AAAS Meeting

Brain cells at the breaking point
Fracture study could lead to insights into traumatic injury

By Laura Sanders

Rigid pathways in brain cell connections buckle and break when stretched, scientists report, a finding that could aid in the understanding of exactly what happens when traumatic brain injuries occur.

Up to 20 percent of combat soldiers in Iraq and an estimated 1.4 million U.S. civilians sustain traumatic brain injuries each year. But the mechanics behind these injuries have remained a mystery.

New research presented February 19 shows that forces similar to those that cause traumatic brain injury can damage tiny conduits called microtubules.

Microtubules extend down the length of axons—which transmit electrical signals in brain cells—serving as “superhighways of protein transfer,” said Douglas Smith of the University of Pennsylvania in Philadelphia, who conducted the research with colleagues. Brain cells rely on microtubules to move important cellular material out to the ends of axons.

Car crashes, bomb blasts and falls can damage these intricate links, and destroying even a small number of them can cause devastating damage.

“You can have very small lesions in very discrete pathways which can have phenomenal impact,” said Geoffrey Manley, a neurosurgeon at the University of California, San Francisco, who did not participate in the research.

When Smith and colleagues quickly stretched brain cells growing on a silicone membrane, the microtubules inside the axons immediately buckled and broke, spilling their contents.

“This disconnection at various discrete points spells disaster, and things are just dumped out at that site,” Smith said. “Microtubules are the stiffest component in axons, and they can’t tolerate that rapid, dynamic stretch.”

Like Silly Putty pulled slowly apart, axons can adjust to gradual stretching, Smith said. But sudden forces, like those that happen in blasts and collisions, can cause the Silly Putty to snap.

In their lab dish experiments with brain cells on silicone, the researchers were able to minimize microtubule damage with a drug called Taxol, commonly used to treat cancer. But it’s too early to say whether the drug would work in people with traumatic brain injuries.

Currently, traumatic brain injury research is in “the abyss between bench and bedside,” Manley said. So figuring out exactly what happens in traumatic brain injuries could lead to new approaches to treatment.

Stem cells fuel prostate tumors
Mouse study also shows role for gene in malignancy

By Laura Sanders

Some self-renewing stem cells may play a role in prostate cancer, and a certain gene in these cells contributes to the malignancy, research presented February 20 suggests. Prostate cancer is the most common malignancy in men in Western nations, affecting one in six men.

Like many other tissues in the body, prostate tissue is made up of several different kinds of cells, including a class called basal stem cells. Normally these cells divide to replenish prostate tissue, but sometimes they become cancerous. Instead of producing normal cells, these stem cells lead to tumors.

“Think about cancer as a disease of stem cells,” said study coauthor Owen Witte, a Howard Hughes Medical Institute investigator at the University of California, Los Angeles. Mutations can cause “normal stem cells to lose their regularized behavior and instead turn into an incipient cancer.”

Witte and his colleagues wanted to determine which class of cells generates prostate cancer in mice. They separated mouse prostate cells into different groups based on type, then introduced mutations often found in prostate cancers. Then the researchers implanted the cells back into mice one type at a time.

Basal stem cells outpaced the other groups by far in their cancer-forming ability, the researchers reported February 9 in the Proceedings of the National Academy of Sciences. Earlier studies suggested that the same thing might also be happening in human prostate cancers.

“When we apply stem cell thinking to cancer, we find that in the run-up to cancer—the premalignant period—many, many genetic and heritable changes occur in the line of stem cells,” commented Irving Weissman of Stanford University.

A gene called BMI1 is important for basal stem cells’ self-renewal and may also play a role in malignancy. When BMI1 activity was knocked down in basal stem cells, the cells were no longer able to self-renew, nor did they form tumors, Witte reported at the meeting. “We get a dramatic change in the rate of growth and the tumor outcome by blocking this one single pathway,” Witte said.