Food Science

Harnessing fatty acids to fight cancer

Fatty acids are straight-chain, carbon-based molecules that are among the building blocks of fats and oils. Three polyunsaturated ones – linoleic, gamma-linolenic (GLA) and arachidonic (AA) – are even essential nutrients. But cancer cells are deficient in polyunsaturated fatty acids (PUFAs). In fact, says Michel Bégin, "they do everything they can to get rid of them." And that led Bégin and his Canadian colleagues at the private Efamol Research Institute in Kentville, Nova Scotia, to explore the tumor/PUFA relationship. Three years ago they reported that PUFAs could kill tumor cells. Now they have identified not only which are the most efficient tumor-cell killers, but also their modus operandi. Bégin presented their findings last week at the American Oil Chemists' Society annual meeting in Phoenix, Ariz.

Working with cultured human breast-cancer cells, the Canadian researchers found that while AA, EPA (eicosapentanoic acid) and GLA were about equally effective in killing tumor cells – and were the most lethal of the seven PUFAs being looked at – their effect on normal cells differed dramatically. EPA, for example, was just about as lethal to normal cells. AA was not quite as toxic to normal cells, but it also wasn't benign. At concentrations of about 0.5 nanogram per cultured cell, however, GLA was quite deadly to tumor cells and innocuous to healthy ones.

Because PUFAs are very susceptible to oxidizing reactions, their presence in cell membranes can easily cause serious cell damage. In search of the mechanism for PUFA-initiated tumor-cell killing, Bégin, Greg Ells and David Horrobin focused on damaging oxygen-based reactions. Their results, first described in the April 6 JOURNAL OF THE NATIONAL CANCER INSTITUTE, suggest the cell killing by GLA and other PUFAs correlates with their generation of superoxide radicals (highly reactive oxygen molecules) and toxic secondary products – primarily singlet oxygen, aldehydes and polymers of peroxides.

Though the GLA concentration needed to kill cultured cancer cells is small, Bégin says it is still at least 5 times higher than that normally found in the body. So he and his coworkers turned to transition metals – like iron and copper – to see if they could enhance GLA's efficacy. As Bégin explains, these metals increase the degradation products of hydroperoxides, reactive chemicals active in this PUFA-initiated tumor-cell killing. The researchers found that adding just 10 micrograms of iron per milliliter of culture medium was sufficient to halve the dose of GLA that killed tumor cells. Alternatively, doubling the iron concentration would double or triple the rate of cell killing.

What this suggests, Bégin says, is that with sufficient iron, it might be possible to trigger the body to kill its own tumor cells – just using the GLA naturally present. The trick, and one Bégin is already at work to engineer in animals and humans, is seeing that the iron and appropriate fatty acids both enter the tumor cells.

A saturated fat to enjoy without guilt

Since saturated fatty acids tend to raise blood-cholesterol levels, people with high cholesterol are often warned to limit their dietary fat – especially saturated fat. But this generic warning against saturated fats is too simplistic, according to a study reported in the May 12 NEW ENGLAND JOURNAL OF MEDICINE. Though stearic acid – one of the primary constituents of beef and other animal fats – is saturated, it does not raise blood-cholesterol levels. In fact, its cholesterol-lowering effects match or surpass that of oleic acid – the monounsaturated fatty acid in olive oil and rapeseed often recommended for cholesterol watchers.

Eleven hospitalized male volunteers, aged 59 and older, were randomly and successively assigned to each of three, three-week-long high-fat (40 percent of calories) liquid diets. The diets were basically identical except for their fat. One contained 45.1 percent palmitic acid, a primary saturated fatty acid in palm oil, and 38.8 percent oleic acid. A second contained 42.9 percent stearic acid and 39.4 percent oleic acid. The third contained 79.7 percent oleic acid, with traces of stearic and palmitic.

The subjects' blood cholesterol was 14 percent lower on the high stearic-acid diet than on the high palmitic-acid diet – and 4 percent lower than it was on the high oleic-acid diet. Similarly, low-density-lipoprotein cholesterol levels on the high-stearic diet were 22 percent lower than on the high-palmitic diet – and 6 percent lower than on the high-oleic diet. Andrea Bonanome and Scott M. Grundy of the University of Texas Southwestern Medical Center at Dallas, the study's authors, speculate that one partial explanation for the stearic effect is that the body quickly converts it into oleic acid. What this doesn't explain is why stearic appeared to outperform oleic acid in cholesterol lowering.

Experts caution that other saturated fats found in meats and oils still pose a health risk.

In an editorial in the same issue of the journal, Irwin Rosenberg and Ernst Schaefer of the Agriculture Department's Human Nutrition Research Center on Aging in Boston, note one advantage of oleic and stearic acids over polyunsaturated fatty acids – like the linoleic found in corn oil – is that they don't reduce blood levels of high-density lipoproteins, the so-called "good lipoproteins." They also say these findings could lead to new cholesterol-lowering margarines that "taste more like butter than the margarines currently available."

Gary Smith, head of animal science at Texas A&M University in College Station, points to another potential application of these findings. "We love the satiety associated with eating things that have fat," he notes. In fact, researchers and physicians find people tend to abandon diets that don't contain enough fat to satisfy that taste craving. So while very lean animals can be developed, he says, you run the risk of creating a meat that people won't want to eat. "But if stearic turns out to be the good guy that it appears it is, we may be able to produce animals with more of this in them," Smith says – and in so doing create a meat with a satisfying amount of fat, yet with the nutritional benefits of formerly unpalatable ultra-lean cuts.

Butter – an anti-tumor agent?

Because of concern about the heart-disease risk posed by saturated animal fats, butter sales have been falling and margarine use increasing, notes Mitsuaki Sakamoto of the Nara (Japan) Medical College. But butter lovers take heart. He and his colleagues now report that, at least in animals, "butter has a protecting effect" against breast-tumor development. Sakamoto reported his findings last week at the American Oil Chemists' Society meeting.

Spontaneous lifelong breast-tumor formation was compared between mice fed an ordinary diet and those fed one enriched with 20 percent dextrin (starch gum), 20 percent butter, 20 percent margarine or 20 percent safflower oil. While those on the margarine and safflower oil had about the same incidence of breast tumors as mice on the ordinary diet – roughly 45 percent – only 7 percent on the butter diet and 21 percent fed the dextrin diet developed tumors. In rats fed similar diets and exposed to a 5-milligram dose of the carcinogen DMBA, again butter-fed animals had the lowest tumor incidence of all (40 percent). Margarine-fed animals, by contrast, had the highest tumor incidence (66.7 percent).