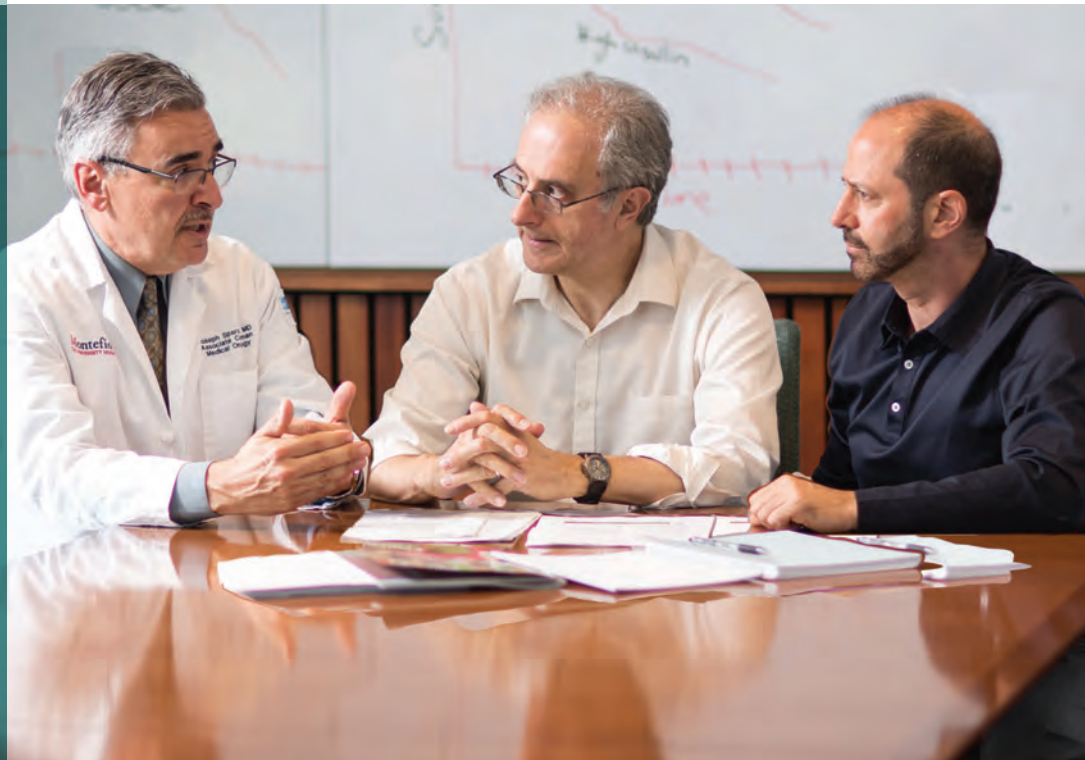


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NEWS

Einstein Cancer Center



Obesity: An Important Cause of Cancer

Beginning about a decade ago, scientific papers started linking obesity to greater risk for developing breast cancer and other types of cancer.

Obesity was already known as a risk factor for major killers such as heart disease, diabetes and stroke. Yet the notion that excessive fat could somehow cause cancer had seemed far-fetched. Not anymore.

"We know that obese patients are more likely to get cancer and to die of cancer," says Joseph A. Sparano, M.D., a professor of medicine (oncology) and of obstetrics & gynecology and women's health at Einstein and associate chair of oncology at Montefiore, the University Hospital and academic medical center for Einstein.

Evidence overwhelmingly links obesity (defined as a body-mass index, or BMI, above 30) to major cancers, including postmenopausal breast cancer and cancers of the colon, endometrium, kidney and esophagus. The American Institute for Cancer Research estimates that obesity, which affects more than one in three Americans and is on the rise, causes more than 100,000 extra cases of cancer in the United States every year.

On the cover: Working together to understand the interrelationship among obesity, diabetes, hormones and cancer are Joseph A. Sparano, M.D.; Thomas E. Rohan, M.D., Ph.D.; and Howard D. Strickler, M.D., M.P.H.

MESSAGE FROM THE DIRECTOR



I. DAVID GOLDMAN, M.D.
Director, Albert Einstein
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Professor of Medicine
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Evolution has provided humans with a variety of survival mechanisms. Since starvation posed a major threat to survival in prehistoric times, we've developed the ability to efficiently store and use the food we eat. However, we've never needed survival mechanisms to address a surplus of food. The resulting obesity has now emerged as a major public health hazard.

One way we learn about obesity's impact is by studying metabolic defects in obese animals to find the molecular basis for these changes. This edition of the newsletter illustrates efforts by investigators in our Cancer Epidemiology Program to understand obesity's connection with cancer based on population studies.

Their studies point to the high blood levels of insulin associated with obesity as a key risk factor for both the development of breast cancer and poor outcome once the disease has occurred. Studies from Einstein and other research centers suggest that carbohydrate restriction and drugs that decrease insulin blood levels can decrease the incidence of breast cancer and improve survival once the disease has occurred.

The many threats to health associated with obesity are clear, but how to address this public health problem is a major challenge. Behavioral scientists at Einstein's NIH-funded cancer and diabetes centers are now collaborating on initiatives that will reduce the prevalence of obesity in our society.

Obesity: An Important Cause of Cancer *(continued from page 1)*

In a study published last year in the journal *Cancer*, Dr. Sparano, also associate director for clinical research at the Albert Einstein Cancer Center (AECC), and his colleagues analyzed data on nearly 7,000 women with stage 1 to stage 3 breast cancer who were treated with optimal chemotherapy and hormone therapy. After ruling out the impact of other diseases associated with obesity, his team found that women who were obese at the time of their breast cancer diagnoses were 30 percent more likely to relapse—and 50 percent more likely to die—than women who were not obese.

Cancer epidemiologist Thomas E. Rohan, M.D., Ph.D., associate director for population sciences at the AECC and leader of its Cancer Epidemiology Program and its Epidemiology Study Management and Informatics Facility, has found similar connections between a high BMI and several types of cancer. In collaboration with researchers at Einstein and other institutions, Dr. Rohan, a Harold and Muriel Block Chair in Epidemiology & Population Health at Einstein and professor and chair of the department of epidemiology & population health at Einstein and Montefiore, has found that high BMI is associated with increased risk for both ovarian and pancreatic cancer (but—interestingly—with reduced risk for lung cancer).

How can extra fat tissue accelerate or even cause cancer? AECC researchers from a wide range of

disciplines are studying factors associated with obesity that may cause people to develop cancer.

The Insulin Connection

Being overweight is the major risk factor for developing type 2 diabetes. Like obese people, those with type 2 diabetes face a heightened cancer risk and are far more likely than nondiabetics to be diagnosed with cancer.

High insulin may be a common factor linking both obesity and type 2 diabetes to cancer susceptibility. The pancreas secretes insulin to help cells absorb glucose from the bloodstream. In people with type 2 diabetes (by far the more common form of the disease) and in some obese individuals, cells become resistant to insulin and are unable to take in glucose and metabolize it. The pancreas responds to insulin resistance by pumping more insulin into the bloodstream, leading to high insulin blood levels. In addition to its well-known role in metabolism, researchers have long recognized that insulin can stimulate cells to multiply, which may increase cancer risk. It turns out that obese people—whether they have type 2 diabetes or not—often have elevated blood levels of insulin too.

Einstein scientists led by Howard D. Strickler, M.D., M.P.H., a professor of epidemiology & population health and a Harold and Muriel Block Chair in Epidemiology & Population Health, investigated insulin's role in causing breast cancer. They did so by analyzing data from one of the largest-ever

cancer



Q: Does losing weight lower the risk of developing cancer?

A: Research on weight loss and cancer risk is still limited. But growing evidence suggests that weight loss may reduce the risk of several types of cancer, including breast cancer that occurs after menopause, more aggressive forms of prostate cancer and possibly other cancers, too.

studies of postmenopausal women—a 12-year federally funded study called the Women’s Health Initiative (WHI). In a study published in 2009 in the *Journal of the National Cancer Institute*, the researchers found that excess insulin in the blood is a strong independent risk factor for breast cancer, suggesting that insulin may have a substantial role in explaining the obesity–breast cancer relationship.



Nicole S. Nevadunsky, M.D.
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Conversely, efforts to lower insulin levels may help prevent or treat cancer. A number of studies suggest that the diabetes drug metformin—developed in the 1920s to lower insulin levels—reduces the risk of breast cancer in postmenopausal women who have diabetes and improves the prognosis of breast cancer patients with diabetes. Through work led by Nicole S. Nevadunsky, M.D., it appears that metformin use helps improve survival of diabetics with endometrial cancer.

In a current study funded by the



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National Institutes of Health (NIH), Gloria S. Huang, M.D., and Mark H. Einstein, M.D., M.S., are assessing how insulin interacts with a related hormone, called insulin-like growth



Ilir Agalliu, M.D., Sc.D.
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factor (IGF), to influence the risk that endometrial cancer will recur. And the American Cancer Society is funding research by Ilir Agalliu, M.D., Sc.D., and his colleagues to examine how obesity, insulin and IGF may interact to influence aggressive prostate cancer phenotype.

The Estrogen Question

Menopause occurs when a woman’s ovaries no longer produce estrogen. But low levels of estrogen can continue being produced even after menopause—primarily by fat tissue.

Scientists have long known that excess body fat can boost estrogen levels in the body and that postmenopausal women with elevated estrogen levels are at increased risk for breast and endometrial cancer. But is estrogen by itself a link between obesity and cancer?

To find out, Dr. Strickler and his Einstein colleagues further analyzed the WHI data. In a paper published in 2012, they reported that while estrogen is a risk factor, the relation of obesity with breast cancer risk is more strongly linked to insulin than to estrogen.

The recent findings by Dr. Strickler’s team underline the potential for targeting the insulin-signaling pathway to identify individuals at high risk of breast cancer, so tumors can be detected early or perhaps even before they fully develop. The findings could even lead to efforts to reduce risk of tumor cells developing in the first place, by blocking the cancer-related component of insulin signaling.



ON THE WEB

To learn more about the Albert Einstein Cancer Center, please visit www.einstein.yu.edu/cancer.

STARVE A CANCER?



Eugene J. Fine, M.D.
Clinical Professor of Radiology (Nuclear Medicine)
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As noted (at left), elevated insulin levels in the blood appear to increase breast cancer risk. This condition, known as hyperinsulinemia, seems to raise the risk for several other types of cancer as well. Since dietary carbohydrates cause insulin levels to spike, Einstein researchers wondered whether putting cancer patients on low-carb diets could be beneficial.

Collaborating with Dr. Sparano, Eugene J. Fine, M.D., carried out a pilot study on carbohydrate restriction in 10 patients with advanced, incurable cancer. The results, published in 2012 in *Nutrition*, indicated that a low-carbohydrate diet for four weeks could suppress insulin blood levels and was “safe and feasible.”

The authors noted that if the results are confirmed in larger studies, “dietary manipulation may have the potential to be used as a complementary non-toxic approach to improve the effectiveness” of standard cancer therapies.





our supporters

The Albert Einstein Cancer Center gratefully acknowledges the generosity of the following individuals and organizations whose support is critical to advancing its mission.

NOTABLE GIFTS AND GRANTS

\$1.3 Million Raised to Benefit Cancer Research

The Grand Ballroom of New York's Plaza Hotel was the setting last fall for a dinner marking the 60th anniversary of Einstein's founding and 60 years of philanthropic leadership by the Einstein Women's Division to help advance the medical school's mission. The evening's honorees—Broadway producer Daryl Roth, a longtime Women's Division board member, and Einstein Overseer Benjamin J. Winter, who together with his wife, Susan, is a leading supporter of biomedical research—received the Albert Einstein Humanitarian Award for their dedicated service to the College of Medicine.

Proceeds from the event totaled \$1,350,000. The funds will help support research into men's and women's

cancers, including ovarian, cervical, uterine, breast, prostate, lung, colon and pancreatic cancers and leukemia.

Carol Roaman, the Women's Division president, chaired the event; dinner co-chairs were Linda and Earle Altman, Judy and Ronald S. Baron, Renée E. and Robert A. Belfer, Carol and Roger W. Einiger, Ruth L. and David S. Gottesman, Janet and Arthur Hershaft, Ronnie Heyman, Karen and David Mandelbaum, Pamela and Edward S. Pantzer, and Kathy and Samuel G. Weinberg. Burton P. Resnick served as journal chair.

Quality-of-Life Research for Patients with Cancer

Bruce D. Rapkin, Ph.D., director of the AECC's Marilyn and Stanley M. Katz Comprehensive Cancer Prevention and Control Program, has received

a grant from the Patient-Centered Outcomes Research Institute to develop a quality-of-life assessment instrument aimed at obtaining information from patients that is more accurate than data gained from previous assessment tools. The results will help pave the way for better-targeted treatment strategies, patient education and supportive care.

The Katzes' generous support for the cancer prevention and control program, including their recent \$500,000 commitment (announced in our last issue), helped fund the pilot research that led to this grant.

Dr. Rapkin is also a professor of epidemiology & population health and of family and social medicine.

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Leonard H. Augenlicht, Ph.D.; Jan Vijg, Ph.D.

Age and Diet: Major Interacting Factors That Drive Sporadic Intestinal Cancer—A Provocative Questions Grant from the National Cancer Institute

To learn more about supporting the work of the AECC, please contact:

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ALBERT EINSTEIN CANCER CENTER

Our mission: to promote and conduct research that will elucidate the origins of cancer and lead to effective new approaches for the prevention, diagnosis and treatment of malignant diseases

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