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Being overweight or obese threatens the health of more than 2 billion people worldwide and more than two-thirds of the U.S. population. As a physician-scientist focusing on obesity and metabolic disease, Cohen investigates the molecular origins of metabolic dysfunction and cancer related to obesity with the ultimate goal of developing therapies to break the link between them.

Obesity can bring with it myriad serious and even potentially fatal health problems, including cardiovascular disease, type 2 diabetes, and cancer. But these conditions and the timing of their onset are not universal; they develop much later for some patients than others, and some escape almost entirely. A number of reasons—genetics, diet, physical activity, and type of fat—contribute to this variability. Cohen focuses on understanding the molecular underpinnings of obesity-related diseases.

Epidemiological studies have shown visceral adipose tissue, stored around the abdomen, increases risk for illness and death. Meanwhile, subcutaneous adipose deposits around the hips and buttocks do not raise these risks and may even be protective. Evidence suggests the type of adipocytes within these two tissues is responsible for the dichotomy.

In visceral fat, white adipocytes warehouse triglycerides in large droplets. In obesity, this tissue is marked by inflammation and an increased accumulation of immune cells. However, other types of adipocytes may have neutral or even beneficial effects. Brown adipocytes can defend body temperature by converting the chemical energy in glucose and triglycerides into heat and may also make significant contributions to adult metabolism. Likewise, a third type, beige adipocytes, can dissipate energy just like brown adipocytes when activated by cold or certain hormones. In rodents, beige adipocytes occur in clusters surrounded by white adipocytes in subcutaneous fat, suggesting the reason for the neutral to beneficial effects of that tissue. The location and physiological role of beige adipocytes, which are also present in humans, is not yet fully defined.

Using animal and cellular models and translational approaches in humans, Cohen investigates the transcriptional basis for the harmful and health-protecting effects of fat deposits and the adipocytes they contain. Ultimately, he hopes to develop ways to engineer healthier fat by manipulating the regulation of traits associated with different types of adipocytes.

One of Cohen's early breakthroughs at Rockefeller was the development of a tissue-clearing imaging technique that allowed his team to visualize structures in fat tissue at molecular resolution. Three-dimensional images provided a striking and unprecedented look at the functional features of beige fat, including blood vessels and projections from nerve cells. It suggested that the most active fat tissue also had the most nerve projections, and that signals between fat cells and nerves are crucial for establishing this interaction.

Cohen's group has identified and characterized proteins fat cells secrete, which interact with surrounding cells and have unexplored biological effects. These proteins mediate diverse functions, which may include obesity-induced inflammation and the regulation of vascular tone and blood pressure.

Cohen and his colleagues have also completed a massive data-mining study of electronic health records, revealing that the presence of brown fat—as shown on PET scans—is associated with reduced prevalence of many common illnesses including type 2 diabetes, coronary artery disease, cerebrovascular disease, congestive heart failure, and hypertension, as well as improved levels of HDL cholesterol and other blood lipids. The findings suggest the possibility that genes associated with brown fat production may confer significant health benefits to those who suffer from these disorders. Studies of these genes could lead to new drugs capable of treating or preventing disease.

EDUCATION

A.B. in biology, 1996
Harvard College
Ph.D., 2003
The Rockefeller University
M.D., 2004
Weill Cornell Medical College

MEDICAL TRAINING

Residency in internal medicine, 2004–2007
Columbia University Medical Center
Fellowship in cardiovascular medicine, 2007–2011
Brigham and Women's Hospital

POSTDOC

Dana Farber Cancer Institute and Harvard Medical School, 2009–2014

POSITIONS

Assistant Professor, 2015–2021
Associate Professor, 2021–
The Rockefeller University
Senior Attending Physician, 2015–
The Rockefeller University Hospital
Cardiologist, 2016–
Memorial Sloan Kettering Cancer Center

AWARDS

Irma T. Hirschl/Monique Weill-Caulier Trust Research Award, 2015
Human Frontier Science Program Young Investigator Grant, 2016
Sinsheimer Award, 2016
American Diabetes Association Accelerator Award, 2017
American Society of Clinical Investigation Young Physician-Scientist Award, 2017
The Rockefeller University Distinguished Teaching Award, 2019
Mark Foundation Emerging Leader Award, 2021
Emerging Leader in Health and Medicine, National Academy of Medicine, 2021

SELECTED PUBLICATIONS

O'Connor, S. et al. AGO HITS-CLIP reveals distinct miRNA regulation of white and brown adipose tissue identity. *Genes Dev.* 35, 771–781 (2021).
Maguire, O.A. et al. Creatine-mediated crosstalk between adipocytes and cancer cells regulates obesity-driven breast cancer. *Cell Metab.* 33, 499–512 (2021).
Chi, J. et al. Early postnatal interactions between beige adipocytes and sympathetic neurons regulate innervation of subcutaneous fat. *Elife* 10, e64693 (2021).
Becher, T. et al. Brown adipose tissue is associated with cardiometabolic health. *Nat Med.* 27, 58–65 (2021).
Chi, J. et al. Three-dimensional adipose tissue imaging reveals regional variation in beige fat biogenesis and PRDM16-dependent sympathetic neurite density. *Cell Metab.* 27, 226–236 (2018).