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Editorial

Role of Inflammasomes in Inflammatory and Infectious Diseases

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Inflammation is an innate immune response protecting the body from invading pathogens and intracellular danger signals. However, chronic inflammation, that is, a repeated and prolonged inflammatory response, involves a progressive change in the type of cells present at the site of inflammation and has been regarded as a major risk factor for a variety of human diseases, including inflammatory, autoimmune, metabolic, and cardiovascular diseases and even cancer.

The inflammatory response consists of two main steps, "priming" and "triggering." Priming is the preparatory step of inflammatory response by increasing the expression of inflammatory genes and the production of inflammatory mediators, while triggering is the activating step of inflammatory response by inducing inflammasome activation and inflammatory cell death, called pyroptosis.

In the last several decades, a large number of studies have mostly focused on the priming step of inflammatory responses; however, there have been recent advances in the understanding that triggering plays a crucial role in inflammatory responses by activating inflammasomes, intracellular protein complexes comprising intracellular pattern recognition receptor (PRR), and inflammatory molecules in response to various extracellular and intracellular activating ligands.

In this special issue, we invited investigators to contribute the latest original research and review articles investigating *in vitro*, *in vivo*, nonclinical, and clinical/translational studies focusing not only on the roles of inflammasomes in inflammatory and infectious diseases but also on the potential therapeutic strategies selectively targeting inflammasomes to prevent and treat various inflammatory and infectious diseases. In this special issue, nine original and two review articles were published regarding the role of inflammasomes in inflammatory and infectious diseases.

The research article by S. A. Tanuseputero et al. investigated the effect of intravenous L-arginine (Arg) supplementation on modulating NLRP3 inflammasome activity in relation to septic acute kidney injury (AKI) and demonstrated that intravenous Arg supplementation immediately after sepsis restores plasma Arg levels and is beneficial for attenuating septic AKI, partly via nitric oxide- (NO-) mediated NLRP3 inflammasome inhibition.

The research article by L. Yang et al. investigated whether hydrogen-rich solution (HRS) could attenuate coagulation disorders and inflammation to improve intestinal injury and poor survival following intestinal ischemia/reperfusion (I/R) and demonstrated the amelioration of coagulation disorders and inflammation by HRS as a mechanism to improve intestinal I/R-induced intestinal injury and poor survival, which might be partially related to inhibition of the nuclear factor kappa B (NF-κB)/NLRP3 pathway.

The research article by M. L. Thorstenberg et al. investigated the involvement of the P2 purinergic receptor $P2Y_2R$ in the activation of NLRP3 inflammasome elements (caspase-1 and 11) and interleukin- (IL-) 1β secretion during *Leishmania amazonensis* infection in peritoneal macrophages as well as in a murine model of cutaneous leishmaniasis. This study suggests that $P2Y_2R$ activation induces caspase-1 activation and IL-1β secretion during *Leishmania amazonensis* infection and that IL-1β/IL-1R signaling is crucial for $P2Y_2R$-mediated protective immune response in an experimental model of cutaneous leishmaniasis.

Another research article by K. Gonzalez et al. also investigated the Th17 and inflammasome responses in the skin lesions of patients with localized cutaneous leishmaniasis (LCL) caused by *Leishmania* (*Viannia*) *panamensis* and demonstrated the participation of Th17 cells and the inflammasome in the *in situ* inflammatory response in localized cutaneous leishmaniasis caused by *Leishmania* (*Viannia*) *panamensis* infection and their roles in the control of the parasites through IL-17 and the IL-1β-dependent NLRP3 inflammasome activation.

The research article by K. Midtbö et al. described the outcome of NLRP3 inflammasome activation and the functional effects of diverse inflammasome inducers and suggests that NLRP3 inflammasome response should be considered a dynamic process, which can be described by taking the ratio between IL-1β and IL-18 into account and moving away from an on/off perspective of inflammasome activation.

The research article by Y. Chen et al. investigated the differences in absent in melanoma 2 (AIM2) inflammasome expression levels between rheumatoid arthritis (RA) and osteoarthritis (OA) and the role of AIM2 in RA fibroblast-like synoviocytes (RA-FLS). This study demonstrated that the AIM2 inflammasome pathway involves in the pathogenesis of RA and suggests that AIM2 inflammasome may be a promising therapeutic strategy for the treatment of RA.

The research article by P. H. Bürgel et al. analyzed the impact of molecules secreted by *Cryptococcus neoformans* B3501 strain and its acapsular mutant *Δcap67* on inflammasome activation in an *in vitro* model. This study demonstrated that conditioned media from a wild-type strain inhibit a vital recognition pathway and subsequent fungicidal function of macrophages, contributing to fungal survival *in vitro* and *in vivo*, which suggests that the secretion of aromatic metabolites, such as DL-indole-3-lactic acid (ILA), during cryptococcal infections fundamentally impacts pathogenesis.

Canonical inflammasomes, such as NLRP3 inflammasome can activate matrix metalloproteinase-9 (MMP-9) in inflammatory responses and diseases, and the research article by C. Li et al. investigated the role of MMP-9 in intrauterine adhesion (IUA) in rats and patients. This study established an animal model for studying IUA mechanisms and suggests that MMP-9 plays an important role in IUA by decreasing MMP-9 expression.

The research article by Q. Su et al. investigated the mechanism by which patients being treated for pulmonary tuberculosis often suffer liver injury due to the effects of anti-TB drugs. This study demonstrated that isoniazid (INH) and rifampin (RIF) can destroy the normal liver tissue, induce an inflammatory response and oxidative stress, and can regulate drug-metabolizing enzymes and the antioxidant defense system by accelerating the activation of NLRP3 inflammasomes, which provide the strong evidence that NLRP3 inflammasomes could be the key factors involved in INH- and RIF-induced liver injuries.

The review article by S. A. Sheweita et al. discussed different bacteria, such as *Helicobacter pylori*, *Salmonella typhi*, *Staphylococcus aureus*, *Klebsiella* spp., and *Proteus mirabilis* that induced cancer via different molecular mechanisms and concluded that a certain bacterium is linked with induction of a specific type of cancer via different molecular and biochemical mechanisms, such as the induction of inflammatory responses. This study suggests that bacterial infection could potentially affect human health in different ways and that it is important to know the possible factors involved in cancer induction for better treatment of cancer patients.

Another review article by M. Michalczyk et al. discussed the current understanding of the mechanisms which underlie the development of preeclampsia (PE) and the significant factors responsible for PE development. This review suggests the mechanisms causing the immune imbalance leading to an enhanced systemic inflammatory response that occurs in PE and potential future researches which may contribute to the identification of new targets for PE therapies. This review also helps readers understand that the pathophysiology of the inflammatory process in PE can largely contribute to the design of new, targeted anti-inflammatory therapies, such as selective NLRP3 inflammasome inhibitors. This review provides a key impact on the development of a targeted therapy that can improve perinatal outcomes in women affected with PE.

We hope that readers will be interested in understanding the roles of inflammasomes in inflammatory response and various human inflammatory and infectious diseases. We also hope that this special issue attracts the interest of the scientific community, thereby contributing and driving further investigations leading to the discovery of unknown inflammasome targets and the development of novel therapeutics to prevent and treat various human inflammatory and infectious diseases.

Conflicts of Interest

The editors declare that there is no conflict of interest regarding the publication of this special issue.

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