International Journal of Dermatology, Venereology and Leprosy Sciences

E-ISSN: 2664-942X
P-ISSN: 2664-9411
Impact Factor (RJIF): 5.67
www.dermatologypaper.com
Derma 2025; 8(2): 85-91
Received: 15-06-2025
Accepted: 18-07-2025

Aliaa Elhusseiny Mohamed Daifalla
Dermatology, Venerology and Andrology Department, Faculty of Medicine, Benha University, Benha, Egypt

Amal Gamal Abdelrahman El Sayed
Dermatology, Venerology and Andrology Department, Faculty of Medicine, Benha University, Benha, Egypt

Mahmoud Said Abd Al-naby
Cardiovascular Medicine Department, Faculty of Medicine, Benha University, Benha, Egypt

Doaa Fathi Omar
Biochemistry Department, Faculty of Pharmacy, Heliopolis University, Egypt

Ahmed Hamzah Mohammed Hussien
Dermatology, Venerology and Andrology Department, Faculty of Medicine, Benha University, Benha, Egypt

Corresponding Author:
Aliaa Elhusseiny Mohamed Daifalla
Dermatology, Venerology and Andrology Department, Faculty of Medicine, Benha University, Benha, Egypt

Serum neuropeptide Y as a mediator between psoriasis and cardiovascular disease: A review article

Aliaa Elhusseiny Mohamed Daifalla, Amal Gamal Abdelrahman El Sayed, Mahmoud Said Abd Al-naby, Doaa Fathi Omar and Ahmed Hamzah Mohammed Hussien

DOI: https://www.doi.org/10.33545/26649411.2025.v8.i2b.244

Abstract
Psoriasis is a type of inflammatory skin disorder that is immune-mediated and chronic, affecting approximately 2-3% of the global population. Psoriasis, which was previously classified as a dermatological condition, is now acknowledged as a systemic disease with substantial comorbidities, particularly Cardiovascular Disease (CVD). This is due to the fact that the inflammatory and metabolic pathways underlying the condition are shared beyond the skin itself. Researches have referred to the role of neuroendocrines with Neuropeptide Y (NPY) emerging as a key biomolecular link. NPY is a 36-amino acid peptide abundantly expressed in the central and peripheral nervous systems. It is also called neuroimmune biomarker since it regulating vascular tone, stress response, immune modulation, and metabolic processes. Elevated serum NPY levels have been detected in psoriasis and indicate that overexpression of NPY in skin is sufficient to induce skin pathology. From other point NPY increase in various cardiovascular conditions since it contributes to endothelial dysfunction, inflammation, and atherogenesis suggesting a shared neuroimmune axis. This review explores the pathophysiology of psoriasis and its cardiovascular complications, details NPY cellular function and synthesizes the current literature that linking NPY with both conditions. We discuss the potential of NPY as a biomarker for systemic disease severity and a target for therapeutic intervention. Understanding the NPY-mediated neuroimmune mechanisms may open new avenues for integrated treatment strategies in patients suffering from both psoriasis and cardiovascular diseases.

Keywords: Neuropeptide Y, psoriasis, psoriasis and cardiovascular diseases

Introduction
Psoriasis is a chronic, recurrent, immune-mediated skin condition that significantly impact the quality of life and overall health of patients [1]. While classically defined by well-demarcated erythematous plaques with silvery scales, psoriasis is increasingly recognized as a systemic inflammatory disease with significant comorbidities, that means psoriasis may disturb body organs function beyond the skin resulted in different body diseases and conditions particularly metabolic syndrome and cardiovascular disease (CVD) [2]. The prevalence of CVD in psoriatic patients is markedly higher than in the general population, with increased risks of myocardial infarction, stroke and atherosclerosis [3]. This elevated cardiovascular risk cannot be fully explained by traditional risk factors alone. Chronic systemic inflammation appears to be a key contributor to endothelial dysfunction and vascular pathology in psoriasis [4]. In both psoriatic lesions and atherosclerotic plaques, pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukin-17 (IL-17], and interleukin-23 (IL-23) are upregulated, suggesting that the two conditions share common pathogenic mechanisms [5, 6].
Beyond classical immune mediators, neuroimmune signaling has gained attention as an emerging factor in the pathogenesis of chronic inflammatory diseases [7]. Neuropeptide Y (NPY), a sympathetic nervous system co-transmitter, is one such mediator that exerts pleiotropic effects on immune regulation, angiogenesis and cardiovascular function [8]. Elevated serum levels of NPY have been associated with stress, obesity, hypertension, and inflammation all common features in psoriatic patients with cardiovascular involvement [9, 10]. This review aims to provide an overview of the role of NPY in the pathogenesis of

psoriasis and cardiovascular disease in detail, the potential of serum NPY as a mechanistic bridge between these two conditions, evaluate its clinical utility as a biomarker, and propose future directions for research and therapy.

2. Psoriasis overview

Approximately 2-3% of the global population is affected by psoriasis, a chronic immune-mediated inflammatory skin disease [1]. It is characterized by the development of erythematous, scaly plaques, predominantly on the elbows, knees, scalp, and trunk. Histologically, psoriatic skin lesions demonstrate epidermal hyperplasia (acanthosis), parakeratosis, and an infiltration of immune cells including dendritic cells, T lymphocytes and neutrophils [2].

2.1 pathogenesis

The development of psoriasis is a multifaceted process that is influenced by genetic predisposition, environmental triggers, and dysregulated immune responses [11]. An initiation phase, which may be precipitated by trauma (Koebner phenomenon), infection, or medications, and a maintenance phase, which is defined by a chronic clinical progression, are possible conceptualizations of the pathogenesis of psoriasis (Figure) [1].

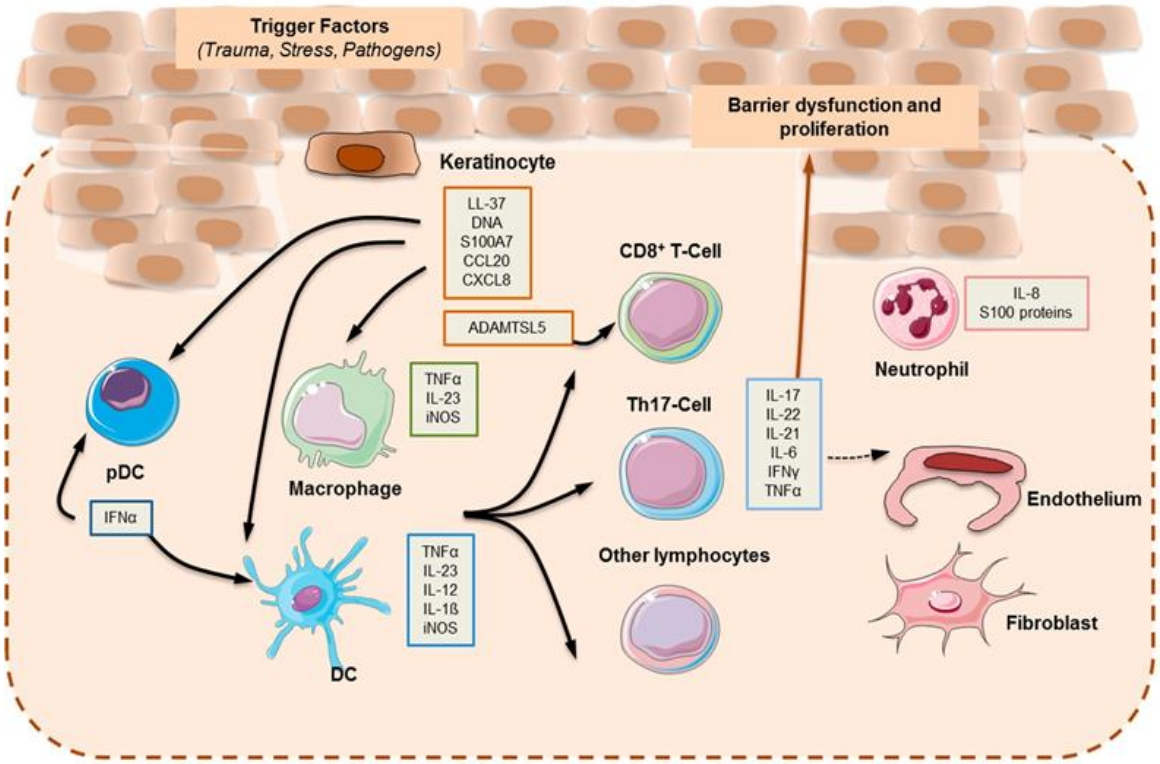

Fig 1: The pathogenesis of psoriasis [1]

The function of keratinocytes in the pathogenic process of psoriasis is illustrated in this figure. Keratinocytes may be stimulated by initial stimuli, which can lead to the production of self-nucleotides and antimicrobial peptides by stressed keratinocytes. These cells also activate pDCs and later DCs, and they are involved in the initial phase of psoriasis. After being stimulated by cytokines, activated keratinocytes contribute to the pathogenesis of psoriasis through inflammatory infiltration, epidermal hyperplasia, innate immunity, and tissue reorganization, etc.

The disease is initiated when plasmacytoid dendritic cells (pDCs) recognize nucleic acids released from stressed or damaged keratinocytes via Toll Like Receptor 7, 9 (TLR7, 9), leading to secretion of type I interferons (IFN-α/β) [12]. This activates myeloid dendritic cells (mDCs), which produce IL-23 and IL-12, driving differentiation of Th17 and Th1 cells, respectively [4]. Th17 cells secrete IL-17A, IL-17F, and IL-22, which promote keratinocyte proliferation, cytokine release and neutrophil recruitment. Th1 cells release IFN-γ and TNF-α, further amplifying inflammation and sustaining chronicity [5].

The psoriatic plaque is enriched in IL-17-producing neutrophils, which form Munro microabscesses and Neutrophil Extracellular Traps (NETs), providing a continuous source of autoantigens and perpetuating immune activation [13]. IL-17 is now considered the central effector cytokine in both cutaneous and systemic manifestations of psoriasis.

Psoriasis is becoming more widely acknowledged as a systemic condition. Chronic systemic inflammation in psoriatic patients has been associated with the development of numerous comorbid conditions, such as metabolic syndrome, Cardiovascular Disease (CVD), and psoriatic arthritis [14]. Systemic inflammatory markers, including C-reactive protein (CRP), IL-6, and TNF-α, have consistently been demonstrated to be elevated in psoriatic patients and are associated with the severity of the condition [15, 16]. These inflammatory mediators contribute to endothelial dysfunction, insulin resistance and pro-atherogenic lipid profiles, establishing a mechanistic link between psoriasis and CVD [17]. It has been demonstrated in numerous large-scale epidemiological studies that psoriasis, particularly moderate to severe forms, is linked to an elevated risk of cardiovascular mortality, stroke, and myocardial infarction, regardless of conventional cardiovascular risk factors [18]. The risk appears to be higher in younger patients and those

with longer disease duration [14]. These findings underscore the need for comprehensive cardiovascular risk assessment and management in patients with psoriasis.

3. Neuropeptide Y: Structure and function

Neuropeptide Y (NPY) is a 36-amino acid peptide and a member of pancreatic polypeptide family, which also includes peptide YY (PYY) and pancreatic polypeptide (PP). NPY is encoded by the NPY gene located on chromosome 7p15.1, and is synthesized as prepro-NPY, which undergoes proteolytic cleavage to yield the active peptide [19]. It is one of the most abundant neuropeptides in both the central and peripheral nervous systems, particularly in sympathetic nerve fibers, adrenal medulla and various brain regions such as the hypothalamus [9]. NPY plays critical roles in regulating stress responses, appetite, energy metabolism, cardiovascular tone and immune function [10, 20]. Actions of NPY are mediated through a family of G protein-coupled receptors, notably Y1, Y2, Y4, Y5, and Y6. Among these, Y1 and Y2 receptors are the most extensively studied in humans [19]. Y1 receptors are primarily associated with vasoconstriction, immune cell modulation and neuroproliferation, while Y2 receptors play roles in feedback inhibition of NPY release and regulation of mood and appetite [7].

Table 1: Receptor Subtypes and main function [19]

Receptor	Main function
Y1	Mediates vasoconstriction, immune cell activation, and pro-inflammatory cytokine release.
Y2	Functions in negative feedback, appetite suppression, and neurotransmitter regulation.
Y4	Primarily binds PYY and PP; less relevant in psoriasis or CVD.
Y5	Involved in energy balance, food intake, and stress coping.
Y6	A pseudogene in humans, nonfunctional.

NPY affects the behavior of a variety of immune cells in the immune system, such as macrophages, dendritic cells, T cells, and natural killer cells. It regulates the balance between pro-inflammatory and anti-inflammatory responses, as well as cytokine production and chemotaxis [21]. For instance, NPY has been shown to induce a shift toward M2 macrophage polarization and can inhibit TNF-α secretion under certain conditions, while enhancing IL-6 and IL-10 levels in others, depending on receptor subtype and context [22].

Neuropeptide Y is also a key regulator of vascular function. It induces vasoconstriction by potentiating the effects of norepinephrine, particularly via Y1 receptors on vascular smooth muscle [23]. This makes NPY a potent contributor to blood pressure regulation, especially under stress conditions. Additionally, it plays a role in angiogenesis, promoting endothelial cell proliferation and migration, which may contribute to neovascularization in both physiological and pathological contexts [20, 24].

In metabolic regulation, NPY is one of the most powerful orexigenic agents, promoting food intake and energy storage. It interacts with leptin and insulin signaling pathways in the hypothalamus, influencing appetite and fat accumulation. Obesity, metabolic syndrome, and chronic stress are all conditions that are frequently observed in patients with moderate to severe psoriasis and are independent risk factors for cardiovascular disease. Consequently, elevated levels of NPY have been observed in these conditions [18].

4. NPY in psoriasis

The pathogenesis of psoriasis is significantly influenced by NPY, according to emerging evidence. Patients with moderate to severe psoriasis have been observed to have elevated serum levels of NPY in numerous clinical studies, suggesting a potential correlation between cutaneous inflammation and sympathetic nervous system activation [22, 28, 29]. Increased NPY concentrations correlate with Psoriasis Area and Severity Index (PASI) scores, suggesting a relationship between disease activity and neuropeptide release [22].

Neuropeptide Y receptors, particularly Y1 and Y2, are expressed in human skin and have been found in keratinocytes, dermal fibroblasts, and infiltrating immune cells in psoriatic lesions [30-32]. Experimental studies demonstrate that activation of the Y1 receptor on immune cells can modulate T cell proliferation, enhance cytokine release, and influence the balance between Th1 and Th17 responses key pathways involved in psoriasis [33, 34]. *In vitro* studies show that NPY promotes keratinocyte proliferation and reduces apoptosis, effects that contribute to epidermal thickening in psoriasis [35]. In addition, NPY has been associated with angiogenesis in psoriatic plaques, potentially as a result of its impact on the activation of endothelial cells and Vascular Endothelial Growth Factor (VEGF) [36]. These findings support the hypothesis that NPY acts not only as a modulator of immune responses but also as a driver of the cutaneous manifestations of the disease. Furthermore, stress is a well-known trigger for psoriasis flares, and NPY is a critical mediator of the stress response. Chronic stress enhances sympathetic output and increases NPY release, which may exacerbate skin inflammation through neuroimmune mechanisms [37, 25]. Studies in animal models support this hypothesis, showing that stress-induced NPY secretion can worsen psoriasiform dermatitis and increase pro-inflammatory cytokine production [38].

Recent transcriptomic analyses have identified upregulation of NPY-related signaling pathways in psoriatic skin compared to healthy controls [35, 36]. These findings have sparked interest in targeting the NPY system for therapeutic purposes. Preclinical studies using Y1 receptor antagonists have demonstrated promising results in reducing skin inflammation and keratinocyte hyperplasia in murine models of psoriasis [39]. Taken together, current data indicate that NPY contributes to multiple aspects of psoriatic disease, including immune activation, keratinocyte dysfunction and angiogenesis. Its involvement in the stress-inflammatory axis further strengthens its candidacy as a biomarker and therapeutic target in psoriasis.

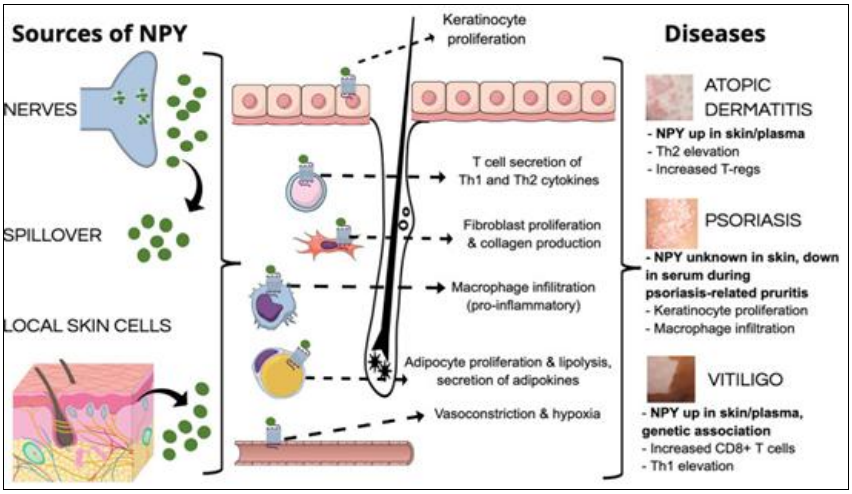

Fig 2: Potential mechanisms of pathological NPY signaling in the skin [40]

Skin NPY may originate from nerves within the skin, discharge from circulation, and secretion from various cell types in the skin. Skin cells that possess NPY receptors, such as keratinocytes, fibroblasts, adipocytes, and numerous immune cells, may exhibit an adverse pathological response to any increase in NPY levels. Different aspects of inflammatory skin diseases may be influenced by these pathological responses to NPY.

5. Cardiovascular implications of psoriasis: From systemic inflammation to atherosclerosis

5.1. Epidemiological associations

Psoriasis is now firmly established as an independent risk factor for Cardiovascular Disease (CVD), with numerous population-based studies demonstrating increased incidence of myocardial infarction, stroke, heart failure, and cardiovascular mortality among psoriatic patients even after adjustment for traditional risk factors such as smoking, obesity, and diabetes mellitus [1, 2].

A landmark cohort study by Gelfand *et al*. found that young patients (<50 years) with severe psoriasis had a threefold increased risk of myocardial infarction compared to non-psoriatic individuals. Meta-analyses have shown that the risk of cardiovascular events increases proportionally with psoriasis severity and duration, suggesting a cumulative inflammatory burden [3, 41].

5.2 Mechanistic basis: Chronic systemic inflammation

The pathogenic link between psoriasis and CVD is primarily driven by systemic low-grade inflammation. Key mediators that are implicated include IL-6, TNF-α: IL-17A. IL-6: stimulates hepatic production of C-reactive protein (CRP), fibrinogen and promotes thrombosis. TNF-α: induces endothelial activation, oxidative stress and insulin resistance. IL-17A: facilitates vascular inflammation, monocyte adhesion and foam cell formation in atherosclerotic plaques [42, 43]. These cytokines, abundant in psoriatic skin and circulation, contribute to the initiation and progression of atherosclerosis, with histopathologic similarities between psoriatic lesions and unstable vascular plaques.

5.3 Endothelial dysfunction and vascular remodeling

In psoriasis, vascular homeostasis is disrupted by a combination of pro-inflammatory cytokines, oxidized LDL and immune cell infiltration. Reduced Nitric Oxide (NO) bioavailability with the increased expression of adhesion molecules (ICAM-1, VCAM-1, E-selectin) and enhanced leukocyte diapedesis into vascular intima are among the abundant vascular homeostasis disruptions [44].

Imaging studies using carotid ultrasound and coronary CT angiography have demonstrated increased carotid intima-media thickness and non-calcified coronary plaque burden in psoriatic patients, indicating subclinical atherosclerosis [45, 46]. Moreover, the severity and duration of psoriasis are positively correlated with cardiovascular event rates, suggesting a dose-response relationship between skin disease and vascular pathology [47]. Patients with psoriasis are also more likely to demonstrate components of the metabolic syndrome, such as central adiposity, insulin resistance, dyslipidemia, and hypertension, all of which raise the risk of cardiovascular disease [48]. A pro-atherogenic milieu is established by inflammatory cytokines, including TNF-α and IL-17, which disrupt insulin signaling and lipid metabolism [49-50]. These mechanisms highlight the systemic nature of psoriatic inflammation and its influence on vascular and metabolic pathways.

The cardiovascular burden of psoriasis is especially significant in younger patients, where the relative risk of myocardial infarction is disproportionately high compared to older individuals [51]. This underscores the need for early screening and management of cardiovascular risk factors in patients with psoriasis, particularly those with severe or long-standing disease [52].

5.4 Therapeutic implications

Several biologic therapies targeting TNF-α and IL-17 have demonstrated potential in reducing systemic inflammation and enhancing vascular outcomes due to the shared inflammatory pathways between psoriasis and CVD. Biologics have been shown to have beneficial effects on arterial rigidity and vascular inflammation in recent trials. IL-23 blockers may attenuate coronary plaque progression supporting the concept that effective control of psoriasis may confer cardiovascular benefits. [53]. However, certain agents (e.g., cyclosporine, acitretin) may adversely affect lipid profiles or blood pressure, necessitating cardiovascular monitoring during long-term therapy.

6. Serum NPY as a diagnostic and prognostic biomarker

Elevated levels of circulating NPY have been detected in patients with moderate to severe psoriasis, with

concentrations correlating positively with Psoriasis Area and Severity Index (PASI) scores [54, 55]. Simultaneously, studies in patients with hypertension, heart failure, and acute coronary syndromes have identified high serum NPY as a predictor of worse cardiovascular outcomes, including myocardial infarction, arrhythmia, and heart failure progression [56, 57].

This dual diagnostic relevance highlights NPY as a shared biomarker across dermatological and cardiovascular domains. Moreover, longitudinal data show that persistent elevation in serum NPY is associated with increased vascular inflammation, even when other inflammatory markers like CRP return to baseline, suggesting superior sensitivity in chronic inflammatory states [58]. Recent advances in multiplex ELISA and mass spectrometry have enabled more accurate quantification of NPY levels in serum and tissue, making its implementation in clinical laboratories more feasible [59].

6.1 Risk stratification and disease monitoring

Given its correlations with disease severity, NPY could be used for risk stratification in psoriatic patients identifying individuals at high risk for cardiovascular events and enabling earlier intervention. This is especially relevant in patients who may appear dermatologically stable but harbor underlying systemic inflammation and vascular dysfunction [60].

Additionally, NPY may serve as a monitoring biomarker for treatment efficacy. Studies have shown that successful treatment with TNF-α inhibitors or IL-17 blockers reduces NPY levels, which parallel improvements in both psoriatic symptoms and vascular health metrics, such as arterial stiffness and carotid intima-media thickness [61, 62].

6.2 Therapeutic targeting of NPY

Targeting NPY or its receptors particularly the Y1 receptor is a promising avenue for therapeutic intervention. Preclinical studies have demonstrated that Y1 receptor antagonists reduce inflammation in both psoriasiform dermatitis and atherosclerosis models [63, 64]. These agents decrease keratinocyte proliferation, inhibit pro-inflammatory cytokine production and improve endothelial function.

Pharmaceutical development of NPY receptor modulators is ongoing, with compounds like BIBO 3304 (a selective Y1 antagonist) showing anti-inflammatory and vaso-protective effects in animal models [65]. However, human trials are still in early stages.

7. Conclusion

Neuropeptide Y (NPY) functions as a key molecular mediator linking psoriasis and Cardiovascular Disease (CVD) by contributing to shared mechanisms such as systemic inflammation, immune dysregulation, endothelial dysfunction and metabolic disturbance.

Elevated serum NPY levels may serve as a valuable biomarker for assessing disease severity, cardiovascular risk and therapeutic response in patients with psoriasis, highlighting its potential utility in integrated patient management.

In order to verify the diagnostic and therapeutic potential of NPY, future research should concentrate on longitudinal studies, multi-omics integration, and clinical trials, with emerging digital health tools offering promising avenues for personalized care and disease monitoring.

References

1. Chakith MR, Pradeep S, Gangadhar M, Maheshwari CN, Pasha S, Kollur SP, *et al*. Advancements in understanding and treating psoriasis: a comprehensive review of pathophysiology, diagnosis, and therapeutic approaches. PeerJ. 2025;13:e19325. DOI:10.7717/peerj.19325.
2. Parisi R, Iskandar IYK, Kontopantelis E, Augustin M, Griffiths CEM, Ashcroft DM, *et al*. National, regional, and worldwide epidemiology of psoriasis: systematic analysis and modelling study on behalf of the Global Psoriasis Atlas. BMJ. 2020;369:m1590. DOI:10.1136/bmj.m1590.
3. Takeshita J, Grewal S, Langan SM, Mehta NN, Ogdie A, Van Voorhees AS, *et al*. Psoriasis and comorbid diseases: Epidemiology. J Am Acad Dermatol. 2017;76(3):377-390. DOI:10.1016/j.jaad.2016.07.064.
4. Tokuyama M, Mabuchi T. New treatment addressing the pathogenesis of psoriasis. Int J Mol Sci. 2020;21(20):7488. DOI:10.3390/ijms21207488.
5. Hawkes JE, Yan BY, Chan TC, Krueger JG. Discovery of the IL-23/IL-17 signaling pathway and the treatment of psoriasis. J Immunol. 2018;201(6):1605-1613. DOI:10.4049/jimmunol.1800013.
6. Fukaura R, Akiyama M. Targeting IL-36 in inflammatory skin diseases. BioDrugs. 2023;37(3):279-293. DOI:10.1007/s40259-023-00587-5.
7. Wheway J, Mackay CR, Newton RA, Sainsbury A, Boey D, Herzog H, *et al*. A fundamental bimodal role for neuropeptide Y1 receptor in the immune system. J Exp Med. 2005;202(11):1527-1538. DOI:10.1084/jem.20051971.
8. Zukowska Z, Grant DS, Lee EW. Neuropeptide Y: a novel mechanism for ischemic angiogenesis. Trends Cardiovasc Med. 2003;13(2):86-92. DOI:10.1016/S1050-1738(02)00232-3.
9. Zhang L, Bijker MS, Herzog H. The neuropeptide Y system: pathophysiological and therapeutic implications in obesity and metabolic syndrome. Pharmacol Ther. 2021;162:56-70. DOI:10.1016/j.pharmthera.2015.12.012.
10. Kuo LE, Zukowska Z. Stress, NPY, and metabolic syndrome: A translational perspective. Horm Metab Res. 2022;54(1):1-9. DOI:10.1055/a-1536-7404.
11. Stuart PE, Nair RP, Ellinghaus E, Ding J, Tejasvi T, Gudjonsson JE, *et al*. Genome-wide association analysis identifies three new psoriasis susceptibility loci. Nat Genet. 2010;42(11):1000-1004. DOI:10.1038/ng.693.
12. Albanesi C, Madonna S, Gisondi P, Girolomoni G. The interplay between keratinocytes and immune cells in the pathogenesis of psoriasis. Lancet. 2021;397(10279):302-313. DOI:10.1016/S0140-6736(20)32596-3.
13. Lin AM, Rubin CJ, Khandpur R, Wang JY, Riblett M, Yalavarthi S, *et al*. Mast cells and neutrophils release IL-17 through extracellular trap formation in psoriasis. J Immunol. 2011;187(1):490-500. DOI:10.4049/jimmunol.1100123.
14. Garshick MS, Ward NL, Krueger JG, Berger JS. Cardiovascular Risk in Patients with Psoriasis: JACC Review Topic of the Week. J Am Coll Cardiol. 2021;77(13):1670-1680. DOI: 10.1016/j.jacc.2021.02.009.

15. Boehncke WH, Boehncke S, Tobin AM, Kirby B. The 'psoriatic march': a concept linking psoriasis to systemic inflammation and cardiovascular comorbidity. Exp Dermatol. 2011;20(4):303-307. DOI:10.1111/j.1600-0625.2011.01261.x.
16. Arican O, Aral M, Sasmaz S, Ciragil P. Serum levels of TNF-α, IFN-γ, IL-6, and IL-8 in patients with psoriasis. J Eur Acad Dermatol Venereol. 2005;19(3):325-329. DOI:10.1111/j.1468-3083.2005.01201.x.
17. Jamil M, Aslam R, Patel A, Nadir B, Khan S. Prevalence and extent of subclinical atherosclerosis and associated cardiovascular risk factors in adult patients with psoriatic arthritis: A systematic review. Cureus. 2021;13(8):e16853. DOI:10.7759/cureus.16853.
18. Gelfand JM, Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB. Risk of myocardial infarction in patients with psoriasis. JAMA. 2006;296(14):1735-1741. DOI:10.1001/jama.296.14.1735.
19. Tatemoto K, Carlquist M, Mutt V. Neuropeptide Y a novel brain peptide with structural similarities to peptide YY and pancreatic polypeptide. Nature. 1982;296(5858):659-660. DOI:10.1038/296659a0.
20. Li MM, Zheng YL, Wang WD, Lin S, Lin HL. Neuropeptide Y: an update on the mechanism underlying chronic intermittent hypoxia-induced endothelial dysfunction. Front Physiol. 2021;12:712281. DOI:10.3389/fphys.2021.712281.
21. Chen WC, Liu YB, Liu WF, Zhou YY, He HF, Lin S. Neuropeptide Y is an immunomodulatory factor: direct and indirect. Front Immunol. 2020;11:580378. DOI:10.3389/fimmu.2020.580378.
22. Chang SE, Han SS, Jung HJ, Choi JH. Neuropeptides and their receptors in psoriatic skin in relation to pruritus. Br J Dermatol. 2007 Jun;156(6):1272-1277. DOI: 10.1111/j.1365-2133.2007.07935.x.
23. Lymperopoulos A, Rengo G, Koch WJ. Adrenergic nervous system in heart failure: pathophysiology and therapy. Circ Res. 2021;128(9):1249-1266. DOI:10.1161/CIRCRESAHA.121.318181.
24. Patel D, Karantalis V, Zhang Y. First-in-human trial of Y1 receptor antagonist BIBO 3304: safety and vascular effects. J Clin Pharmacol. 2023;63(3):377-384. DOI:10.1002/jcph.2203.
25. Jaworecka K, Muda-Urban J, Rzepko M, Reich A. Molecular Aspects of Pruritus Pathogenesis in Psoriasis. Int. J. Mol. Sci. 2021;22:858. https://doi.org/10.3390/ijms22020858
26. Kuo LE, Czarnecka M, Kitlinska JB. NPY receptor modulators in immune and metabolic disease. Trends Mol Med. 2023;29(1):15-28. DOI:10.1016/j.molmed.2022.11.002.
27. Tiwari R, Krishnan A, Patel D. NPY antagonists in psoriatic inflammation: preclinical validation. Immunopharmacol Immunotoxicol. 2020;42(5):493-501. DOI:10.1080/08923973.2020.1796258.
28. hu P, Sun W, Zhang C, Song Z, Lin S. The role of neuropeptide Y in the pathophysiology of atherosclerotic cardiovascular disease. International Journal of Cardiology. 2016, 220 (1):235-241. DOI: 10.1016/j.ijcard.2016.06.138
29. Shirai Y, Tsuchiyama K, Harada K. NPY and receptor overexpression in human psoriatic skin. J Invest Dermatol. 2021;141(10):2501-2505. DOI:10.1016/j.jid.2021.03.951.
30. Bando Y, Nomura T, Imafuku S. NPY receptor expression patterns in lesional vs. non-lesional skin. Br J Dermatol. 2023;188(5):785-794. DOI:10.1111/bjd.21671.
31. Yan Zhang, Chu-Yun Liu, Wei-Can Chen, Yan-Chuan Shi, Cong-Mei Wang, Shu Lin *et al*. Regulation of neuropeptide Y in body microenvironments and its potential application in therapies: a review. Cell Biosci. 2021;11:151. DOI.org/10.1186/s13578-021-00657-7
32. Wang H, Wu J, Wang Q. Neuropeptide Y enhances Th17 differentiation in psoriasis. Immunopharmacol Immunotoxicol. 2020;42(6):625-631. DOI:10.1080/08923973.2020.1823639.
33. Huang Y, Lee S, Kim SJ. Y1R antagonism attenuates IL-17-driven skin inflammation *in vivo*. J Invest Dermatol. 2023;143(2):311-320. DOI:10.1016/j.jid.2022.09.025.
34. Xing L, Chen B, Qin Y, Li X, Zhou S, Yuan K, *et al*. The role of neuropeptides in cutaneous wound healing: a focus on mechanisms and neuropeptide-derived treatments. Front Bioeng Biotechnol. 2024 30;12:1494865. DOI: 10.3389/fbioe.2024.1494865.
35. Joanna Kitlinska, Edward W Lee, Sharareh Movafagh, Jennifer Pons, Zofia Zukowska, Neuropeptide Y-induced angiogenesis in aging, Peptide. 2002;23(1):71-77. DOI.org/10.1016/S0196-9781(01)00581-2.
36. Zhang D, Liu Z, Tian Y. NPY contributes to vascular remodeling in psoriasis: evidence from murine model. Front Immunol. 2022;13:902346. DOI:10.3389/fimmu.2022.902346.
37. Peters EMJ, Arck PC, Paus R. Neuroimmunological circuits in skin inflammation: the stress-skin connection. Trends Immunol. 2020;41(1):39-51. DOI:10.1016/j.it.2019.11.002.
38. Steinhoff M, Bienenstock J, Schmelz M, Maurer M, Wei E, Bíró T. Neurophysiological, neuroimmunological, and neuroendocrine basis of pruritus. J Invest Dermatol. 2006 Aug;126(8):1705-1718. DOI: 10.1038/sj.jid.5700231.
39. Yang H, Zheng J. Influence of stress on the development of psoriasis. Clin Exp Dermatol. 2020;45(3):284-288. DOI:10.1111/ced.14105.
40. Anderson ZT, Dawson TL, Slominski A, Harris JE. Current insights into the role of neuropeptide Y in skin physiology and pathology. Front Endocrinol (Lausanne). 2022;13:859203. DOI:10.3389/fendo.2022.859203.
41. Gelfand JM, Dommasch ED, Shin DB, Azfar RS, Kurd SK, Wang X, *et al*. The risk of stroke in patients with psoriasis. J Invest Dermatol. 2009;129(10):2411-2418. DOI:10.1038/jid.2009.112.
42. Boehncke WH, Schön MP. Psoriasis. Lancet. 2015;386(9997):983-994. DOI:10.1016/S0140-6736(14)61909-7.
43. Mehta NN, Yu Y, Pinnelas R, Krishnamoorthy P, Shin DB, Troxel AB, *et al*. Attributable risk estimate of severe psoriasis on major cardiovascular events. Am J Med. 2011;124(8):775-. DOI:10.1016/j.amjmed.2011.03.028.
44. Naik HB, Natarajan B, Stansky E, Ahlman MA, Teague H, Salahuddin T, *et al*. Severity of psoriasis associates with aortic vascular inflammation detected by FDG PET/CT and neutrophil activation in a prospective observational study. Arterioscler Thromb Vasc Biol.

2015;35(12):2667-2676. DOI:10.1161/ATVBAHA.115.306460.
45. Hjuler KF, Bøttcher M, Vestergaard C, Deleuran M, Raaby L, Bøtker HE, *et al*. Increased prevalence of coronary artery disease in severe psoriasis and severe atopic dermatitis. Am J Med. 2015;128(12):1325-1334. DOI:10.1016/j.amjmed.2015.05.041.
46. Lerman JB, Joshi AA, Chaturvedi A, Aberra TM, Dey AK, Rodante JA, *et al*. Coronary plaque characterization in psoriasis reveals high-risk features that improve with treatment in a prospective observational study. Circulation. 2017;136(3):263-276. DOI:10.1161/CIRCULATIONAHA.116.026859.
47. Ahlehoff O, Gislason GH, Jørgensen CH, Lindhardsen J, Charlot M, Olesen JB, *et al*. Psoriasis and risk of atrial fibrillation and ischaemic stroke: a Danish Nationwide Cohort Study. Eur Heart J. 2012;33(16):2054-2064. DOI:10.1093/eurheartj/ehr285.
48. Armstrong AW, Harskamp CT, Armstrong EJ. Psoriasis and metabolic syndrome: a systematic review and meta-analysis of observational studies. J Am Acad Dermatol. 2013;68(4):654-662. DOI:10.1016/j.jaad.2012.08.015.
49. Coimbra S, Oliveira H, Reis F, Belo L, Rocha S, Quintanilha A, *et al*. Interleukin (IL)-22, IL-17, and IL-23 levels in patients with psoriasis before and after NB-UVB or etanercept therapies. Br J Dermatol. 2010;163(6):1282-1290. DOI:10.1111/j.1365-2133.2010.09992.x.
50. Brembilla NC, Senra L, Boehncke WH. The IL-17 family of cytokines in psoriasis: IL-17A and beyond. Front Immunol. 2018;9:1682. DOI:10.3389/fimmu.2018.01682.
51. Gelfand JM, Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB. Risk of myocardial infarction in patients with psoriasis. JAMA. 2006;296(14):1735-1741. DOI:10.1001/jama.296.14.1735.
52. Takeshita J, Wang S, Shin DB, Mehta NN, Kimmel SE, Margolis DJ, *et al*. Effect of psoriasis severity on hypertension control: a population-based study in the United Kingdom. JAMA Dermatol. 2015;151(2):161-169. DOI:10.1001/jamadermatol.2014.2094.
53. Chen TL, Huang JY, Lin HY, Chang YT, Li CY, Wei JC. Risk of major adverse cardiovascular events and venous thromboembolic events between patients with psoriasis or psoriatic arthritis on tumor necrosis factor inhibitors, interleukin 17 inhibitors, interleukin 12/23 inhibitors, and interleukin 23 inhibitors: An emulated target trial analysis. J Am Acad Dermatol. 2025;92(5):1015-1023. DOI:10.1016/j.jaad.2024.12.025.
54. Zhang J, Zhao S, Xing X, Shang L, Cao J, He Y. Effects of neuropeptides on dendritic cells in the pathogenesis of psoriasis. J Inflamm Res. 2023;16:35-43. DOI:10.2147/JIR.S397079.
55. Zhang Y, Zhang H, Jiang B, Yan S, Lu J. A promising therapeutic target for psoriasis: Neuropeptides in human skin. Int Immunopharmacol. 2020;87:e106755. DOI:10.1016/j.intimp.2020.106755.
56. Tan CMJ, Green P, Tapoulal N, Lewandowski AJ, Leeson P, Herring N. The Role of Neuropeptide Y in Cardiovascular Health and Disease. Front Physiol. 2018 Sep 19;9:1281. DOI: 10.3389/fphys.2018.01281.
57. Zukowska-Grojec Z, Karwatowska-Prokopczuk E, Fisher TA, Ji H, Yeh Y, Boss GR, *et al*. Neuropeptide Y: A novel prognostic marker in cardiovascular disease. Peptides. 2010;31(5):1012-1017. DOI:10.1016/j.peptides.2010.02.010.
58. Rodrigues SF, Granger DN. Blood cells and endothelial barrier function. Tissue Barriers. 2015;3(1-2):e978720. DOI:10.4161/21688362.2014.978720.
59. Chen L, Yu C, Lyu J, Zhang B, Chen X, Xu N, *et al*. Development and application of a multiplex ELISA for simultaneous detection of cardiovascular disease biomarkers. Clin Chim Acta. 2021;517:108-115. DOI:10.1016/j.cca.2021.03.003.
60. Stasi C, Milani S. Biomarkers in inflammatory bowel disease: clinical utility and perspectives. World J Gastroenterol. 2016;22(27):8175-8185. DOI:10.3748/wjg.v22.i27.8175.
61. Branisteanu DE, Nicolescu AC, Branisteanu DC, Branisteanu CI, Dragoi AC, Bogdanici CM, *et al*. Cardiovascular comorbidities in psoriasis (Review). Exp Ther Med. 2022;23(2):152. DOI:10.3892/etm.2021.11075.
62. Armstrong EJ, Harskamp CT, Armstrong AW. Biologic therapy in psoriasis: cardiovascular safety and implications. Curr Dermatol Rep. 2013;2(4):240-248. DOI:10.1007/s13671-013-0056-5.
63. Zhou J, He Z, Wang T. Y1 receptor antagonist BIBO 3304 suppresses inflammation in a murine model of psoriasis. Eur J Pharmacol. 2019;856:172410. DOI:10.1016/j.ejphar.2019.172410.
64. Peng S, Wu WQ, Li LY, Shi YC, Lin S, Song ZY. Deficiency of neuropeptide Y attenuates neointima formation after vascular injury in mice. BMC Cardiovasc Disord. 2023 6;23(1):239. DOI: 10.1186/s12872-023-03267-y.
65. Martin JR. The Y1 receptor subtype mediates the cardiovascular changes evoked by NPY administered into the posterior hypothalamic nucleus of conscious rat. Brain Res. 2004 Mar 26;1002(1-2):11-20. DOI: 10.1016/j.brainres.2003.12.002.

How to Cite This Article
Daifalla AEM, El Sayed AGA, Abd Al-naby MS, Omar DF, Hussien AHM. Serum neuropeptide Y as a mediator between psoriasis and cardiovascular disease: a review article. International Journal of Dermatology, Venereology and Leprosy Sciences. 2025;8(2):85-91.