

## Diabetes antibody best marker so far

A specific antibody found in blood from people who eventually developed Type I diabetes might be the best early warning yet for the disease, say researchers at the University of Florida College of Medicine in Gainesville. Called 64K autoantibody, it raises to three the number of known autoantibodies involved in Type I diabetes, which is widely believed to be an autoimmune reaction to the body's own insulin-producing beta cells in the pancreas.

A reliable antibody marker would single out future diabetics, and if it proved to be the primary cause of the disease, it could provide the key to therapy that would halt its course before insulin-dependent diabetes occurred. The Florida researchers have found the two previously known antibodies in at most 75 percent of those who later developed the disease. However, the 64K autoantibody has shown up so far in all the subjects who later became diabetic.

These findings, presented in New Orleans this week by Mark Atkinson and his colleagues at the 48th annual meeting of the American Diabetes Association, are based on blood samples drawn from 5,000 schoolchildren and 3,000 close relatives of Type I diabetics selected at random. Twelve have since become diabetic, with all 12 testing positive for the 64K autoantibody — so named because it attacks a 64,000-molecular-weight protein on the surface of beta cells. Blood samples taken as early as seven years before the onset of diabetes harbored the 64K autoantibody.

Researchers also tested for the two other Type I-associated antibodies. Insulin antibodies were in the blood of five of the 12 who developed diabetes, and islet-cell antibodies were found in nine.

"We're very sure it's a specific marker," Atkinson says, referring to the 64K autoantibody. He also notes that the antibody's target protein has been found only on beta cells.

Type I is the more acute form of diabetes, usually striking during childhood or adolescence. Insulin injections become routine for these patients, since their bodies do not produce enough of the hormone to control blood-glucose levels. Late-onset diabetes, Type II, often can be controlled with a diet low in sugar.

Atkinson says previous autoantibody studies tested newly diagnosed patients rather than prediabetics. For purposes of comparison, his group also tested newly diagnosed Type I patients, finding 64K autoantibodies in 18 out of 20 patients. None of 18 controls carried the 64K autoantibody.

"Our current studies are isolating and sequencing the surface protein [attacked by the antibody]," Atkinson says. "Our hope is that we could attach toxins to it that would destroy the antibody." He

suggests that, being a surface protein, the antibody's target site might be the first in a cascade of reactions that eventually whittle away beta cells.

Atkinson says a toxin specific for the autoantibodies would not have the side effect of suppressing the body's entire immune system, as does cyclosporine, which is currently in clinical trials as a Type I treatment (SN: 11/7/87, p.132). This immunotoxin approach, using the body's immune system as a drug courier, is already under study as a cancer therapy (SN: 4/4/87, p.219). By locking ricin, a plant toxin, onto antibodies that target

tumor cells, an immunotoxin can destroy cancer cells without harming other body tissues. The Florida study will be a mirror image of that: The toxin will be attached to the beta-cell surface protein and destroy the antibody when it binds to the cell.

Atkinson predicts his group will begin testing such a therapy in mice later this year. In the meantime, scientists in Denmark also are examining the 64K autoantibody.

The test for 64K autoantibodies currently costs about \$500 and takes four to five weeks to process. Atkinson says the assay would have to cost about \$2 per test and be much faster to have commercial value. — L. Beil

## Will cancer spread? Sound out NMR

A Canadian scientist has adapted a standard chemical assaying technique to identify whether solid cancerous tumors have the ability to spawn secondary growths, called metastases. In a recently completed study of 200 human adenocarcinomas — 70 percent colon cancers, 30 percent breast tumors — Ian C.P. Smith correctly diagnosed 27 cancers as having apparently "no metastatic potential." It is significant, he notes, that none of his diagnoses falsely predicted that a cancer would not spread.

If such metastatic diagnoses prove as reliable as the preliminary studies suggest, they might one day offer physicians the option of prescribing postsurgical radiation or chemotherapy directed only at the primary tumor, says Smith, director of the Canadian National Research Council's Division of Biological Sciences in Ottawa. Thus some patients might qualify for a more benign therapy than the treatment used to tackle unseen metastases today, he says.

Over the past decade, most major hospitals have adopted nuclear magnetic resonance (NMR) imaging, also known as magnetic resonance imaging, as a noninvasive tool for peering into the body. But chemists have used NMR spectroscopy — which can identify and quantify chemical species within complex samples — for at least 30 years. And a technique based on this spectroscopic side of the technology lies behind Smith's work, which he described in Toronto last week at the Third Chemical Congress of North America.

Smith irradiated samples (from tumors removed during surgery) with radiofrequency radiation. This energy "excited" nuclei of certain atoms in the cancerous tissue to a higher energy. When the NMR beam shut off, the atoms "relaxed" to their initial energy state. Each chemical constituent has a unique relaxation profile, or signature, that allows its identification.

Smith focused on relaxation rates for

the methylene (CH<sub>2</sub>) component of fat, because an Australian study in rats had suggested its association with metastasis. None of the 27 patients whose tumors' methylene spectra relaxed quickly — usually in about 154 milliseconds — had metastases at the time of surgery or in the two to three years they have been followed since then. However, Smith found, among those patients whose tumor spectra had relaxation times above 350 milliseconds, many had metastases at surgery. Moreover, among the initially metastases-free patients with tumors showing slowly relaxing methylene spectra, "a number have since developed metastases," Smith says.

He also reports that the width of the CH<sub>2</sub> spectral peak — at least in the colon tumors — appears to correlate with the tumor's invasiveness. "The narrower it is," he says, "the further the tumor has [invaded] the wall of the colon."

"What I think we are seeing is a unique cancer-cell antigen," Smith says — a sort of identity marker on the outside of cancer cells that "gives us the slow [NMR relaxation] response." Because this particular signature may be specific to the class of tumors he studied, it cannot yet be extrapolated to solid tumors in general. But if type-specific signatures do occur, Smith says, spectroscopists might be able to read such signatures noninvasively before patients undergo surgery — learning not only what type of cancer they have but also whether it has spread.

Several researchers, including Smith, have experimentally used NMR spectroscopy to screen blood for signs a patient has cancer. However, Smith found, unusual fat ratios in the blood — which can be caused by diabetes, heart disease or even pregnancy — may yield a false indication of cancer. Where NMR monitoring of blood might be useful, Smith says, is in following high-risk persons, like those who have had cancer surgery, to look for early signs of recurring disease. — J. Raloff