Immunomodulating Activity of the Host Defence Peptides

Ernesto M. Martell[1], Melaine González-García[1], Ludger H. Ständker[2], and Anselmo J. Otero-González[a1]

[1]Center for Proteins studies, Faculty of Biology, Havana University, La Habana, Cuba
[2]Core Facility of Functional Peptidomics, Ulm University, Ulm, BW, Germany

Host defence peptides can complement the efficacy of conventional antibiotics amid the current strain resistance crisis. In addition to their microbicidal actions, they may have an immunomodulatory function, reinforcing an antimicrobial fight in a way that conventional antibiotics cannot efficiently address.[b]

The anti-infectious therapy is in a critical crossroad due to the resistance of emerging and reemerging pathogens to conventional antibiotics which are scarce in terms of new mechanisms of action. Host defence peptides (HDPs) including antimicrobial peptides (AMPs) are a promising option for their therapeutic potential because they exhibit a broad spectrum of activity against various infectious agents and they are less prone to provoke microbial resistance [1, 2, 3].

Immunomodulatory activity of HDPs has been recognized in the last 20 years as a promising field which has been in continuous growing. In a clear distinction to their direct antimicrobial killing actions, the immunomodulatory activities of host defence peptides are more effective in vivo. They offer a great opportunity for promising therapeutic applications in the fields of anti-infective therapy, chronic inflammatory diseases treatment, novel vaccine adjuvants development and anticancer immunotherapy.

These immune related functions of HDPs includes chemoattraction of leukocytes, modulation of inflammation enhancement of antigen presentation and polarisation of adaptive immune responses [4].

The complex mechanisms on which these activities are based are not fully understood and may be different for each HDP [5] which also is applied to the innate defence regulatory peptides (IDR) [6]. Previous studies suggest that the mechanism of action of the immunomodulatory activities of some of them on immune cells could be shown in Fig. 1.

Realising and maximising the therapeutic potential of these peptides requires a shift in perspective in HDP development [7]. Each immunomodulatory activity of HDPs can be linked to specific applications and they can work together to enhance their effects, as shown in Fig. 2.

The ability of immunomodulatory HDPs to promote anti-inflammatory cytokine production while exhibiting anti-infective activities reduces the development of excessive inflammation. This clearly represents an advantage compared to most immunostimulatory drugs, which commonly increase the production of proinflammatory cytokines and increase the risk of inflammatory

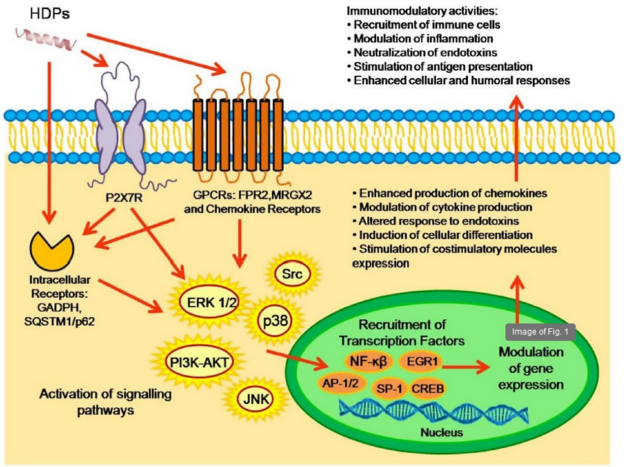

Figure 1: Overview of the mechanism of action of immunomodulatory HDPs in immune cells based on the mechanisms of LL37, human defensins and IDRs (Source: Reference [4]).

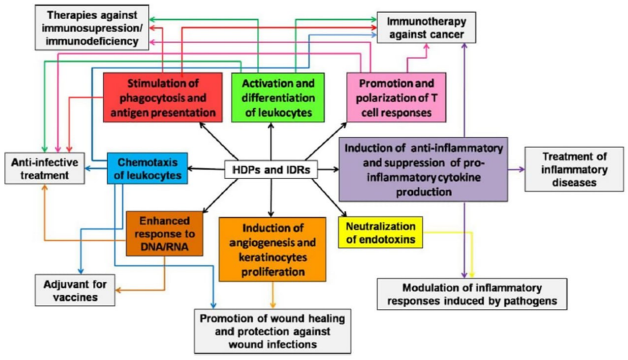

Figure 2: Connection between the main immunomodulatory activities of HDPs and IDRs and their potential therapeutic applications. Each immunomodulatory activity is represented with a specific color (Source: Reference [4]).

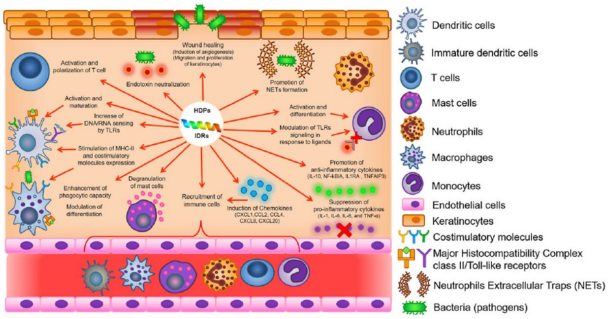

Figure 3: Immunomodulatory activities of HDPs/ IDRs against infections. HDPs exhibit a broad range of immunomodulatory activities that work together during infections to enhance immune response (Source: Reference [4]).

lesions [4]. Figure 3 shows the immunomodulatory activities of HDPs discussed above and how they work together in the context of infection.

The wide range of immunomodulatory activities of HDPs underlines their key role in immunity. In the context of the immune response, they promote immune cell recruitment, antigen presentation, and adaptive responses. It is known that in living organisms all the immunomodulatory effects of HDPs act simultaneously, connecting many immunological networks.

However, to improve the development of natural HDPs and IDRs for immunomodulatory therapies, it is particularly important to clarify more aspects of their immune system-related activities and to consider a systemic view of their impact on human physiology.

This is crucial to reduce the potential adverse effects of these therapies and uncover potential new applications of the attractive and promising immunomodulatory side of the HDP coin.

Notes

a. Email: aoterogo@yahoo.com

b. Original version of this article is reference [4]

References

[1] González-García M. *et al*, Antimicrobial peptides and multiresistant respiratory infections, *Rev Cub Med Trop* **71** (2) (2019) e343

[2] Otero-González A.J. *et al*, Antimicrobial peptides from marine invertebrates as a new frontier for microbial infection control, *FASEB J* **24** (2010) 1320-1334

[3] López-Abarrategui C. *et al*, Cm-p5: an antifungal hydrophilic peptide derived from the coastal mollusk *Cenchritis muricatus* (Gastropoda: Littorinidae), *FASEB Journal* **29** (8) (2015): 3315-25

[4] Martell, E.M. *et al*, Host defense peptides as immunomodulators: The other side of the coin, *Peptides* **146** (2021), 170644

[5] Hilchie, A.L. *et al*, Immune modulation by multifaceted cationic host defence (antimicrobial) peptides, *Nat. Chem. Biol.* **9** (2013) 761–768

[6] Scott, M.G. *et al*, An anti-infective peptide that selectively modulate the innate immune response, *Nat Biotechnol* **25** (2005) 465-472

[7] Nicholls E.F. *et al*, Immunomodulators as adjuvants for vaccines and antimicrobial therapy, *Ann. N. Y. Acad. Sci.* **1213** (2010) 46–61