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Editorial

Electronic medical records, genetics, and childhood obesity: A new direction for scientific discovery?

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Childhood obesity is a public health disorder of global concern, in part because of its medical comorbidities, which include lipid disorders. A challenge to obesity prevention and treatment is the complex etiology of childhood obesity, which includes the interplay of genetic and environmental factors [1,2]. Body mass index (BMI) (kg/m^2) is highly heritable, however the search for specific genes driving elevated BMI has been challenging. As with other complex traits, only a handful of genes have shown associations, most notably polymorphisms in the fat mass and obesity associated genes [3,4] and melanocortin 4 receptor [5,6] genes. Yet, many other findings do not replicate, and effect sizes generally are small. A challenge for the field is the required sample sizes to detect genotype-phenotype associations, which is daunting. Innovative methodologies that can help overcome these challenges may have huge implications for discovering the etiology of obesity and its comorbities.

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The study by Wang et al. [7] in this issue of the *Journal of Pediatric Genetics* is an impressive one. It demonstrates the potential of electronic medical records (EMR) as a methodology to drive insights into the genetics of pediatric childhood obesity and its comorbities. Using a genetic bank of over 300,000 children enrolled in the health care network of the Children's Hospital of Philadelphia, the investigators identified a number of genes associated with high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglyceride levels. Associations previously discovered with adults were replicated in children, and new findings were reported as well. The results build up prior reports using this cohort to identify genes influencing child BMI [8,9].

The "marriage" of genetic information with EMR technology is neither simple nor inexpensive, however it deserves the attention it is increasingly receiving [10,11]. Developments are still unfolding, yet one can imagine potential scientific innovations beyond establishing initial genotype-phenotype associations for obesity. First, because EMRs capture weight and height data prospectively (i.e., across childhood and adolescence), the influence of genes on dynamic changes in BMI could be tested [2]. This is important because emerging evidence suggests that there are different subgroups or clusters of BMI trajectories

during development, and these subgroups differ in metabolic profile [12–14]. Linking genetic and prospective growth data may drive insights into these issues.

A second potential opportunity is for studies of gene-environment (G*E) interaction. Documenting G*E interactions for childhood obesity has been most challenging because, in part, [1] direct measures of the environment are obtained infrequently and [2] studies are underpowered to detect interactions. However, if EMRs could be linked to indexes of the "obesigenic-" or "built- environment" (e.g., household proximity to playgrounds or grocery markets), might this allow for G*E studies that have been elusive to date? Moreover, if EMRs could be linked to measures of mothers' health status, diet, or other lifestyle behaviors during pregnancy, might this pave the way for innovative epigenetic analyses? It is too early to answer these questions, although prior research already has linked EMRs with sophisticated social-environmental maps [15]. Linking environmental measures to EMRs and genetic data could open the door to examining these issues.

Third, uniting genetic information with EMRs would allow for selective recruitment of children based on genotype for more intensive laboratory experiments related to diet, physical activity, or metabolic response to interventions. That is, children would be identified *a priori* from the biobank and then recruited (or not) based on their polymorphisms at candidate genes of interest. For example, investigators might hypothesize that children with only select polymorphisms of the fat mass and obesity associated gene will overeat at controlled test meals (for example, see ref 16,17); EMR biobanks could allow investigators to efficiently identify and contact the legal guardians of children regarding potential participation in such studies. This may be more efficient than an open recruitment for "all comers" in which child genotype is unknown at screening.

In summary, Wang et al.'s [7] study is most important. However, its significance goes beyond the particular genotype-phenotype associations that are reported. Their work opens the imagination to other potential scientific discoveries; this approach may drive regarding the causes of childhood and its comorbidities. New findings ultimately may inform novel prevention strategies for this pressing public health problem.

References

[1] Lajunen HR, Kaprio J, Keski-Rahkonen A, Rose RJ, Pulkkinen L, Rissanen A, et al. Genetic and environmental effects on body mass index during adolescence: a prospective study among Finnish twins. Int J Obes (Lond) 2009;33(5):559–67.

[2] Silventoinen K, Rokholm B, Kaprio J, Sørensen TI. The genetic and environmental influences on childhood obesity: a systematic review of twin and adoption studies. Int J Obes (Lond) 2010;34(1):29–40.

[3] Dina C, Meyre D, Gallina S, Durand E, Körner A, Jacobson P, et al. Variation in FTO contributes to childhood obesity and severe adult obesity. Nat Genet 2007;39(6):724–6.

[4] Haworth CM, Carnell S, Meaburn EL, Davis OS, Plomin R, Wardle J. Increasing heritability of BMI and stronger associations with the FTO gene over childhood. Obesity (Silver Spring) 2008;16(12):2663–8.

[5] Farooqi IS, Keogh JM, Yeo GS, Lank EJ, Cheetham T, O'Rahilly S. Clinical spectrum of obesity and mutations in the melanocortin 4 receptor gene. N Engl J Med 2003;348(12):1085–95.

[6] Loos RJ, Lindgren CM, Li S, Wheeler E, Zhao JH, Prokopenko I, et al. Common variants near MC4R are associated with fat mass, weight and risk of obesity. Nat Genet 2008;40(6):768–75.

[7] Wang, K, Zhang H, Mentch FD, Bradfield JP, Glessner JT, Qiu H, et al. Examination of genetic variants influencing lipid traits in pediatric populations J Pediatr Genet 2012; 1(2):85–99.

[8] Grant SF, Bradfield JP, Zhang H, Wang K, Kim CE, Annaiah K, et al. Investigation of the locus near MC4R with childhood obesity in Americans of European and African ancestry. Obesity (Silver Spring) 2009;17(7):1461–5.

[9] Grant SF, Li M, Bradfield JP, Kim CE, Annaiah K, Santa E, et al. Association analysis of the FTO gene with obesity in children of Caucasian and African ancestry reveals a common tagging SNP. PLoS One 2008;3(3):e1746.

[10] Ritchie MD, Denny JC, Crawford DC, Ramirez AH, Weiner JB, Pulley JM, et al. Robust replication of genotype-phenotype associations across multiple diseases in an electronic medical record. Am J Hum Genet 2010;86(4):560–72.

[11] Roden DM, Pulley JM, Basford MA, Bernard GR, Clayton EW, Balser JR, et al. Development of a large-scale de-identified DNA biobank to enable personalized medicine. Clin Pharmacol Ther 2008;84(3):362–9.

[12] Ventura AK, Loken E, Birch LL. Developmental trajectories of girls' BMI across childhood and adolescence. Obesity (Silver Spring) 2009;17(11):2067–74.

[13] Huang RC, de Klerk NH, Smith A, Kendall GE, Landau LI, Mori TA, et al. Lifecourse childhood adiposity trajectories associated with adolescent insulin resistance. Diabetes Care 2011;34(4):1019–25.

[14] Li C, Goran MI, Kaur H, Nollen N, Ahluwalia JS. Developmental trajectories of overweight during childhood: role of early life factors. Obesity (Silver Spring) 2007;15(3): 760–71.

[15] Liu GC, Cunningham C, Downs SM, Marrero DG, Fineberg N. A spatial analysis of obesogenic environments for children. Proc AMIA Symp 2002:459–63.

[16] Wardle J, Llewellyn C, Sanderson S, Plomin R. The FTO gene and measured food intake in children. Int J Obes. (Lond) 2009;33(1):42–45.

[17] Cecil JE, Tavendale R, Watt P, Hetherington MM, Palmer CN. An obesity-associated FTO gene variant and increased energy intake in children. N Engl J Med 2008;359(24): 2558–66.