

Paternal Imprinting of $G\alpha_s$ and Human Obesity

▶ Albright hereditary osteodystrophy (AHO) is caused by heterozygous *GNAS* mutations that disrupt the stimulatory G protein α -subunit $G\alpha_s$. Maternal inheritance of AHO leads to short stature, obesity, brachydactyly, subcutaneous ossifications, dental abnormalities, and cognitive impairment, often accompanied by multi-hormone resistance [pseudohypoparathyroidism type 1a (PHP1a)]. Because $G\alpha_s$ is silenced in certain hormone target tissues when inherited paternally,

similar developmental defects develop without the hormonal resistance, termed pseudopseudohypoparathyroidism (pseudoPHP). The obesity has been considered similar in both conditions.

To test this assumption, a team led by Emily L. Germain-Lee, M.D., at Johns Hopkins University School of Medicine, examined body mass index (BMI) in 40 patients with PHP1a and 13 with pseudoPHP, all with confirmed *GNAS* mutations, and 2 with progressive osseous heteroplasia. Their results will soon be published in *The Journal of Clinical Endocrinology & Metabolism*.*

The team found that mean PHP1a BMI z scores were significantly higher than those in pseudoPHP, and 25 of 40 PHP1a patients had mean BMI z scores more than two standard deviations above the mean, whereas none with pseudoPHP had BMI z scores in this range. This brought the researchers to conclude that obesity is more prominent in PHP1a—and severe obesity is specifically characteristic of PHP1a. “PHP1a can be considered a potentially important model ... to evaluate the usefulness of anti-obesity agents that influence levels of cAMP in the central

nervous system or other organ systems,” according to the authors. ■

* Long DN, McGuire S, Levine MA, Weinstein LS, Germain-Lee EL. Body mass index differences in pseudohypoparathyroidism type 1a versus pseudopseudohypoparathyroidism may implicate paternal imprinting of $G\alpha_s$ in the development of human obesity. *J Clin Endocrinol & Metab*, in press.

Body Composition Changes in Menopause

▶ Fat mass is an active contributor to the metabolic profiles affecting health, rather than merely a passive fat depot. Understanding how menopause changes body composition will help determine women's health risks later in life, including for stroke, incident cardiovascular disease, and cardiovascular mortality.

MaryFran Sowers, Ph.D., and colleagues at the University of Michigan School of Public Health, Ann Arbor, Mich., studied whether changes in body size and composition in women at

mid-life were related to chronological and/or ovarian aging. Their paper will be published shortly in *The Journal of Clinical Endocrinology & Metabolism*.*

Of the 543 subjects who participated in the Michigan Site of the Women's Health Across the Nation (SWAN) study and also this new study, 60% were African American and the others Caucasian. The women's mean measurements were age 45, body mass index (BMI) 32.1 kg/m², and waist circumference 94.1 cm. African American women had a mean baseline follicle-stimulating hormone (FSA) level of 18.9 mIU/mL (SD 13.9) and Caucasians of 16.3

(SD 12.0), and their mean fat mass was 8.1% higher than the Caucasian women's.

During a 6-year period, the women gained 3.4% in weight (2.9 kg), and lost 0.38 cm in height, causing a 4% increase in BMI (about 1.2 kg/m²). Waist circumference expanded 6.2% (5.7 cm), fat mass rose 10.1% (3.4 kg), and skeletal muscle mass declined 1.06% (0.23 kg). FSA concentrations rose progressively and 24% of women experienced their last menstrual period (LMP). Annual measurements of lean mass did not change during the 6 years.

The authors attributed the body composi-

tion changes, similar in the two races, to the passing years and also to the ovarian aging reflected in the higher FSA and LMP. Waist circumference expanded throughout, but its increase rate ebbed a year after LMP (along with a flattening out of FSA), for reasons under active investigation. Mean fat mass increased at a steady rate throughout the study. The data indicate that waist circumference is more sensitive to ovarian aging than to that the increase of fat mass, the authors concluded. ■

* Sowers MF, Zheng H, Tomey K, et al. Changes in body composition in women over six years at mid-life: ovarian and chronological aging. *J Clin Endocrinol Metab*, in press.