**Implications of LEP and LEPR Within the Human Body Pertaining to Obesity**

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**Key Words:**

Leptin, leptin receptor, and obesity.

**Abstract:**

The critical examination of the following study by Fairbrother aims to review the current information on genes and their expression regarding their involvement with obesity. With a specific focus on the genes LEP and LEPR, an underlying basis of contextualization, interpretation, and totality are implemented to further the comprehension on just how essential these genes are as a causative agent of glucose levels and metabolism regulation, thus impacting body weight. Variants in genes are present and their involvement in signaling pathways present that monogenic variants are contributive in obesity. Identifying such genes that are responsible for severe obesity and the distinction between types of obesity is now conflated as rare and common obesity share similarities of variants across the general population. This is not unforeseen as leptin is a complex protein; such technological advancements in genotype and their sequencing allows them to be associated with a character for all variants.

**Introduction:**

 Obesity has seemed to situate itself in a customary notion in modern time becoming more pervasive. Obesity is concomitant with an ample number of complications such as cardiovascular disease, type 2 diabetes, and cancer. Although its underlying causes have been difficult to elucidate, it is evident that obesity and one of its causative agents is influenced by such genetic components. The human monolog of the gene is characterized by a capitalized O. Encoded by the LEP gene and through its receptor LEPR, both genes are instrumental in the transduction of leptin messages via signaling pathways. As a complex phenotype (derived from more than one gene) in which behavioral, environmental, and genetic features all play a role, leptin is a 167 amino acid that is an enzyme; it suppresses appetite and galvanizes metabolism. It is essentially a peptide that is released by fat cells. Other functions and capabilities of leptin include its role of acting as a hormone requiring a specific cell receptor for binding before they cause the effect. Leptin is a cascade of events entailing the process of leptin stimulating the hypothalamus, the hypothalamus embracing the pituitary gland, the pituitary gland invigorating the thyroid gland to release thyroxine, thus raising the metabolism rate. However, there are several factors which inhibit this enzyme from operating optimally and correctly. Induction of a cascade to generate the thyroid gland affects NPY suppression of appetite (Marley, 2018); the suppression of neuropeptide y (NPY) – an appetite stimulant – results in the loss of appetite. Moreover, leptin blocks transcription of mRNA for NPY, resulting in appetite decreasing. In addition, leptin has the possibility of making the intramitochondrial membrane pregnable or leaky to protons. By stimulating the release of uncoupling proteins, the membrane is therefore weakened. Furthermore, this leads to the rapid release of electrons from the body as thermogenesis; the lack of ATP increases the demand for more electrons from carbohydrates and fats, causing more carbs and fats to enter the respiratory pathway. Scotee states that leptin also conditions inflammation, immune responses, infection, and bone metabolism; all which are physiological features (Scotece et al., 2014). Correspondently, Procaccini mentions the LEPR gene being expressed across somatic cells associated with the innate and adaptive immune system, eliciting the gene leptin as an imperative bridge of immune systems and neuroendocrine (Procaccini et al., 2017). The scientific report by Fairbrother that I intend on analyzing encompasses the focus of obesity as an idiosyncratic disease with a specific genetic cause rather than common polygenic obesity.

 Recent studies from as early as this year by Ali and company (Ali et al., 2019) address the role of fat mass, leptin receptor, and obesity-concomitant polymorphisms for the impressionability of obesity among various individuals; by using the methodology of PCR genomic DNA was genotyped to illustrate the relationship of the gene and obesity.

**Discussion:**

 Upon reviewing, Fairbrother establishes the connection between severe obesity and postulates theory of a specific disease in conjunction with a particular gene(s). LEP and LEPR are illuminated on as variants that give rise to obesity and monogenic obesity within the universal population. In a study by Adams, selected genes with variants showed to contribute to acute obesity (Adams et al., 1993). Tests with mouse at the helm as subjects implicated leptin and its receptor in monogenic obesity. Fairbrother and company also stress the hormone cascade in which leptin acts and influences the transcription factors in relation to homeostatic pathways, including sugar and calorie levels. In addition to the behavioral portioning regarding food intake, leptin induces its effects of another receptor, LepRb. LepRb is specifically expressed in the region of the brain responsible for energy expenditure and food regulation. The complexity of leptin is extrapolated in this report. Fairbrother and all are not linear in approaching the signaling process. While the rudimentary disposition focuses on leptin pertaining to obesity or individuals with a significantly above average weight, individuals with a normal weight or body mass are not just used as the control experiment for comparative measures. Normal body weight people are mentioned with fluctuating levels of leptin; reported is decreased levels of leptin lead to a direct relationship of decreased levels of sugar and energy use. This highlights the functionality of leptin and leptin receptors as a main component in metabolism and glycaemic control.

Shifting its focus back on LEP and LEPR in obese individuals, Fairbrother involves pathways mechanism factors that have multitude levels of influences such as inflammatory responses and feedback inhibitions. Leptin levels are increased in obese humans and animal models, but the imperative feedback loop that generates reduction in the behavior of food and great energy expenditure fails. Interestingly, Fairbrother comes to the revelation that an obese final point is reached despite increased leptin to leptin receptor gesturing, and that increased levels of leptin signaling eventually creates leptin resistance limiting the full scope of the amplitude of the process. This is mentioned by Al-Suhaimi and Shehzad as they report how leptin resistance caused by impairment of leptin signaling and transportation is thought to be the central risk factor for the obesity pathogenesis (Al-Suhaimi and Shehzad, 2013). Allelic variation and mutation are even discussed examining the genetic impact on identification of positive associations of leptin in association with body maintenance.

Furthermore, such genes, like BMI and MC4R, and their expression have been found to be in people who are similar in phenotype (obese). This study attests to the newly found comprehension and relatedness between obesity and genetics and implicates for the future variants within the genome that can be worked upon in a nuanced fashion broaching the issues obesity proposes on the population.

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