The earliest studies of the non-microbicidal properties of CHDP focused on their effects on immune cells, particularly their ability to recruit leukocytes. Over the past two decades, research has uncovered a wide range of immune-related functions for CHDP, with these functions dependent on environmental stimuli, cell and tissue type, interactions with cellular receptors, and peptide concentration. The molecular mechanisms underlying CHDP's selective modulation of immune responses are intricate and involve intracellular uptake, potentially mediated by GPCRs, interactions with proteins like GAPDH and p62, alterations in signaling pathways (NF-□B, p38 and JNK MAPK, MKP1, and PI3K), and engagement of transcription factors. These processes are influenced by peptide concentration, response kinetics, and environmental stimuli. The diverse immunomodulatory functions of CHDP raise questions about their primary biological role. This review summarizes the activities of CHDP on immunity and inflammation, focusing on cathelicidins and defensins. Comprehending the mechanisms behind CHDP's ability to modulate immunity for infection protection, inflammation resolution, and immune homeostasis is crucial for developing novel therapeutic approaches based on CHDP-derived peptides.