

## Bone marrow cells can build new muscle

Scientists may have found the source of Mighty Mouse's strength. They've discovered that mouse marrow, the soft tissue inside bone, harbors cells capable of forming new muscle. This finding suggests novel avenues to explore in treating muscular dystrophies and other muscle-wasting diseases.

In the March 6 *SCIENCE*, Italian scientists describe the ability of marrow cells to journey to the site of a muscle injury, where they seem to help mend damaged tissue. "They are recruited from the marrow, travel through the blood, actively pass through the blood vessel barrier, and repair muscle," says study

author Fulvio Mavilio of the H. San Raffaele-Telethon Institute for Gene Therapy in Milan.

Bone marrow has long been known as a reservoir of hematopoietic stem cells, which develop into white and red blood cells. Indeed, that's why bone marrow transplants are used to reconstitute a person's immune system.

In recent years, researchers have also gathered evidence that some marrow cells, grown in the laboratory under particular conditions, can form bone, cartilage, fat cells, and muscle, says Darwin J. Prockop of Allegheny University of the Health Sciences in Philadelphia.

## Dyslexia tied to disrupted brain network

Children and adults who exhibit the reading disability known as dyslexia have a difficult time applying appropriate sounds to the letters that make up written words. A new brain-imaging study indicates that a widespread network of brain regions critical to this ability malfunction in people with dyslexia.

Further work is needed to determine whether this brain disturbance acts as a "neural signature" for the fundamental problem in dyslexia, say pediatrician Sally E. Shaywitz of Yale University School of Medicine and her colleagues.

"These brain activation patterns now provide us with hard evidence of a disruption in the brain regions responsible for reading—evidence for what has previously been a hidden disability," Shaywitz holds.

The Yale researcher's group recruited 14 male and 15 female dyslexic readers, as well as 16 male and 16 female volunteers with no reading impairments. Participants ranged in age from 16 to 63.

During a series of tasks that tapped into progressively more complex manipulations of letter sounds in words, a functional magnetic resonance imaging scanner measured changes in oxygen use in the participants' brains. Brain cells use more oxygen as they work harder.

Dyslexic readers had the most trouble when asked to identify nonsense words that rhyme, such as "leat" and "jete." Actual words that rhyme, many of which had already been memorized by the dyslexic readers, usually proved less vexing for them.

Compared to unimpaired readers performing these tasks, dyslexic readers lacked neural activity in several regions toward the back of the brain, Shaywitz and her coworkers report in the March 3 *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES*. These include Wernicke's area, which contributes to language comprehension, as well as parts of the visual cortex and a section of the association

cortex considered pivotal to integrating the sight of printed letters with their corresponding sounds.

At the same time, dyslexic readers showed greater than average activity in areas at the front of the brain. The most prominent such sites were the inferior frontal gyrus, especially during nonsense word rhyming, and Broca's area, a crucial location for speech processing.

The areas affected in dyslexic readers largely correspond to sites of brain damage in adults who developed severe reading problems after having suffered a tumor or stroke, the scientists contend.

Other studies of the brain have suggested that dyslexia derives from perceptual disturbances, such as underactivation of a structure called V5. This brain structure facilitates the visual processing of printed letters and other fast-moving images (*SN*: 2/17/96, p. 104). The extensive reading network identified in the new study appears to maintain anatomical connections to that area, according to Shaywitz and her coworkers.

"This is an interesting and exciting new study," comments neuroscientist Guinevere Eden of Georgetown University Medical Center in Washington, D.C. "But the relationship of the Shaywitz data to the V5 findings is unclear." Eden directed the V5 research.

Jonathan Demb, a neuroscientist at the University of Pennsylvania School of Medicine in Philadelphia, has found reduced brain activity in several visual regions linked to reading problems. Many dyslexia-related disturbances cited by the Shaywitz group occur within or near primary sensory areas of the brain, he notes. Scientists need to clarify the proposed reading network's relationship to auditory and visual regions already implicated in dyslexia, he remarks.

Increased activity in the Broca's area of dyslexic readers is another intriguing and unexplained finding in the new study, Eden adds.

—B. Bower

Yet there has been little proof that marrow cells actually pursue such career choices inside the body. Mavilio's evidence came serendipitously. In experiments unrelated to muscle research, a colleague injected bone marrow cells into muscle and noticed that they appeared to form new muscle.

To examine this unexpected phenomenon further, the researchers used snake venom to destroy limb muscle. They then took bone marrow from mice engineered to include a gene that expresses a marker protein only in muscle cells. When they transplanted this marrow into the damaged muscles of the other mice, they found that some regenerated muscle tissue displayed the marker, indicating that the foreign marrow cells had developed into muscle.

Mavilio and his colleagues also injected bone marrow into the bloodstream of mice with damaged muscles and later saw muscle cells with the marker protein at the site of regeneration.

The damaged muscle tissue must somehow lay down a chemical trail that attracts the marrow-derived muscle precursors, suggests Mavilio. "We don't know what those signals are. We have no idea at all," he says.

Noting that most new muscle develops from so-called satellite muscle cells near the injured tissue and thus does not carry the marker, Mavilio cautions that his group has not yet proved that the marrow cells contribute significantly to regeneration.

Indeed, Eric P. Hoffman of the University of Pittsburgh School of Medicine told *SCIENCE NEWS* that several years ago, he and his colleagues found that bone marrow transplants had no therapeutic effect on a mouse version of a muscular dystrophy.

Nevertheless, Hoffman says this latest research should renew interest in whether marrow-derived cells are more effective in treating muscular diseases than transplants of myoblasts, or mature muscle cells. That controversial technique has been abandoned by most investigators.

"If we could identify the muscle stem cells—a true population that lives, proliferates, and regenerates skeletal muscle—that would be critical for developing transplants as a true form of therapy," says Hoffman. He notes that few of the transplanted myoblasts have survived for long in patients.

Furthermore, while physicians inject myoblasts into muscles, they might be able to inject the marrow-derived muscle precursors into the bloodstream, which would carry them to the appropriate muscles, speculates Mavilio.

He warns that scientists have yet to show that marrow-derived muscle precursors exist in people. "All of this could still be a biological curiosity," he says.

—J. Travis