Editorial

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Chemerin: The Regulation of Glucose Homeostasis and the Development of Obesity

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ABSTRACT

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Editorial

Adipokines have been connected to the metabolic syndrome since the discovery of leptin because of its influence on biological functions such as blood pressure, homeostasis, adipogenesis, and glucose metabolism. Several researchers have indicated that the adipokine chemerin is implicated in adipogenesis, glucose homeostasis, and the prevention of obesity in adipose tissue, and that it is implicated in the control of glucose homeostasis. Chemerin's function, particularly its association to obesity and insulin resistance, is currently the subject of a lot of research. Chemerin gene expression and circulation levels have repeatedly been linked to increased BMI and obesity biomarkers in people [1]. Obese mice on a diet reported increased plasma chemerin concentrations, which were reduced by fasting. This effect is unaffected by the mouse strain (FVB or C57BL/6) utilized [2]. This disparity could be attributed to the fact that certain mouse strains are more vulnerable to diet-induced obesity than others. Genetically obese (ob/ob) mice showed greater plasma chemerin levels, but leptin receptor-deficient mice (db/db mice) had reduced serum chemerin levels and enhanced insulin signaling [3]. Chemerin intraperitoneal injections resulted in a startling reduction in body weight in rats [4]. This appears to refute the idea that increased plasma chemerin concentrations cause obesity. Some research, which used chemerin injections directly into the brain, found a heterogeneous effect to body weight and food intake. Chemerin intracerebroventricular bolus injections reduced body weight, however continuous chemerin infusions raised it [5]. As a result, based on the period studied, chemerin may have varied biological effects. Given that rising chemerin values are generally associated with modifications in body composition, a proinflammatory effect over time may correlate it to insulin resistance in obesity. Another information relating chemerin to glucose homeostasis was found in studies on animals without the GPR1 receptor.

Gpr1-knockout animals on a high-fat diet displayed elevated glucose intolerance compared to wild-type mice, but no differences in body weight, body composition, or energy expenditure [6]. Morbid obesity is a condition known as adiposity. Adiposity indices that take into account waist circumference instead of body weight reveal the quantity of WAT, a reliable indicator of metabolic dysfunction in humans [7]. White fat tissue produces a variety of adipokines that affect inflammation, adipocyte metabolism, and adipose tissue homeostasis. Chemerin is just one of these adipokines. High levels of Chemerin and Cmklr1 expression are found in WAT, but only at very low levels in BAT [8]. The fact that BAT is linked to thermogenesis would imply that chemerin affects weight via regulating adipogenesis rather than thermogenesis. But new research has revealed that CMKLR1 deletion decreases the expression of genes linked to thermogenesis in WAT and BAT [9]. BAT has been discovered as a possible target for the treatment of obesity since it has the ability to produce heat instead of ATP, which results in weight reduction. A crucial component in the control of

BAT thermogenesis is retinoic acid [10]. The intriguing prospect that chemerin could encourage BAT activity and/or browning of WAT is raised by the fact that chemerin is downstream of retinoic acid signaling. A metabolic condition known as type 2 diabetes mellitus (T2DM) is characterized by insulin resistance and high blood sugar levels (hyperglycaemia). Obesity-related increases in serum chemerin are strongly associated with human T2DM development [4]. Despite widespread agreement that chemerin controls glucose homeostasis, its function in controlling glucose tolerance is still unknown as a result of inconsistent findings from numerous in vivo and in vitro research [11].

Here, we summarize the role of chemerin in controlling insulin secretion and sensitivity because the insulin signaling pathway is the key to maintaining glucose homeostasis by boosting the absorption of glucose into fat and muscle and decreasing the synthesis of glucose in the liver [12]. The correct control of glucose tolerance depends on both insulin release from the pancreas and insulin-stimulated glucose absorption in peripheral tissues. The fact that pancreatic beta cells also make chemerin and its receptor, CMKLR1, suggests that both molecules may play a role in controlling insulin secretion [5]. Furthermore, chemerin and CMKLR1 deletion animals produce less insulin in response to glucose, but gain-of-function studies using chemerin transgenic mice revealed an increase in insulin production during glucose tolerance testing [5,13]. In pancreatic cells, chemerin serves as a glucose sensor and a transporter; in mice, chemerin elimination reduces the transcription of these genes. In turn, this promotes the hormone insulin's synthesis [14]. Therefore, it is suggested that low GLUT2 expression in chemerin-deficient cells is the cause of the insufficient glucose-stimulated insulin production [14]. Because sustained overexpression of chemerin in low-density lipoprotein receptor (LDLR)-knockout rats did not impact the amount of insulin circulating, there is a probability that GLUT2 and LDLR interact in beta cells [15]. Similar to CMKLR1, the second chemerin receptor, GPR1, also binds chemerin [16]. Under conditions of a high-fat diet, the GPR1-deficient mice exhibit not only a little reduction in glucose-stimulated insulin release but also a much lower level of fasting blood insulin [17].

The specific mechanisms are still unclear, despite prior research offering some insight into the function of the chemerin-CMKLR1 or chemerin-GPR1 axis in coordinating glucose-induced insulin production [5]. Additionally, chemerin has been shown to control glucose absorption and insulin sensitivity [18]. The fact that 3T3-L1 adipocyte in vitro investigations have shown that chemerin has both stimulatory and inhibitory effects on glucose uptake is contradictory [19]. The disparity could be brought on by varying doses, chemerin treatment periods, and culture conditions. Chemerin injection decreases the insulin-stimulated glucose uptake and enhances the phosphorylation of insulin receptor substrate 1 in skeletal muscle cells [20]. Moreover, all of the mutant mice for Chemerin, CMKLR1, and GPR1 exhibit glucose intolerance. Chemerin-knockout mice have altered insulin sensitivity in the liver and adipose tissue, which leads to higher blood sugar levels, decreased glucose uptake by fat, and increased hepatic glucose synthesis [21]. Reduced glucose absorption by adipose tissue and skeletal muscle but not liver occurs in mice with CMKLR1 genetic deletion [22]. Mice fed a high-fat diet experience worsened glucose intolerance, elevated insulin levels, and enhanced insulin resistance [23]. Heterozygous and homozygous Gpr1-knockout mice fed a high-fat diet consistently experience severe glucose intolerance but show lower levels of glucose-stimulated insulin [5,24]. Overall, these mutant mice had higher blood glucose levels. However, greater study of the underlying processes is required. Conversely to these results, the lack of CMKLR1 in mice had no impact on body weight, food intake, blood lipid levels, or insulin resistance [5,25]. Thus, the role of chemerin signalling in the regulation of glucose homeostasis and in the development of obesity needs to be validated.

Disclosure Statement

The authors declare that there are no conflicts of interest.

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