “How did we physically evolve?” It is, instead, “How did we become human?” For this world-renowned paleoanthropologist it is a humbling reminder that no matter how complete the skeleton, how perfect the fossil, there is a gap in our knowledge. Our ancestors evolved from two-legged scavengers into creatures that *create*. They learned to make stone tools, to communicate, to build shelters, and to hunt for food.

This realization sparked Leakey to return to his earlier work — especially his 1977 book, *Origins* — to poke holes in his previous beliefs and to reflect anew on what makes us who we are. As he gently admits, considerations like these are usually left to philosophers, not scientists. But again and again, he is faced with his own guiding principle: “The past is the key to our future.”

In this seminal work, Leakey incorporates ideas from philosophy, anthropology, molecular biology, and even linguistics, to investigate not only how we evolved anatomically, but how we acquired the qualities that make us human — consciousness, creativity, and culture.

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