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Short Communation

Metabolic Syndrome and Inflammasomes: A Framework of Situation

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Innate immune response and metabolic pathways have evolved to be essential for survival in all species. As a result, immunological responses are intricately linked to the regulation of whole-body and cellular metabolism. Therefore, introducing novel elements to this sensitive evolutionarily conserved physiological link can have detrimental consequences for species due to erroneous immune responses. The prevalence and incidence of metabolic illnesses linked to obesity have risen considerably in recent decades around the world. Obesity, as a newly acquired human trait, has revealed the crucial role of innate immune pathways in a variety of metabolic pathophysiological processes [1]. Type 2 diabetes (T2D), obesity, gout, and cardiovascular disease have all become substantially more widespread in recent years. According to new studies, persistent inflammation plays a key role in the etiology of metabolic disorders. Oxidative stress is defined by high levels of circulating inflammatory mediators such cytokines and chemokines, which have recently been related to the start and progression of metabolic diseases [2]. The inflammasome complex, which converts dormant pro-IL-1 and IL-18 into mature versions, has been discovered to govern chronic inflammation and alter physiological metabolic pathway. Identifying the mechanism(s) of inflammasome activation could lead to the development of particular therapy approaches, hence this field of study has promise [3].

The formation of key innate immune pathways, such as the Toll-like receptors and c-type lectin receptors, which are largely membrane-associated and respond to pathogen-associated substances, has resulted from the finding of similar structure conserved gene families [4]. The identification of NLRs (nucleotide-binding domain, leucine-rich repetition including, commonly described as nucleotide-oligomerization domain-like receptors), a huge gene family generating intracellular proteins that reflect changes in cellular homeostasis and/or microbial infection, is a major step advance. NLRs have a conserved nucleotide binding domain (NBD) preceded by a leucine rich region, as indicated by their name (LRR). These genes are located in both plants and animals, however unlike TLRs found in Drosophilia, NLRs are not found in lower species such as fruit flies and nematodes, and hence represent a distinct family of transcription factors for higher creatures [5]. Plants, on the other hand, have a lot of NLRs, which are classified as disease resistance (R) genes, which are a powerful weapon in the fight against pathogens [6]. Vegetation NLRs are located in both the cytoplasm and the nucleus and get an intracellular activity. Acidic transactivation, pyrin, CARD (caspase activation and recruitment domain), and baculoviral inhibitory repeat (BIR)-like domain are the four subgroups of the NLR family in mammals. In some circumstances, additional domains might be found in the C-terminus [7].

The NLR family consists of 22 members with a wide range of functional tasks. Multiple have been observed to play roles in cell death processes such as pyroptosis, apoptosis, necrosis, and autophagy, and two have been found to intervene as master transcriptional regulators of class I and II Major Histocompatibility Complex (MHC) gene transcription. Many of these are positively or negatively regulators of key transcription factors such as NFB and MAPK [8]. Some NLRs have multiple functions in the cell, and subsequent research is anticipated to broaden their functional repertoire [9].

The NLR sub-family that triggers the inflammasome and activates the cysteine protease CASPASE-1, which then cleaves pro-IL-1 and pro-IL-18 to their mature forms, is the most thoroughly investigated, and this issue has been intensively studied [10-12]. Despite the fact that there are ten NLRs which could stimulate the inflammasome in response to a variety of agonists (NLRP1, NLRP2, NLRP3, NLRP6,

NLRP7, NLRP12, NOD2, NLRC4/IPAF, NAIP2, NAIP5), the protein NLRP3, which is a pyrin-containing NLR, has been the most increasingly investigated due to the wide range of adequate incentives in a variety of disease [13].

Gain-of-function mutations in NLRP3 were first identified as the cause of a kind of inherited recurrent sickness marked by arthritis, fever, skin rashes, and high serum levels. IL-1β/IL-18 [14]. These SNPs are seen in a series of auto-inflammatory disorders described as FCAS (Familial Cold Auto inflammatory Syndrome) or CAPS (Cryopyrin-associated Periodic Syndrome), which can be managed efficiently with Anakinra/Kineret, an IL-1 receptor antagonist (IL-1Ra) [15]. Clinical evidence between NLRP3 and IL-1 was found in these genetic analysis of individuals. The inflammasome was discovered after in vitro studies of NLRP1, and later NLRP3, using cell free lysates focused for NLRP1, the adaptor ASC (apoptosis-associated speck-like protein comprising CARD), and pro-CASPASE-1/5 [16].

The inflammasome complex is the outcome of the proteolytic cleavage of CASPASE-1 after these components were assembled. The adaptor ASC, which has both pyrin and CARD domains, interacts biochemically with NLRP1's pyrin domain and pro-caspases' CARD domain to form the inflammasome [17]. CASPASE-1 is auto-catalytically cleaved after complex assembly, and it then converts pro-IL-1 and pro-IL-18 to their review of previous studies [18]. In terms of pathogen- or microbial-associated molecular patterns (PAMPs or MAMPs), as well as products from injured tissues, Nlrp3/ mice studies show that this gene is essential for the secretion of IL-1 and IL-18 by myeloid macrophage cell types in terms of a variety of pathogen- or microbial-associated molecular patterns (PAMPs or MAMPs), as well as products from injured tissues, referred to as damage-associated molecular patterns (DAMPs) [19]. Several metabolic processes linked to metabolic disorders are hypothesized to act as DAMPs, causing sterile inflammation that is unrelated to microbial pathogens. These haven't been researched in relation to metabolic illnesses, or they haven't been found to have a role in them. Despite evidence that NLRP6 potentially play a role in non-alcoholic fatty liver disease models, research on metabolic illnesses and its links to the inflammasome has mostly concentrated on the NLRP3 protein, as in other fields [20].

Conclusion

In conclusion, the increased prevalence of metabolic illnesses necessitates the development of novel therapeutic and preventative treatments, taking into account that each involves nutritional, genetic, and immunological components. Changes in diet and exercise, as well as innovative medicines to alleviate the accompanying immunopathology, will almost certainly be required for effective treatment regimens. The NLRP3 inflammasome and its derivatives, IL-1 and IL-18, are good targets for drug development because they are generated in response to a wide range of DAMPs linked to metabolic illness.

Disclosure Statement

The author declares that there are no conflicts of interest.

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