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Editorial

Secreted Proteins and their Role in Type-2 Diabetes

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Editorial

Secreted proteins based on its origin can be of exocrine or endocrine in nature and play a key role in maintaining physiological environment within the body by inter-and intra-organ communications. These proteins are secreted in response to a stimulus and their levels changes during a disease state. Now these altered levels of secreted protein may provide regulatory effects on its target tissue in an autocrine, paracrine or endocrine dependent manner.

The Tumor Necrosis Factor (TNF) a cytokine superfamily is one of the major classes of soluble secreted proteins and play important role in variety of cellular functions like regulating inflammation, cell differentiation, apoptosis, innate immunity, synapse homeostasis, and energy metabolism [1]. Another important cytokine adiponectin which is called as adipokine due to its exclusive secretion from adipose tissue also plays vital role in glucose and lipid metabolism and has insulin-sensitizing effects in obesity [2]. Adiponectin is a first identified member of the Complement-C1q TNF-Related Proteins (CTRP) superfamily and these proteins have been shown to have anti-inflammatory and anti-diabetic effects in mice [2]. In addition to adiponectin, other 15 CTRP family members have been reported [3] and these CTRP family members have been implicated in the pathophysiology of obesity and type 2 diabetes [4,5]

The members of CTRP family are characterized by the presence of a C-terminal globular domain with sequence homology to the immune complement protein C1q [3] and show remarkable similarity among structure and biochemical properties with adiponectin. The metabolic function and regulation of adiponectin has been extensively studied in the past decade [6,7] however, not much is known about the regulation and function of CTRPs.

CTRP1 is primarily expressed in adipose tissue and studies have suggested that CTRP1 may have beneficiary effects during metabolic stress and is a novel regulator of skeletal muscle fat metabolism [4,8]. Another member CTRP3 is also present in adipocytes but other tissue like brain, liver also have significant expression levels of CTRP3[4,9,10]. It has been reported that CTRP3 might play an important role in metabolic stress induced by obesity and type 2 diabetes [11,12]. On the other hand CTRP5 is known to express in eye in higher levels and also in adipocytes where it acts mainly in autocrine manner [13]. However its role in metabolism is ambiguous. Exclusively, CTRP9 is the closest member of the CTRP family to adiponectin having more than 50% structural similarity with very high expression levels in adipocytes [5]. Similar to adiponectin CTRP9 has beneficiary effects in obesity, type 2 diabetes and cardiovascular complications [15,16]. CTRP11 is known to express in white and brown adipose tissue and may have regulatory effects in adipogenesis [17]. Unlike other CTRPs, CTRP12 may exist in two isoforms differing in structure and signaling pathway [18]. Reports have suggested that CTRP12 ameliorates metabolic complications through both insulin-dependent and insulin-independent manner [18]. CTRP13 expresses adipocytes and also in hypothalamus and studies have suggested that CTRP13 may play an important role in regulating food intake [19]. CTRP 15 is also called myokine or myonectin due to its very high expression levels in skeletal muscles and studies have suggested that muscles secretedCTRP15 play a role in response to nutrients levels in circulation [20].

Although identification of CTRP family is not new and a good progress has been made learning the role and functions of CTRPs in metabolic stress, a lot of questions still need to be answered. Identifying definitive receptors for these CTRPs is one of the significant questions yet to be addressed as developing tools to these CTRP receptors could be of therapeutic significance and can help in the treatment of obesity and type 2 diabetes.

References

1. Ressl S, Vu BK, Vivona S, Martinelli DC, Sudhof TC, et al. (2015) Structures of C1q-like proteins reveal unique features among the C1q/TNF superfamily. Structure 23: 688-699.

2. Díez JJ, Iglesias P (2003)The role of the novel adipocyte-derived hormone adiponectin in human disease. Eur JEndocrinol. 148: 293-300.

3. Kishore U, Gaboriaud C, Waters P, Shrive AK, Greenhough TJ, et al. (2004) C1q and tumor necrosis factor superfamily: modularity and versatility. Trends Immunol. 25: 551-561.

4. Wong GW, Krawczyk SA, Kitidis-Mitrokostas C, Revett T, Gimeno R, et al. (2008)Molecular, biochemical and functional characterizations of C1q/TNF family members: adipose-tissue-selective expression patterns, regulation by PPAR-gamma agonist, cysteine-mediated oligomerizations, combinatorial associations and metabolic functions. Biochem J 416: 161-177.

5. Wong GW, Krawczyk SA, Kitidis-Mitrokostas C, Ge G, Spooner E, et al. (2009) Identification and characterization of CTRP9, a novel secreted glycoprotein, from adipose tissue that reduces serum glucose in mice and forms heterotrimers with adiponectin. FASEB J 23: 241-258.

6. Kadowaki T, Yamauchi T, Kubota N, Hara K, Ueki K, et al. (2006) Adiponectin and adiponectin receptors in insulin resistance, diabetes, and the metabolic syndrome. J Clin Invest116:1784-1792.

7. Turer AT, Scherer PE (2012) Adiponectin: mechanistic insights and clinical implications. Diabetologia 55: 2319-2326.

8. Peterson JM, Aja S, Wei Z, Wong GW (2012) CTRP1 protein enhances fatty acid oxidation via AMP-activated protein kinase (AMPK) activation and acetyl-CoA carboxylase (ACC) inhibition. J BiolChem 287:1576-1587.

9. Schäffler A, Ehling A, Neumann E, Herfarth H, Paul G, et al. (2003) Genomic organization, promoter, amino acid sequence, chromosomal localization, and expression of the human gene for CORS-26 (collagenous repeat-containing sequence of 26-kDa protein). BiochimBiophys Acta1630:123-129.

10. Maeda T, Jikko A, Abe M, Yokohama-Tamaki T, Akiyama H, et al. (2006)Cartducin, a paralog of Acrp30/adiponectin, is induced during chondrogenic differentiation and promotes proliferation of chondrogenic precursors and chondrocytes. J Cell Physiol 206: 537-544.

11. Peterson JM, Wei Z, Wong GW (2010) C1q/TNF-related protein-3 (CTRP3), a novel adipokine that regulates hepatic glucose output. J BiolChem285: 39691-36701.

12. Peterson JM, Seldin MM, Wei Z, Aja S, Wong GW (2013) CTRP3 attenuates diet-induced hepatic steatosis by regulating triglyceride metabolism. Am J PhysiolGastrointest Liver Physiol 305: G214-G224.

13. Schmid A, Kopp A, Aslanidis C, Wabitsch M, Müller M, et al. (2013) Regulation and function of C1Q/TNF-related protein-5 (CTRP-5) in the context of adipocyte biology. ExpClinEndocrinol Diabetes 121:310-317.

14. Yamauchi T, Kamon J, Minokoshi Y, Ito Y, Waki H, et al. (2002) Adiponectin stimulates glucose utilization and fatty-acid oxidation by activating AMP-activated protein kinase. Nat Med 8:1288-1295.

15. Uemura Y, Shibata R, Ohashi K, Enomoto T, Kambara T, et al. (2013) Adipose-derived factor CTRP9 attenuates vascular smooth muscle cell proliferation and neointimal formation. FASEB J27:25-33.

16. Wei Z, Seldin MM, Natarajan N, Djemal DC, Peterson JM, et al. (2013) C1q/tumor necrosis factor-related protein 11 (CTRP11), a novel adipose stroma-derived regulator of adipogenesis. J BiolChem 288:10214-102129.

17. Wei Z, Lei X, Seldin MM, Wong GW (2012) Endopeptidase cleavage generates a functionally distinct isoform of C1q/tumor necrosis factor-related protein-12 (CTRP12) with an altered oligomeric state and signaling specificity. J BiolChem 287: 35804-35814.

18. Byerly MS, Swanson R, Wei Z, Seldin MM, McCulloh PS, et al. (2013) A central role for C1q/TNF-related protein 13 (CTRP13) in modulating food intake and body weight. PLoS One 8: e62862.

19. Seldin MM, Peterson JM, Byerly MS, Wei Z, Wong GW, et al. (2012) Myonectin(CTRP15), a novel myokine that links skeletal muscle to systemic lipid homeostasis. J BiolChem 287: 11968-11980.