Smooth-muscle cells: Twist and clout

Researchers at the University of Vermont in Burlington may have uncorked the secret of how smooth-muscle cells contract. Physiologist David M. Warshaw and his colleagues have found evidence that, unlike skeletal muscle, which shortens like an accordion, smooth-muscle cells contract in a corkscrew-like manner. This finding, says Warshaw, could help explain why smooth muscles contract more efficiently and slowly than do skeletal muscles.

Smooth-muscle cells line hollow organs such as the stomach and bladder and are partly responsible for maintaining blood pressure in the blood vessels as well as other involuntary bodily processes. But in spite of their prevalence and obvious importance, relatively little attention has been paid to their contraction machinery, according to Warshaw. More is known about skeletal and cardiac muscles because patterns of striations, or alternating dark and light bands, on these muscle fibers have enabled scientists to study the movement and alignment of the protein strands, called myosin and actin, which do the work of contraction inside the cell.

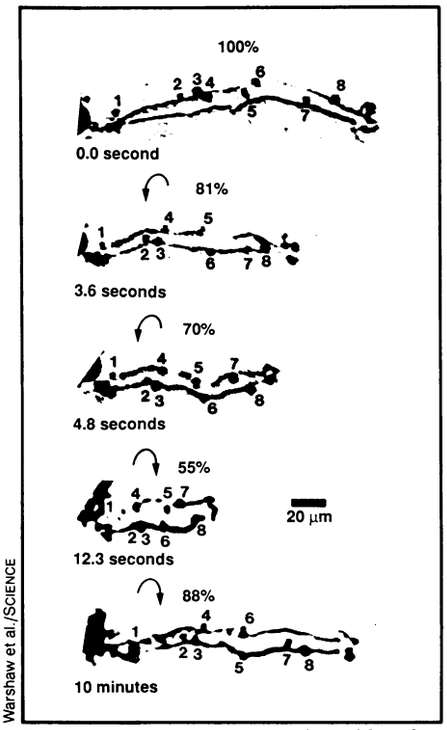
Smooth muscles, on the other hand, are not striated and, when viewed under a microscope, do not appear to be obviously organized in any fashion that would suggest an underlying structure. Past optical microscopy had suggested that the contracting myosin and actin are arranged in helices, but this view has not been widely accepted.

In the June 12 SCIENCE, Warshaw, Whitney J. McBride and Steven S. Work offer more support for the helical camp. They electrostatically attached small resin beads to the outside of smooth-muscle cells taken from a toad's stomach. When the researchers analyzed the movement of the beads on a cell electrically stimulated to contract, they found that the cell twisted in a helix as it shortened. Moreover, as the cell relaxed and reextended, the beads rotated back in the opposite direction. Warshaw says the next step is to use fluorescent antibodies to actin and myosin to see whether the protein "contractile units" inside the cell are arranged in twisting helices as well.

In skeletal muscle cells, the contractile units of myosin and actin are laid out head to tail along the length of the muscle. What advantage might contractile helices offer smooth muscles, which require less myosin and about 1/300th the amount of energy to generate the same force as skeletal muscles?

When the contractile units begin to shorten in a skeletal muscle cell, says Warshaw, each individual unit works against the contraction of its neighbor, so while the cell is able to shorten quickly, only the units at the cell ends are directly pulling on the cell and the resultant net force equals that of only one unit.

In contrast, Warshaw thinks that in smooth muscle, the contractile units are arranged as if they were wrapped around a barber pole inside the cell, with each unit having both its head and tail attached to the sides of the cell. With this arrangement, he says, the helical units work together to a much greater extent so that more force is generated per cross-sectional area in smooth muscle. But because only a component of the force generated by each helix is applied to shortening the cell along its length, the contraction of the cell is slower.



On these video images, numbered beads show coiling and uncoiling of a smooth-muscle cell as it shortens and expands.

What happens "when you take thousands of these cells and put them into a tissue isn't exactly clear," says Warshaw. But because his group found as many cells that twist in a right-hand sense as those that twist the other way, Warshaw speculates that opposite-twisting cells are paired in the muscle tissue, "almost like a gear mechanism . . . [so that these cell partners] somehow additively enhance the transmission of force to the muscle tissue." — *S. Weisburd*

Drug 'nukes' ovarian cancer

Ovarian cancer strikes some 19,000 U.S. women each year, ultimately killing almost three out of five of them — or about twice as many of its victims, proportionately, as breast cancer. Now researchers at the University of Chicago and Argonne (Ill.) National Laboratory have teamed up to tackle ovarian cancer with a new radioactive drug. Though tests are very preliminary, the drug appears to hold great promise of fighting this and estrogen-dependent cancers.

Cancers of the ovaries, breast, cervix and uterus frequently involve cells that have many hundreds or thousands of estrogen-receptor sites. Because most of these cancers also require estrogen for growth, postsurgical treatment to seek out and destroy metastatic disease (minute secondary tumors spawned by the original cancer) usually involves endocrine therapy — starving these cancers of estrogen or providing a drug that counteracts the effects of estrogen.

Ovarian cancers, notes Eugene DeSombre of the University of Chicago, are the exception. Though roughly half carry estrogen receptors that in fact bind with estrogen, these cancers apparently do not need or use the estrogen and therefore "have not responded at all well to any endocrine therapy." But a new estrogen treatment he is investigating shows promise of hunting down and killing metastasized ovarian cancers despite this limitation, he says.

The treatment employs an estrogen or estrogen-like drug to which a form of radioactive bromine (Br-80m) has been attached. Since estrogen receptors are "very tightly associated with DNA," DeSombre explains, when the drug binds to a cell it locks in the bromine very close to its genetic material. As the bromine decays, its locally deposited Auger-electron radiation (SN: 2/22/86, p.124) destroys the cell's DNA.

Micrographs picturing the drug's damage to cells grown in culture show "very dramatic" results, DeSombre says: "The cells look like they've had a miniature atom blast in the middle of them." Moreover, he told SCIENCE NEWS, because each cell suffers so many DNA breaks, "we're confident that they would not be able to recover."

Though the drug might also harm normal ovarian tissue, in most cases surgery for the primary tumor would have removed the ovaries prior to treatment, he says. And because most other tissues reached by the drug would have far fewer estrogen receptors per cell than the cancers, DeSombre says, they should be much less vulnerable to the drug.

The drug, shown to work in cultured cells, is expected to undergo animal testing soon. If all goes well, human trials could get under way in as little as three years. — *J. Raloff*