

Are behavioral practices for overcoming nature the hope for personalized medicine?

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There is a divergence of opinions with regard to the success of genetic research in clinical aspects of obesity. Some scientists share a “glass half full” perspective, arguing that the field has made substantial contributions identifying ~100 genetic markers associated with overall adiposity (1). Others share the “glass half empty” position, criticizing the small portion of heritability explained by association studies in BMI. Regardless of opinions, scientists have joined efforts to deliver the message that, when it comes to obesity, genes contribute to genetic predisposition rather than genetic determinism. Consequently, research initiatives have emerged to bridge genetic association findings with behavioral practices that improve health at the individual level. Efforts have been redirected to understand the interactions of genes with other genetic structures, environmental targets, or behavioral practices, all with hopes of integrating new discoveries into strategies for improving health through individualized approaches.

In this issue of the Journal, Xiang et al. (2) explored how behavioral practices can challenge genetic predisposition by evaluating the effect of the fat mass and obesity-related (*FTO*) gene as a mediator of weight-loss response to diet/lifestyle interventions. The authors conducted a meta-analysis of 14 studies that considered the *FTO* variant rs9939609 (or its proxy) and concluded that, compared with the *TT* genotype, those carrying 1 of 2 copies of the obesity-predisposing allele A tend to lose a greater amount of weight when exposed to a diet/lifestyle intervention. The investigators logically focused on the *FTO* gene, whose first-intron single nucleotide polymorphisms have been one of the most studied common variants influencing overall body fatness. *FTO* has been associated with greater food intake and increased hunger/lower satiety (3), and data suggest that regulatory elements of the genes interact with other gene clusters (4) in processes related to energy metabolism. Undoubtedly, the study findings show a step in the direction of personalized medicine. Contrary to other recently published comparable meta-analyses, the study brings an element of awakening to the possibilities of implementing behavioral preventive strategies in the midst of genetic predisposition to improve individual health outcomes, which is the ultimate goal of personalized medicine.

The authors indicated in their discussion that it is probable that the clinical implications of the reported findings are not relevant. Careful reading of their article invokes a realization that the im-

plications of the study cannot be underestimated for at least 3 main reasons. First, it confirms the importance of broadening the scope of genetics obesity research to include the action and interaction of behavioral variables with documented genes, and probably with different combinations of gene variants. Second, it contributes to disseminating a message that, when it comes to genetics of obesity, and probably to complex diseases, a conforming deterministic fatalism is unviable or not a justifiable reason to be obese. Third, it exemplifies that, regardless of how much we believe that “genetics loads the gun, and environment pulls the trigger,” the individual has the power to set the shot target. And at the end of the day, the gift of individual autonomy may somehow be regulating our own genes; the same genes we cannot change but whose expression it appears we can alter.

As with any scientific investigation, the findings from Xiang et al. bring concerns about the generalizability of the results, particularly when taking into account the heterogeneity of the studies included in the analyses. Questions with regard to the most effective intervention method and duration, as well as the potential population differences, prevail. It is probable that within the scientific community, the findings of this study would represent the half-full part of the glass for those enthusiastic about the magnitude of environmental effects in potential gene regulation and expression and the half-empty part of the glass for those with hopes of an obesity gene whose expression should be silenced through, for example, pharmacotherapies. Nonetheless, there is public health relevance in Xiang et al.’s findings, particularly when delivering the message that a genotype that appears to predispose individuals to obesity also could have a beneficial effect on weight loss when individuals are exposed to diet/lifestyle interventions. This is the type of message that should resonate in the public health arena because it might help in overcoming the misconception that obesity-associated genetic markers justify genetic determinism.

There are no doubts that the results and discussion of the study provide insights into the role of *FTO* in obesity and create a platform for future hypotheses in search of *FTO* mechanisms of action. However, perhaps the most remarkable contribution from this study is the realization that behavioral practices conducive to improved health have the ability to counteract predisposing

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genetic effects that, for a portion of the population, could have been thought of as deterministic fatalism.

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