Case School of Medicine and Cancer Center to work with University Hospitals and Cleveland Clinic on Major Research Project Looking at Obesity and Cancer

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The Case Western Reserve University School of Medicine through its Comprehensive Cancer Center is one of four institutions to share a $54 million federal grant over five years to research the relationship between obesity and cancer. The grant was awarded by the National Cancer Institute (NCI). Case will receive about $10 million for its role in the program called the Transdisciplinary Research on Energetics and Cancer (TREC). The initiative will examine diet, weight, and physical activity and their molecular effects on developing cancer. The project will involve researchers from Case, University Hospitals of Cleveland, and the Cleveland Clinic and is reflective of the cooperation among the institutions working under the umbrella Case Comprehensive Cancer Center.

Nathan A. Berger, M.D., of Case and UHC, is the principal investigator of the study. He said obesity is increasing at epidemic levels in the United States and the risk of developing cancer increases with obesity. “New studies suggest that weight gain at all stages of life may increase the association between obesity and cancer. Even weight gain early in life may have an important impact. For example, high birth weight increases a womanís risk of getting breast cancer as an adult. We need to learn more about why this occurs on genetic, cellular, metabolic and environmental levels,” he said.

The grant consists of three main projects and two pilot projects. The first project, led by Sanford Markowitz, M.D., Ph.D., the Ingalls Professor of Cancer Genetics at Case and UHC, and Joseph Nadeau, Ph.D., Jewell Professor and Chair of Genetics, will use two strains of genetically modified mice. One strain is susceptible to obesity when fed a high fat diet, the other strain is not. The mice will be further engineered with a tumor initiating gene. They then will be compared to determine if a high fat diet leads to tumor formation in the colon or if obesity leads to it. The mice were developed in part with funding from Ohioís Third Frontier program and tobacco settlement funds.

Project 2 will use genomic technologies to examine genetics and intermediate biologic signaling molecules that may connect weight gain to cancer in patients with pre-malignant polyps. Li Li, M.D, Ph.D., assistant professor of family medicine, at Case and UHC will lead this project.

Susan Redline, M.D., professor of pediatrics at Case and UHCís Rainbow Babies and Childrenís Hospital, will lead project 3, which will examine the issue of weight gain in early childhood using a large group of children who have been followed for several years in the Cleveland Childrenís Sleep and Health Study. Statistics have been kept of these childrenís behavior, sleep and biochemical risk factors for obesity. This group of children, 41 percent of which are ethnic minorities, provides a powerful opportunity to identify and measure specific risks, especially sleep disturbances, for obesity, metabolic dysfunction, and cancer. They will be studied for the biological markers in Project 2.

One of the pilot projects, led by Henri Brunengraber, M.D., Ph.D., the Mt. Sinai Professor of Nutrition Research and chair of nutrition at Case, will explore the use of new metabolomic technologies to simultaneously study thousands of molecules involved in energy metabolism to explore differences in the metabolic systems of mouse strains under conditions where they do or do not form tumors. Once identified, these metabolic signatures will be examined as possible markers to identify cancer prone individuals.

A second pilot project will be led by Bryan Williams, Ph.D., chairman and professor of the Department of Cancer Biology at the Lerner Research Institute of the Cleveland Clinic. He will conduct a molecular biologic study to determine mechanisms by which anti-inflammatory agents may interrupt the linkage between obesity and cancer.
The three other research institutions sharing in the large grant are the Fred Hutchinson Cancer Research Center in Seattle, Wash., which will focus on prevention of new or recurrent breast cancer and colon cancer with a particular focus on physical activity; the University of Minnesota, Minneapolis, Minn., which will focus on population studies on the causes and effective prevention strategies for obesity in youth and families; and the University of Southern California, Los Angeles, Calif., which will explore the physiologic, metabolic, genetic, behavioral and environmental influences on obesity and cancer risk in minority children.

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