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Mini Review

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Leptin: an immunomodulatory molecule of animals

Abstract

Leptin, an adipocyte-derived cytokine (adipokine), has plethora of physiological roles in the body, particularly in onset of puberty, reproduction and immune function of an animal. Leptin binds with leptin receptor (*LEPR*) and activates different intracellular signaling pathways to activate downstream gene expression process to execute its functions. The present mini-review focuses on our current understanding about the immunomodulatory and immunodiagnostic potential of leptin in domestic mammalian species. This warrants future research efforts to explore its immunological role that can be exploited for augmenting immunological protection of livestock.

Keywords: animal leptin, cytokine, immunomodulation, innate immunity

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Introduction

Leptin, a non-glycosylated peptide cytokine, is a product of the *obese* (*ob*) or *leptin (LEP)* gene. Leptin which is mainly produced by white adipose tissue (WAT)[1] has pleiotropic effects on a variety of metabolic pathways. Circulatory leptin concentration is directly proportional to the total body fat mass.[2] The molecular weight of leptin is within the range of 16-18kDa.[3] The molecular mass of affinity–purified recombinant human leptin protein was estimated to be approximately 16kDa by SDS-PAGE, whereas the molecular mass of endogenous human leptin was reported as 16,026±9 Da by MALDI-TOF analysis.[4] In our laboratory, molecular mass of affinity–purified native goat (*Capra hircus*), mithun (*Bos frontalis*) and rohu fish (*Labeo rohita*) was ascertained as 15,948.72 Da, 17,214.26 Da and 16,283.38 Da, respectively by MALDI-TOF mass spectrometric analysis.[5–7]

Role of leptin in inflammation and immunological responses of animals against infection and stress is well established.[8] The present mini-review reveals our understanding about the immunomodulatory and immunodiagnostic potential of leptin in domestic mammalian species.

Pro-inflammatory actions of leptin in the immune system act as a potent enhancer of immune functions.[9] Activation of the immune response is a complex mechanism that might be involved in both initiation and/or perpetuation of inflammatory conditions. Certain adipokines can enhance the aforementioned inflammation and, in that context, the modulation of innate immunity by leptin has been well-established.

Leptin binds with leptin receptor (Ob-R or *LEPR*), a single transmembrane-spanning protein and member of the class I cytokine receptor family to exert its function. The primary site of action is the central nervous system, especially the hypothalamus. *LEPR* has several isoforms (Ob-Ra to Ob-Rf) which are produced by alternative mRNA splicing.[10] The isoforms are classified as long, short, or soluble based on their structure. The long form controls cellular activities, while the short form is responsible for its transport through the cell membrane and blood-brain barrier, and the soluble form aids in its circulatory transport.[11] Depending on the target cell type, leptin stimulates numerous signaling pathways after binding to its receptor, including Janus kinase-signal transducer and activator of transcription (JAK-STAT), 5' adenosine monophosphate-activated protein kinase (AMPK), mammalian target of rapamycin (mTOR), phosphoinositide 3-kinase (PI3K), and mitogen-activated protein kinase (MAPK) signaling pathways.[12,13]

Leptin can act on different immune cells, specifically by promoting activation of monocytes or macrophages and natural killer (NK) cells, inducing chemotaxis of neutrophils and degranulation of basophils, among other functions.[14] Various roles played by leptin to modulate innate and adaptive immunity have been depicted in Figure 1. In our laboratory serodiagnostic potentiality of goat, fish and mithun leptin was explored.[5–7]

Recurrent gut parasite infections induce under performance in ruminants due to nutritional conflict between the immune system and growth, and anorexia is a frequent symptom of nematode infection.[15] The influence of leptin molecules on T-cells and pro-inflammatory cytokines IL-6 and TNF-α help well-fed animals to withstand or eradicate illness.[16] Amarante et al.[17] reported that faster-growing Suffolk lambs are more vulnerable than slower-growing breeds and that their anorexia is more severe and lasts longer. A non-significant rise in leptin was reported in restricted Merinos infected with *Trichostrongylus colubriformis* and *Teladorsagia circumcinctav*.[18] Zaralis et al.[19] infected Scottish Blackface and Suffolk × Greyface lambs with *T. circumcincta* for 12 weeks and observed that infected lambs had greater leptin levels than non-infected lambs with equal feed consumption.

Although extensive studies have been done on leptin of human and laboratory animals, information in small ruminants (e.g. sheep, goats etc.) is scarce. The 2D-gel electrophoresis analysis revealed that goat leptin is having isoelectric point (P.I.) of 5.8. In our laboratory, serodiagnostic potentiality of goat besides fish and mithun leptin was explored.[5–7]. Dip-stick ELISA based tool (s) might be prepared to detect goat leptin from unknown (test) samples.[5]

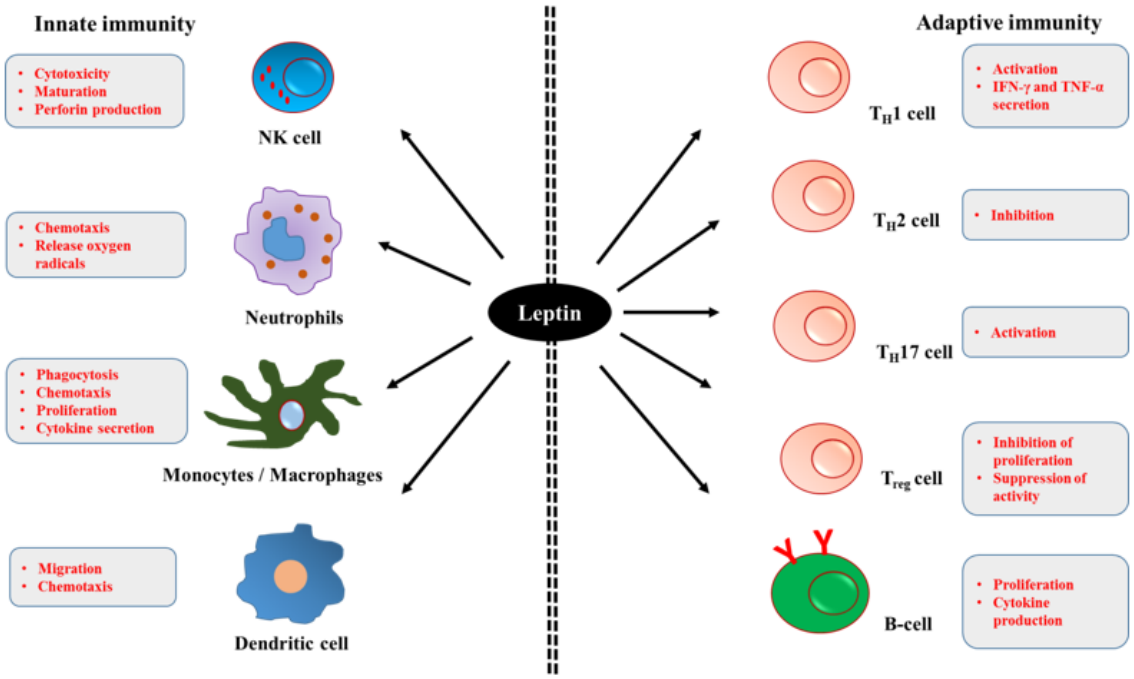

Figure 1 Effects of leptin on innate and adaptive immunity.

Since the discovery of leptin, research have shown that adipose tissue plays a critical role in metabolic and immune function regulation and undoubtedly, there is still plenty to reveal, especially in the context of livestock immunobiology. Future research efforts are much-needed to delineate the leptin machinery in different immune cell types so that they can be manipulated effectively for augmenting immunological protection in livestock.

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Conflicts of interest

Author declares there is no conflict of interest in publishing the article.

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