Scientists outline key challenges and promising avenues in obesity genetics

July 31 2024

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Research on the genetics of obesity dates to the early 1920s, with many of the initial findings indicating the complexity and multifaceted nature of obesity perfectly resonating with more modern discoveries.

Researchers at Pennington Biomedical have collected nearly a century's worth of considerations and advancements to frame their perspectives on modern research into the genetics of obesity.

The paper, "Considerations on efforts needed to improve our understanding of the genetics of obesity," was published in the *International Journal of Obesity* as part of a special issue commemorating 100 years of obesity research. It highlights topic areas in obesity genetics that deserve attention due to their potential for enhancing the quality and power of future studies on the subject.

In addition to the many signature advances in the field so far, Drs. Sujoy Ghosh and Claude Bouchard of Pennington Biomedical in Baton Rouge also outline a number of current challenges and obstacles that can hinder research and limit discoveries into the genetics of obesity.

"The history of genetic obesity research dates back to the early 20th century, but the subsequent decades, powered by extraordinary technological advances and vastly improved computing capabilities, have brought to light many new discoveries, resulting in a much better understanding of the genetic underpinnings of obesity," said Dr. Ghosh, Professor of Functional Genomics.

"Acknowledging this comprehensive history provides us with a backdrop as we enter a new and exciting era of obesity research, straddling the line between opportunity and obstacle."

The publication explores the evolving landscape of genetics research into obesity, emphasizing both new discoveries and challenges. It begins by revisiting the historical context of genetic studies in obesity, highlighting the complexity and multifactorial nature of body weight regulation.

It then underscores some limitations of using BMI as the sole indicator

of obesity in the genetic studies, and advocates for more precise phenotyping methods targeting more relevant and refined phenotypes related to adiposity.

The paper further explores how an individual's genes can result in obesity or thinness, suggesting that both traits are hereditary. Other complex factors of obesity are examined, including the interaction between genes and the environment, how weight control varies from person to person, and how certain modifications of gene function can affect a person's weight.

The paper also covers recent examinations of obesity, including the role of acquired mutations, the potential for large-scale discoveries through bioinformatics, the link between biological and genetic findings, and the successes of genetic medicine in special types of genetic obesity.

"For the researchers who are pursuing solutions from all corners, the purpose of this paper was to emphasize the wide range of variables, considerations and opportunities as they continue their research," said Dr. Claude Bouchard, Emeritus Professor of Human Genomics.

The paper's comprehensive evaluation of the rich history and future challenges to investigations into the genetics of obesity taps into the bedrock of Pennington Biomedical's mission to discover the triggers of obesity and diet-related diseases and improve health for all people. Obesity genetics is currently positioned at an exciting inflection point.

While technological advances and the feasibility of big data analytics portend immense promise for advances in genetic studies, the complexity of genetic interactions, small variant effect sizes and the need for precision in phenotyping poses significant hurdles. Such hurdles further emphasize the paper's recommendation to embrace an integrative approach that incorporates diverse scientific fields.

"This publication advances the broader understanding of the genetic basis of obesity and the link between genes and the environment, and I'm proud that our researchers are planting such a guidepost at this fascinating period in obesity research," said Pennington Biomedical Executive Director Dr. John Kirwan.

"Drs. Ghosh and Bouchard have clearly and comprehensively highlighted the signature advances of obesity genetics while also drawing our attention to underserved areas that will be critical for future success in this very exciting field."

More information: Sujoy Ghosh et al, Considerations on efforts needed to improve our understanding of the genetics of obesity, *International Journal of Obesity* (2024). DOI: 10.1038/s41366-024-01528-0

Provided by Pennington Biomedical Research Center