Do suicidal cells prevent colon cancer?

Cancer may kill, but its deadliness depends upon the ability to keep alive the dividing cells that feed its malignant growth. It's not surprising, then, that cancer cells often have mutations that prevent them from undergoing apoptosis, a form of cellular suicide.

Beyond their role in sustaining tumors, mutations that hinder apoptosis may initiate certain cancers. A new report suggests that precancerous polyps form in the colon because defects in a gene called *APC* stop the cells that line the colon from dying when they should.

"It's the first link between *APC* and programmed cell death," says Patrice J. Morin, an author of the report.

Investigators discovered *APC* while studying familial adenomatous polyposis (FAP). People with this rare inherited disorder commonly have thousands of polyps lining their colon. Because the polyps frequently progress to cancer, some FAP patients resort to having their colon removed as a preventive measure.

In 1991, researchers announced that people with FAP inherit a mutation in one of their two *APC* genes (SN: 8/10/91, p. 86). When mutations strike their second *APC* gene, cells in the colon can turn into polyps. The tumors of people struck at random by colon cancer almost always have *APC* mutations.

What does *APC* do in the cell that is so important? It encodes a protein that cells need to undergo apoptosis, contends Morin of the Howard Hughes Medical Institute at John Hopkins Medical Institutions in Baltimore. Morin, along with Hopkins colleagues Bert Vogelstein and Kenneth W. Kinzler, presents evidence supporting that assertion in the July 23 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

The researchers introduced functioning versions of *APC* into some colon cancer cells growing in petri dishes. These cells normally lack APC, the gene's protein, because both of their copies of the gene are mutated. The colon cancer cells making APC did not proliferate as quickly as the unaltered cancer cells. On a closer look, the investigators discovered that the cancer cells making APC were undergoing apoptosis.

Combining that discovery with recent research showing that *APC* turns on in colon cells only when they near the inner surface of the colon, the researchers offer a possible role for the gene's protein.

Like the skin, the inner lining of the colon is self-renewing. The oldest layers are continuously sloughed off and replaced by newer cells. As a cell nears the surface of the lining, it may synthesize APC in order to commit suicide, say the investigators. If the gene is mutated, however, the cell doesn't die and can form a polyp that may turn cancerous.

Linking *APC* to apoptosis may help explain the apparent ability of aspirin, ibuprofen, and similar drugs to prevent the formation of polyps and thus ward off colon cancer (SN 9/9/95, p. 165). Known collectively as nonsteroidal anti-inflammatory drugs, recent research indicates that they induce colon cells to undergo apoptosis. In effect, says Morin, they may substitute for *APC*.

The new findings, says David E. Fisher of the Dana Farber Cancer Institute in Boston, "suggest *APC* plays a role in life-death decisions. It's a very enticing result, but there's a lot more to do with this observation in terms of verifying the mechanism by which this happens."

The gene's role in apoptosis may simply be that its protein transmits the complex signal to commit suicide. Another molecule that may be involved in that death signal is beta-catenin, to which APC binds tightly.

Yet investigators caution that APC probably does more than command cells to die. "APC is an enormous protein. It has the potential to interact with many other proteins in a cell," notes Jeffrey I. Gordon of the Washington University School of Medicine in St. Louis, who suggests that APC's interactions may also influence cell proliferation and migration.

—J. Travis

Ancient bread rises in gourmet status

Separating the wheat from the chaff was no easy task for the ancient Egyptians, who used a tough-hulled type of wheat called emmer to make bread and beer. Modern interpretations of ancient documents portray their bread as coarse and gritty. A new study, however, suggests that the ancient Egyptians were better bakers and brewers than these documents had let on.

An analysis of some very stale bread loaves—up to 4,000 years old—and beer residues clinging to shards of pottery shows that ancient Egyptians actually used fairly sophisticated processing techniques. The conclusions, published in the July 26 SCIENCE, offer insight into the evolution of food preparation. They have even inspired a beer that made its debut earlier this month.

Delwen Samuel, an archaeobotanist at the McDonald Institute for Archaeological Research at the University of Cambridge in England, examined the samples with both optical and scanning electron microscopes. The bread loaves came from several ancient Egyptian sites, dating from 2000 to 1200 B.C. The beer residues were found at two sites where workmen lived—Deir el-Medina (1550 to 1307 B.C.) and Amarna (1350 B.C.).

Samuel could distinguish the different baking methods from the shapes of the microscopic starch granules. "Unprocessed starch takes a spherical shape," she says, "but the round balls change shape if they've been processed. Heating causes them to swell and bend. Enzymes make pits and channels in the granules."

From these features, Samuel deciphered several recipes for the bread. In one, the emmer wheat was allowed to sprout before being dried and ground into flour. The flour was then mixed with a lot of water, kneaded slightly, and baked, producing a dense bread.

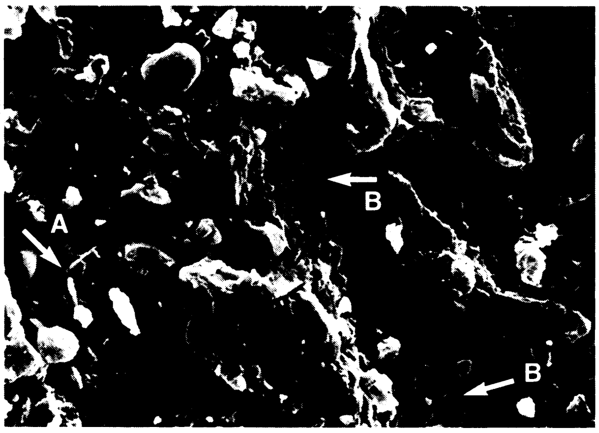
To verify the recipe, Samuel baked several loaves of the sweet, "rather tasty" bread. "When I looked at the microstructure, it matched [that of the ancient bread] very well," she says.

She determined a basic recipe for ancient Egyptian beer too, although it was much more difficult because of beer brewing's complexity. The variety of starch granules on the pottery shards showed that Egyptian brewers used a two-part process. After sprouting the emmer grain to make malt, they divided it into two batches, cooking one and leaving the other alone. Then they mixed the two together and strained out the liquid for fermentation.

Not to let this knowledge go to waste, Scottish and Newcastle Breweries in England came out with Tutankhamun Ale on July 2, brewed with specially grown emmer wheat and using methods based on Samuel's work. "They produced 1,000 bottles and sold them at Harrods," Samuel says. "As far as I know, they've all sold out."

—C. Wu

Samuel/SCIENCE



Starch granules from ancient Egyptian bread, shown in this scanning electron microscope image, contain hollows (A) and channels (B) from processing.