

LAY ABSTRACT

TITLE: Faster ticking rate of the epigenetic clock is associated with faster pubertal development in girls

JOURNAL: Epigenetics. 2018; 13:1, 85-94.

AUTHORS: Alexandra M. Binder^a, Camila Corvalan^b, Verónica Mericq^c, Ana Pereira^b, José Luis Santos^d, Steve Horvath^e, John Shepherd^f & Karin B. Michels^{a*}

INSTITUTIONS:

^aDepartment of Epidemiology, Fielding School of Public Health, University of California, Los Angeles, 650 Charles E Young Drive South, Los Angeles, CA 90095, USA

^bInstitute of Nutrition and Food Technology, University of Chile, Av el Libano 5524, Santiago, Chile

^cInstitute of Maternal and Child Research, University of Chile, Santa Rosa 1234, 2° piso, Santiago, Chile

^dDepartment of Nutrition, Diabetes and Metabolism, School of Medicine, Pontificia Universidad Católica de Chile, Av Libertador Bernardo O'Higgins 340, Santiago, Chile

^eDepartment of Biostatistics, School of Public Health, and Department of Human Genetics, Gonda Research Center, David Geffen School of Medicine, University of California, Los Angeles, 695 Charles E Young Drive South, Los Angeles, CA 90095, USA

^fDepartment of Radiology and Biomedical Imaging, University of California, San Francisco, 400 Parnassus Avenue, San Francisco, CA 94117, USA

*Coordinating author

This is attributed to the BCERP grant U01ES026130 and the National Institutes of Health grant R01CA158313 from the National Cancer Institute

SCIENTIFIC ABSTRACT (current count: 250; max 250 words)

Epigenetic age is an indicator of biological aging, capturing the impact of environmental and behavioral influences across time on cellular function. Deviance between epigenetic age and chronological age (AgeAccel) is a predictor of health. Pubertal timing has similarly been associated with cancer risk and mortality rate among females. We examined the association between AgeAccel and pubertal timing and adolescent breast composition in the longitudinal Growth and Obesity Cohort Study. AgeAccel was estimated in whole blood using the Horvath method at breast Tanner 2 (B2) and 4 (B4). Total breast volume, absolute fibro-glandular volume (FGV), and %FGV were evaluated at B4 using dual X-ray absorptiometry. The impact of AgeAccel (mean: 0; SD: 3.78) across puberty on the time to breast development (thelarche), menarche, and pubertal tempo (thelarche to menarche) were estimated using accelerated failure time models; generalized estimating equations were used to evaluate associations with breast density. A five-year increase in average adolescent AgeAccel was associated with a significant

decrease in time to menarche (hazard ratio (HR): 1.37; 95% CI: 1.04, 1.80) adjusting for birth weight, maternal pre-pregnancy BMI, maternal height, maternal education, B2 height, fat percentage, and cell composition. AgeAccel displayed a stronger inverse association with pubertal tempo (HR: 1.48; 95% CI: 1.10, 1.99). A five-year increase in AgeAccel was associated with 5% greater %FGV, adjusting for B4 percent body fat, and maternal traits (95% CI: 1.01, 1.10). Our study provides unique insight into the influence of AgeAccel on pubertal development in girls, which may have implications for adult health.

LAY ABSTRACT

Where we are and what we do affects how fast we age. These factors can change which genes are turned on or off through something called DNA methylation. Specific patterns of DNA methylation can tell whether our body is aging faster than most people of the same age. We investigated whether this specific measure of our “biological clock” predicts when girls will begin puberty, the time when her breast develop and when she gets her first period. The age when girls begin puberty predicts their health as adults. Among 94 girls in Santiago, Chile, we measured biological aging in blood twice during adolescence. Girls who had faster ticking of the “biological clock” were about 5 months younger when they got their first period than those with slower biological aging. They also went through puberty about 6-7 months more quickly. We also studied the structure of the developing breast using a very low dose x-ray. We found that faster aging was linked with a higher proportion of tissue compared to fat in the breast (increased breast density). Both earlier age of first period and increased breast density are linked with greater risk of breast cancer later on. Future studies will be needed to learn more about the effects on adult health from a faster-ticking of this biological clock during puberty.