

# A Problem of Adhesion

## More evidence of sickle-cell stickiness

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A protein found on red blood cells in sickle-cell disease binds these cells to blood vessel walls, disrupting circulation, a new study suggests. The protein, which makes a cell sticky, may serve as a prime target for drugs to ease the condition.

People with sickle-cell disease make elongated versions of hemoglobin, the protein in red blood cells that totes oxygen. The abnormal hemoglobin can become stiff, bending many of the cells into a sickle shape. Like twigs collecting in a downspout, these misshapen blood cells are apt to clog a vessel. The result can be intense pain and damage to internal organs.

For decades, scientists assumed that the

cells' shape was the primary cause of vessel blockage in sickle-cell patients. But since 1980, researchers have been turning up evidence that specific molecules on the deformed cells make them stickier than healthy cells.

In the latest report, Julia E. Brittain, a pharmacologist at the University of North Carolina at Chapel Hill, and her colleagues find that in a lab dish, three proteins—alpha-4-beta-1 integrin, CD47, and thrombospondin—interact in a complex dance that results in red blood cells attaching to vessel walls.

The scientists report their discovery in the Oct. 8 *Journal of Biological Chemistry*.

Two of the proteins—alpha-4-beta-1 integrin and CD47—reside on the surface of red blood cells, whereas the other—thrombospondin—can either float freely in the bloodstream or serve as part of a blood vessel wall.

In people with sickle-cell disease, deformed red blood cells can't transport oxygen efficiently. Research has shown that the body responds to the oxygen shortage by cranking out new red blood cells. Unlike mature cells, immature red blood cells have abundant alpha-4-beta-1 integrin on their surface.

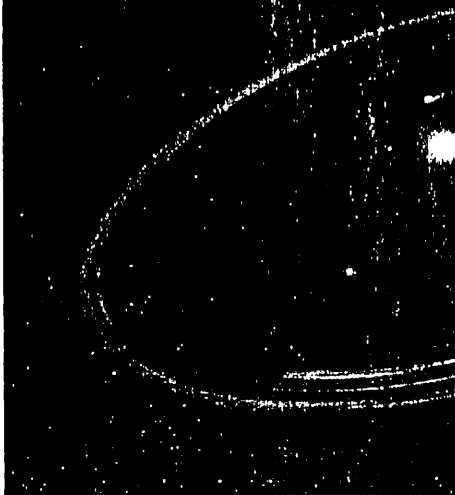
Brittain and her colleagues found that the integrin molecules could bind a cell to a vessel wall by attaching to thrombospondin there. But first, free-floating thrombospondin has to bind to CD47 on the blood cell surface. In response, the integrin changes conformation, making the cell stickier.

"We think this is a primary reason why blood begins to slow down—you get a log-jam" of red blood cells, says Brittain.

Other evidence supports the theory that the unnatural stickiness of red blood cells in sickle-cell patients could contribute to circulation problems, says Timothy M. Wick, a biomolecular engineer at the Georgia Institute of Technology in Atlanta.

For example, Wick and his colleagues have identified other proteins that orchestrate the binding of sickle cells to endothelial cells lining blood vessels. "Once we start to understand the total-ity of binding interactions, we can start . . . to find therapies to stop adhesion. That's the benefit of these kinds of [research] papers," he says.

Using mice with sickle-cell disease, Brittain and her colleagues are planning to test



**UNSETTLING DUST** Depiction of a young star illustrating one of the collisions that could produce

compounds that inhibit alpha-4-beta-1 integrin to see whether they can avert vessel blockage. —N. SEPPA

## Messy Findings

### Planets encounter a violent world

Rocky planets such as Earth are born through countless acts of violence—the collision and merging of many smaller bodies. A new study reveals that some planets continue to take a beating hundreds of millions of years after they've formed.

The evidence comes from an infrared survey of 266 youthful stars, revealing that 71 of them have disks of dusty debris. The disks are a sign that newborn planets are being clobbered by asteroids and that the asteroids—planet-formation leftovers—are banging together (*SN: 10/9/04, p. 227*) and making dust that glows at infrared wavelengths.

Using NASA's Spitzer Space Telescope, which detects disks dimmer than other infrared telescopes can, researchers now have dozens of debris disks to study. The images show that some stars are swaddled by bright disks even if they're several hundred million years old. Many theorists had expected that by that time, most of the dust would have dissipated—either blown outward or dragged inward by the star's radiation.

"The only way to produce as much dust as we are seeing in these older stars is through huge [recent] collisions," says George Rieke of the University of Arizona in Tucson. He