Commentary

Can We Change the Way Our Genes Behave and Pave the Way Forward for Childhood Obesity Prevention?

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Despite a recent plateau in obesity rates among preschool children, childhood obesity continues to be a significant public health concern, particularly among Latino and African-American children who are at a higher risk for childhood obesity (Ogden et al., 2014). While genetic and environmental factors, including diet and physical activity, are known contributors to obesity risk (Brantley et al., 2005; Li et al., 2011; Witkos et al., 2008), we now believe that individual variations in genetic expression result from interactions between one's environment and genetics through epigenetic mechanisms (Herrara et al., 2011; Boyce and Kobor, 2015). The epigenome is highly dynamic and appears to change in response to age and environmental exposures including diet and physical activity (Institute of Medicine, 2015). This could provide a crucial link to understanding developmental plasticity in early childhood.

Epigenetic mechanisms affecting obesity have been identified in prepregnancy and fetal developmental periods, but little is known about the epigenome in the preschool years (Institute of Medicine, 2015). This early childhood period is typically when children experience adiposity rebound (the point at which a child's body mass index [BMI] begins to gradually increase after a period of nonlinear growth when height velocity is higher than weight velocity) and could have a significant influence on a child's later BMI trajectory (Whitaker et al., 1998). DNA methylation (the attachment of methyl groups to sites within a gene) and other epigenetic processes are thought to control gene expression by acting as an "on" or "off" switch for specific genes, and thus they can alter the epigenome in ways that are either stable or subject to environmentally influenced alterations (Fraga et al., 2011; Herrara et al., 2011). This distinction is crucial to understanding the heritability of obesity risk through epigenetic mechanisms as well as potential targets for interventions at loci where methylation patterns could be responsive to treatment.

Key to improving the practical utility of research into epigenetic mechanisms is establishing tissue specificity for relevant markers of obesity risk and identifying easily accessible tissues for sampling in children. Saliva has emerged as a peripheral tissue with promising potential for noninvasive sampling of DNA methylation patterns, with recent studies exploring its use in revealing markers of early childhood adversity and obesity-related characteristics (Gardner et al., 2015; Melas et al., 2013; Weder et al., 2014). Moreover, saliva is a functionally relevant tissue for the epigenetic study of obesity due to its role in digestive functions, including carbohydrate metabolism (Segata et al., 2012). While DNA methylation in saliva demonstrates some correlation with methylation in blood and other tissues, the tissue specificity of methylation at certain genes necessitates further studies into obesity-related methylation patterns in easily accessible tissues (Wang et al., 2012).

Recent studies demonstrate evidence that epigenetic signatures (such as the presence of a methyl group on the DNA within genes) for obesity development may persist across generations (Marco et al., 2014; Ost et al., 2014), underscoring the importance of understanding how these markers change and the potential for identifying biomarkers for obesity risk and/or treatment resistance before the development of obesity. For example, maternal adiposity and nutrition are known to be significantly associated with altered DNA methylation in umbilical cord blood (Liu et al., 2014; Sharp et al., 2015) and recent studies provide evidence that paternal obesity is also associated with altered methylation levels in obesity-related genetic loci in newborns (Soubry et al., 2013).

What we do not know, however, is if and how these epigenetic markers for obesity can be altered during early childhood, and whether they are responsive to nutrition and behavioral interventions. Recent studies in animal models have demonstrated potential mechanisms to explain the transmission of epigenetic signatures of obesity across generations (Marco et al., 2014; Ost et al., 2014); however, more research is needed into these mechanisms in humans to understand the development of epigenetic-based-risk factors for childhood obesity. Additionally, it is important to understand "whether the [epigenetic] signature is present before the development of the phenotype (i.e., obesity) and therefore could be used as a biomarker of disease risk" (Ozanne, 2015).

To move the field forward, we need to explore the use of saliva and other easily accessible tissues as sources of epigenetic material and to identify specific epigenetic markers for early onset of obesity and treatment resistance. The early childhood period of developmental plasticity is a period of epigenetic modification that has significant impacts on adult health. By identifying children at increased risk for obesity before the actual onset of obesity, we could potentially tailor interventions to the child's particular epigenetic signature and perhaps even prevent the onset of childhood obesity and associated chronic conditions later in life.

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