Dairy alliance proves a delight

William Kinlaw, M.D., has been working since 1990 on uncovering the secrets of a gene called Spot 14 (S14), a switch that controls fat production in breast cancer. Most breast cancers need S14 because it allows tumor cells to make fat, which acts as a sort of dry kindling to ignite metastasis. "If we turn off this gene, it kills breast-cancer cells," says Kinlaw.

Last year, he published a series of papers identifying S14 as, says Kinlaw, "a heck of a biomarker" for breast cancer. That would have been good news all by itself. He never imagined that the papers would lead to a collaboration with a Cornell dairy scientist.

Fat: But one day, out of the blue, Kinlaw's phone rang. It was Cornell scientist Dale Bauman, Ph.D., who'd come upon Kinlaw's name by doing a web search for S14. Bauman was trying to solve a problem for dairy farmers whose cows, when they consume a certain kind of grass, produce milk that is useless because it has no milk fat.

"There was something being absorbed from the fermented products of this grass that was shutting down fat production in the mammary gland of the cow and ruining the milk," says Kinlaw. "The bacteria that are in the cow's rumen ferment the grass and rearrange the double bonds on a fatty acid." (The rumen is the part of the bovine digestive system where most fermentation occurs.)

The fatty acid turned out to be conjugated linoleic acid (CLA), which is produced naturally in a cow's rumen; as grass is digested, fermentation converts a normal fatty acid into CLA. Bauman biopsied a cow's mammary gland and subjected the tissue to a gene chip analysis. Of the 24,000 genes he analyzed, the most significant change was in one he knew nothing about: S14.

Clearly there was a connection between CLA and S14. The linkage became evident when Bauman went back to the cows and, instead of feeding them the grass that made the CLA, fed them commercially available CLA; the substance has been on the market since the 1970s in health-food stores and can be purchased online as a human weight-loss supplement. When Bauman gave it to the cows, the S14 gene was promptly turned off.

Before he published a paper on his results, Bauman called Kinlaw to ask about his work with S14, the mysterious gene at the center of Bauman's milk problem. "In essence, it looked like this CLA might be a drug that can be absorbed orally [and] that might turn off the S14 gene, not only in normal mammary tissues but perhaps in cancerous mammary tissue," Kinlaw says. To his surprise, he discovered a number of papers about the connection between CLA and breast cancer. No one, however, had figured out how it affects breast-cancer cells.

S14 appears to be the missing link scientists have been looking for.

"There are several weird theories in the bona fide scientific literature about how CLA works. Well, I think we know how it works," Kinlaw says. S14 appears to be the missing link scientists have been looking for—potentially a very important discovery.

Unfazed: So Kinlaw began his own experiments with CLA. He tried exposing a breast-cancer cell line, which requires fatty acid synthesis to survive, to CLA. The CLA proceeded to shut off the S14 gene and kill the cells. Wondering if the results might be a fluke, he tried the same experiment using a type of cervical-cancer cell that does not need to make its own fatty acids. "We figured that this would be a good . . . test, to see if the CLA was just a general toxin," says Kinlaw. Those cells remained unfazed by the CLA.

JON GILBERT FOX

DMS's Bill Kinlaw, above, got a phone call out of the blue from a Cornell dairy scientist that led to a new way to stop breast tumors from growing.

In a parallel line of investigation, he's been working with surgeon Burton Eisenberg, M.D., the deputy director of Dartmouth's Norris Cotton Cancer Center, on a deadly tumor called a liposarcoma—basically a malignant fat cell. CLA had the same effect on the liposarcoma as on breast-cancer cells; it killed them. "We've actually proven that it is the turning off of the fat metabolism that causes them to go belly-up," says Kinlaw.

Block: Now, in a joint effort with a couple of DMS colleagues, Kinlaw is looking at how CLA—as well as another weight-loss drug, Orlistat, which also kills breast-cancer cells by turning off fat metabolism—might work when combined with drugs like Herceptin and tamoxifen, which can block breast cancer from spreading. "Our overall hypothesis is that blocking both fat metabolism and the systems that drive breast-cancer proliferation and metastasis will kill tumors more completely than either alone," he says.

When he uncovered the mechanism by which CLA's long-suspected antitumor effect works against breast cancer, Kinlaw succeeded in linking, for the first time, two disparate lines of scientific investigation. Thanks to years of meticulous research—and an unexpected phone call.

LEE MCDAVID