Sheep chimera makes human blood cells

Indiana Univ. School of Medicine

This 1-year-old lamb was born with millions of human blood cells after receiving a transplant of human bone marrow while still in the womb.

What has four hooves, fluffy wool and millions of human bone marrow cells? A part-human lamb that could pave the way for curing genetic blood diseases – such as sickle-cell anemia – in the womb.

The sheep/human chimera, so named because it contains cells from both species, is the creation of blood researchers at Indiana University School of Medicine in Indianapolis and the Veterans Administration Medical Center in Reno, Nev. The researchers, led by Edward F. Srour of Indiana University, embarked on the project while developing strategies for transplanting bone marrow from unmatched donors.

Physicians use bone marrow transplants to treat a variety of blood diseases, from leukemia to potentially fatal genetic disorders such as beta thalassemia. But in many cases, doctors cannot find a bone marrow donor with the same tissue type as the patient in need of the transplant. This generally rules out transplantation, since an unmatched graft would trigger rejection by the recipient's immune system.

To surmount the problem, Srour and his colleagues hit on the idea of transplanting blood "stem cells" – which give rise to all types of red and white blood cells – into diseased fetuses before they develop a functioning immune system. To test their idea, the researchers decided to perform the transplant between some widely divergent subjects: an adult human donor and a group of fetal sheep.

Srour's group used a centrifuge and a series of antibodies to separate the tiny stem cells from the human donor's marrow. They selected only those cells that bore a membrane protein called CD34 – a marker for early stem cells – but lacked another membrane protein called major histocompatibility complex class II, which the donor cells could use to recognize and attack their new host. The researchers injected the isolated cells into the bellies of seven sheep fetuses still being carried by their dams.

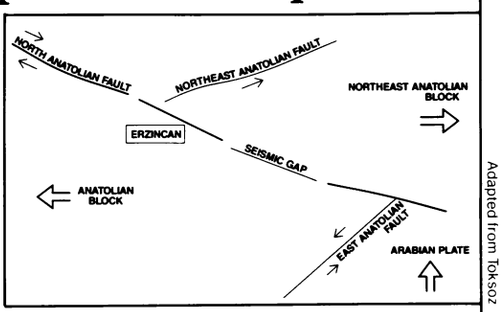
In the March 15 Blood, they report that three of the seven fetal sheep took up the human stem cells. Srour's group found that the marrow of two of the fetuses, which were killed for study before birth, contained up to 4 percent human cells. The marrow of the third lamb, which was born in late 1990, consisted of more than 6 percent human cells. At age 3 months, this chimeric lamb also contained mature human blood cells, they found.

Srour says his group plans to adapt the strategy to treat human fetuses with genetic blood disorders that can be diagnosed during the first trimester of pregnancy, before the immune system begins working. Candidates for the treatment would include fetuses with sickle-cell anemia, severe combined immunodeficiency or chronic granulomatous disease, in which the body's white blood cells lack the chemical ammunition to kill disease-causing invaders. "If we can establish a small degree of chimerism [in such patients] using normally functioning cells, then 99 percent of the symptoms would be alleviated," he asserts. He adds that the treatment "is not difficult to administer at all," because it does not require surgery.

Malcolm Moore, a hematologist at Memorial Sloan-Kettering Cancer Center in New York City, agrees. "We could use this technique to treat many genetic diseases of the blood. . . . I'm very excited by these data." – *C. Ezzell*

Tectonic squeeze sparks Turkish quake

The earthquake that hit eastern Turkey last week apparently emanated from a seismic holdout – a fault segment that had waited decades to let loose. Seismologists believe the recent shock failed to release stress along this entire segment, leaving room for another large earthquake in the near future.



Adapted from Toksoz

Arabia's northward push forces the Anatolian block to escape westward. The recent quake occurred along a seismic gap on the North Anatolian fault.

Seismic activity in this part of Turkey stems from an ongoing collision between the Arabian plate to the south and the Eurasian plate to the north. As the two land masses converge at a rate of about 5 centimeters each year, they squeeze Turkey, forcing most of the country to slide westward in a phenomenon called continental escape, says M. Nafi Toksöz, a Turkish-born seismologist at the Massachusetts Institute of Technology.

Satellite measurements suggest the escaping region, called the Anatolian block, is heading westward at a rate of 2 to 5 centimeters per year.

Last week's magnitude 6.8 quake devastated the town of Erzincan, which lies almost on top of the North Anatolian fault, a 1,200-kilometer-long tear in the Earth running from the Aegean Sea into eastern Turkey. Like California's San Andreas fault, the North Anatolian forms the border between two large blocks of crust that are slowly slipping past one another. In the Turkish case, the fault allows the Anatolian block to slide out of Arabia's path.

In the middle part of this century, most segments of the North Anatolian fault spawned major earthquakes, one of which killed more than 30,000 people in Erzincan in 1939. All of the midcentury shocks, however, bypassed one section of the fault to the southeast of Erzincan. Seismologists had identified that gap as a prime candidate for a major earthquake.

Seismic analysis indicates that both last week's main shock and a magnitude 5.8 aftershock occurred on the seismic-gap section of the fault, Toksöz says. Because of the size of the earthquake and aftershock, seismologists believe stress was released in only about half the gap. "We now feel reasonably confident that the seismicity will migrate eastward on the fault," says Toksöz. The remaining gap could produce a magnitude 7 earthquake in the near future, probably within the next 10 years, he says. – *R. Monastersky*