

Genes link puberty timing and body fat in women

EurekAlert

(Boston) - Scientists have discovered 30 new genes that control the age of sexual maturation in women. Notably, many of these genes also act on body weight regulation or biological pathways related to fat metabolism. The study, which appears in *Nature Genetics*, was a collaborative effort by the international ReproGen consortium, which included 175 scientists from 104 worldwide institutions, including Boston University School of Medicine (BUSM) and Boston University School of Public Health.

Menarche, the onset of first menstruation in girls, indicates the attainment of reproductive capacity and is a widely used marker of pubertal timing. Age of menarche varies widely and is highly dependent on nutritional status. Early menarche is associated with many adverse health outcomes later in life, including breast cancer, endometrial cancer, obesity, type 2 diabetes and cardiovascular disease, as well as shorter adult stature.

To identify loci for age at menarche, the researchers performed a meta-analysis of 32 genome-wide association studies on more than 87,000 women from the U.S., Europe and Australia and performed replication studies in nearly 15,000 additional women. In addition to the known loci at LIN28B and 9q31.2, the researchers identified 30 new menarche loci and found suggestive evidence for a further 10 loci. According to the researchers, the new loci included four previously associated with body mass index, three in or near other genes implicated in energy homeostasis and three in or near genes implicated in hormonal regulation. Ingenuity and gene-set enrichment pathway analyses identified coenzyme A and fatty acid biosynthesis as biological processes related to timing of menarche.

"Our study found genes involved in hormone regulation, cell development and other biological pathways associated with mechanisms age at menarche, which shows that the timing of puberty is controlled by a complex range of biological processes," said senior author Joanne Murabito, MD ScM, an associate professor of medicine at BUSM and Clinic Director and Investigator of the Framingham Heart Study.

"Several of the genes for menarche have been associated with body weight and obesity in other studies suggesting some women may have a genetic susceptibility to weight gain and early puberty. It is important to understand that these 'genetic factors' can be modified by changes in lifestyle. Efforts to reduce or prevent childhood obesity should in turn help reduce the early onset of puberty in girls," added Murabito.

The next steps according to the researchers are to examine the findings in women of other race/ethnic groups, as well as to examine whether these genetic loci influence growth and to determine whether the associations are driven by measures of body fatness. This future work will help to unravel the biologic mechanism

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underlying the associations.

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