New ingredient completes marrow recipe

In bone marrow, where blood cells are born, a few cells have the unique ability to develop into any type of blood cell, as needed, and to produce offspring that can do the same.

After years of experiments failing to reveal what maintains this remarkable population of self-perpetuating cells, called hematopoietic stem cells, researchers working with mice have now discovered a way to propagate the cells in the laboratory. If the method works for human blood cells, it would likely be a windfall for the treatment of cancer and genetic disorders.

Scientists have established that in order to thrive and multiply, stem cells need the support of two other types of cells found in bone marrow: marrow fibroblasts and endothelial cells. In the laboratory, however, the presence of these support cells is not enough to keep a culture of stem cells from dying off within a few weeks. Instead of spawning more of their own kind during that time, the stem cells give rise only to ordinary, mortal blood cells.

Researchers have now discovered the need for a third crucial ingredient, a chemical messenger called thrombopoietin. "We're just completely mind-boggled," says study coauthor Stephen H. Bartelmez of the Seattle Biomedical Research Institute. "No one has ever guessed that this was what was going on."

When the researchers added thrombopoietin to samples of bone marrow that contained blood stem cells and the support cells, the stem cells survived and reproduced for 4 months, they report in the July 6 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES. The group has now maintained a population of living stem cells in the laboratory for 9 months.

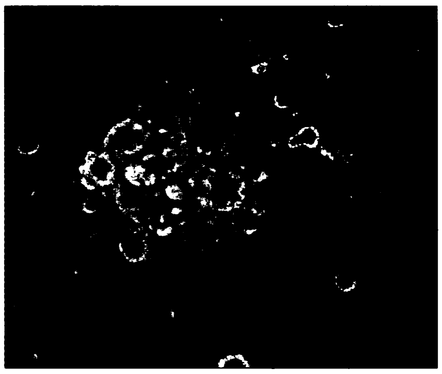
The team transplanted some of the cultured cells into mice whose own blood cells the scientists had killed by radiation. Without the ability to make blood, the mice would die rapidly. After the transplants, however, the mice have now survived for more than a year.

Although thrombopoietin appears to act directly by binding to receptors on the stem cells, Bartelmez says the most important action may be indirect. Thrombopoietin seems to signal the growth of cells called megakaryocytes, which help direct stem-cell production.

"We have finally determined the microenvironment that stem cells live in inside the body and have recreated that outside of the body," Bartelmez says. "We have great hopes that this will work in humans because we now know that we were missing an entire cell type before."

If physicians can also control human stem-cell growth, it may aid cancer patients whose blood cells are obliterated by radiation or chemotherapy. The ability to grow blood stem cells may also help scientists treat genetic disorders by replacing patients' stem cells with cells that contain engineered genes.

Bartelmez



Blood stem cells proliferated in cultures enriched with thrombopoietin.

E. Richard Stanley of the Albert Einstein College of Medicine in New York City comments that the new method's relative simplicity suggests that researchers may easily translate it to human cells.

Darwin J. Prockop of MCP Hahnemann University in Philadelphia, however, is more doubtful. "It's a long way away from saying you could do the same thing in humans," he cautions. "There are a lot of important differences between mice and people." —*S. Carpenter*

Death risk drives shocking love songs

The risk of getting killed often has a dampening effect on the silly excesses of courtship, but the opposite may have been true in electric fish.

The need to evade predators could have driven the electric serenades of knife fish to evolve from a simple zap . . . zap . . . zap to a variety of zippity doo-dahs, according to an analysis by Philip K. Stoddard of Florida International University in Miami. In the July 15 NATURE, he reports that a predator can't detect the complex signals as easily as the simple ones.

"Predators really have been a creative force," he says.

Knife fish mostly cruise murky water at night and emit weak signals to communicate and scan for obstructions. More than 100 species, which include predatory electric eels, roam the fresh waters of Central and South America. Another group, in Africa, evolved electrical signals independently.

Stoddard argues that ancestors of New World knife fish made a one-phase signal. He draws it as a single peak. Many modern fish have gone multiphasic, adding foothills and sunken gorges before and after that main peak.

At first, Stoddard suspected that female fancy had inspired complex signals, just as it sent male peacocks to fashion excess in tail feathers. Males and females typically differ in such exaggerated traits, Stoddard says, yet he saw fewer sex differences in fish than expected.

Electric eels and catfish home in on electric signals when they hunt small knife fish. To assess a typical predator's capabilities, Stoddard trained an eel named Sparky to swim toward electric signals. Sparky responded to one-blip signals about twice as often as he did to multiphasic signals. Predators don't seem daunted by electrified mouthfuls. As Stoddard points out, "We eat wasabi on sushi."

Some modern knife fish species still send risky one-blip signals. The electric eels do, but have little to fear. They kick out about 100 volts per foot of body length. One species of small knife fish seems to have lost its signal complexity, but it lives far from eels and catfish. A third one-blip species may be masquerading as an eel.

Prevailing wisdom decrees that predators limit flashy, sexy traits in their prey, comments Marlene Zuk of the University of California, Riverside. Guppies in waters beset with predators, for example, sport colors less conspicuous than neon orange. However, after writing a review article exploring the dampening effect of predators, Zuk says, "There's very little evidence for it." Stoddard's claim that predators had the opposite effect does not surprise her.

Stoddard

Females of four Brachyhypopomus *fish emit different electric signals.*

Her own work focuses on the serenades of male crickets in places where flies track the songs, land on the singer, and give birth to larvae that burrow into the cricket's body. Crickets in fly-infested areas sound different from crickets in fly-free zones, but Zuk hesitates to rank one's sound as more complex.

Sounds and colors have gotten most of the attention, according to knife fish specialist Carl D. Hopkins of Cornell University. He looks forward to seeing if theories hold up in the electric realm. "The electric fish [research] has a lot to offer because it's so new," he says. —*S. Milius*