Review paper

Dialogue between programmed cell death and psoriasis

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Abstract

Psoriasis is a chronic inflammatory skin condition, associated with both physical and psychological burden. The aetiology of psoriasis is not fully understood. Physiologically programmed cell death (PCD) pathways are crucial for maintaining organismal homeostasis. Several investigations have highlighted the link between dysregulated PCD and the initiation of psoriasis. This review aims to outline various forms of programmed cell death pathways, encompassing the psoriasis distinctive features, triggers, implications in psoriasis pathogenesis, and therapeutic opportunities. It aspires to offer a comprehensive exploration of the role of programmed cell death in the context of psoriasis, providing a rational framework for further investigation and potential therapeutic interventions.

Key words: psoriasis, programmed cell death, apoptosis, ferroptosis, pyroptosis, autophagy.

Introduction

Psoriasis is a non-communicable, chronic inflammatory skin condition, which causes rapid proliferation of skin cells, resulting in the formation of plaques of thickened skin covered in scales. Psoriasis considerably impacts patients' quality of life and may contribute to psychological stress in a multitude of aspects in these patients [1, 2]. Programmed cell death (PCD) stands pivotal in various cellular processes, governing tissue growth, embryogenesis, cell turnover, immune response, and diverse biological mechanisms [3, 4]. Psoriasis is caused by a complex interplay between the immune system and the epidermis, which results in a multifaceted process that includes dysregulation of inflammatory responses and hyperproliferative epidermis [5, 6]. Notably, the evidence underscores the association between PCD and psoriasis, hinting at PCD as a prospective therapeutic avenue for addressing psoriasis [7–11].

This review navigates recent advancements in programmed cell death studies, encompassing the evolving understanding of the potential roles of distinct cell death mechanisms in psoriasis. Emphasis is placed on elucidating apoptosis, autophagy, pyroptosis, and ferroptosis concerning their implications in psoriasis pathology (Table 1).

Psoriasis and apoptosis

Apoptosis is a regulated and fundamental programmed cell death, crucial for maintaining the homeostasis and normal physiological function of living organisms [12]. However, aberrations in the apoptosis process can lead to various diseases. Psoriasis is a prevalent chronic inflammatory skin disease characterized by hyperproliferation and incomplete differentiation of epidermal keratinocytes, resulting in marked thickening of the epidermis. This condition is associated with abnormal apoptotic processes [13–15]. The viewpoint is different, some scholars believe that there are pro-apoptotic genes in psoriatic lesions, but some scholars believe that the expression of genes that inhibit apoptosis is up-regulated and there is apoptosis resistance in psoriatic lesions. Psoriatic keratinocytes exhibit robust anti-apoptotic capabilities, potentially representing a key pathogenesis of psoriasis. Psoriasis is characterized by abnormal expression of molecules involved in epidermal apoptosis, leading to the inhibition of apoptosis processes [16].

In recent years, an increasing number of studies have focused on apoptosis in psoriasis, exploring a diverse array of genes, proteins, and pathways. Below, we enumerate several key mechanisms of apoptosis in psoriasis. In keratinocytes from patients with psoriasis, a crucial death receptor signalling inhibitor is present: cellular FADD-like interleukin-converting enzyme inhibitory protein (C-FLIP). It acts on Fas-associated death domain protein (FADD) and procaspase-8, preventing FADD binding to caspase-8, thereby inhibiting the occurrence of the apoptotic cascade, enabling continuously proliferation of keratinocytes [17]. This is one of the pathogenetic factors in psoriasis. Caspase-9 is primarily involved in apoptosis, and Oztas *et al.* [18] observed a significantly decreased

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Table 1. Programmed cell death involved in psoriasis

Classes	Role in psoriasis	Function in psoriasis	Pathway	Reference
Apoptosis	Inhibit	keratinocytes	TNF-α/Bcl-xL	16
Apoptosis	Promote	Keratinocytes	Caspase-1/IL-lβ	18
Apoptosis	Promote	Keratinocytes	p38 MAPK/caspase-1/IL-18	19
Apoptosis	Inhibit	Keratinocytes	C-FLIP/FADD/caspase-8	20
Apoptosis	Inhibit	Keratinocytes	Caspase-9	21
Apoptosis	Inhibit	Keratinocytes	Fas	22
Apoptosis	Inhibit	Keratinocytes	Methylation levels in the WIF1 promoter region	24, 25
Ferroptosis	Promote	Psoriasis vulgaris	Lipid ROS/ferrous iron	36
Ferroptosis	Promote	NA	PEBP1, PRKAA2, ACSF2	37
Ferroptosis	Promote	Keratinocytes	MDA/ROS/Fe^{2+} accumulation, ACSL4/TNF-α/IL-6/IL-8	43
Pyroptosis	Promote	Keratinocytes	SLC46A2-NOD1	58
Pyroptosis	Promote	Macrophages	IL-1β, IL-6, TNF-α, NLRP3 and p-p65	59
Pyroptosis	Promote	Macrophages	GSDMD/caspase1/NLRP3	60
Pyroptosis	Promote	Macrophages	NLRP3, IL-1β and caspase-1	61
Autophagy	Inhibit	Keratinocytes	AP1S3	74
Autophagy	Inhibit	Keratinocytes	PI3K/Akt/mTOR	78
Autophagy	Inhibit	CD4+T	IL-17A/RORC/IFN-γ	80
Autophagy	Inhibit	Keratinocytes	lncRNA MEG3 blocks the PI3K/AKT/mTOR signalling activation	81
Autophagy	Inhibit	Keratinocytes	Fisetin inhibited Akt/mTOR	84

caspase-9 expression in psoriatic lesions, explaining the reduced apoptosis in these lesions. Additionally, Takahashi *et al.* [16] demonstrated increased expression of the anti-apoptotic Bcl-xL protein in psoriatic epidermis compared to normal epidermis. TNF-α has been shown to upregulate the expression of the Bcl-xL gene, as well as Bcl-2 and genes encoding Bax pro-apoptotic proteins in psoriasis. A member of the TNF family, the Fas receptor, is believed to play a significant role in the development of psoriasis. Takahashi *et al.* clearly demonstrated a significant increase in Fas expression in psoriatic keratinocytes compared to normal epidermis. In another study, Mysliwiec *et al.* [19] found a significant increase in soluble Fas protein, considered an inhibitor of apoptosis, in the serum of psoriasis patients compared with healthy individuals. DNA methyltransferases (DMNTs) are important for maintaining DNA methylation in cells. Keratinocytes express DNMT1, DNMT3A, and DNMT3B [20]. Under physiological conditions, DNMT1 plays an important role in maintaining epidermal progenitor cell function and inhibiting epidermal differentiation. Recent studies have shown that ingenol can improve psoriasis model symptoms in mice by inhibiting DNMT1 activity thereby reducing methylation levels in the WIF1 promoter region, inhibiting keratinocyte proliferation and inducing apoptosis [21, 22].

It is evident that restoring normal apoptosis mechanisms plays an important role in enhancing the homeostasis of psoriatic epidermal cells. Research has increasingly focused on various treatments for psoriasis related to apoptosis. Biopharmaceutical studies of TNF-α have demonstrated its significant role in modulating the activity of apoptotic and pro-apoptotic protein. Kokolakis *et al*. [23] showed that TNF-α antagonists have significant efficacy for the treatment of psoriasis. Yu *et al*. similarly reported a positive effect of biopharmaceuticals in psoriasis patients [24]. This implies that gaining a better understanding of the mechanism of action of TNF-α in psoriasis could pave the way for innovative treatments. Etanercept has proven effective in treating psoriasis and demonstrates increased efficacy when combined with methotrexate [25]. Methotrexate monotherapy has also been shown to markedly decrease the expression of genes encoding Bcl-xL, c-FLIP, NFκB, p65, and pAkt1, and significantly increase caspase-9 expression. This suggests that methotrexate plays an important role in inducing the mitochondrial apoptosis pathway [26]. In a recent study by Shi *et al.* on the effect of oxymatrine on apoptosis in psoriatic epidermal cells, oxymatrine inhibited apoptosis by increasing the expression of anti-apoptotic Bcl-2 protein, and the study confirmed that oxymatrine significantly reduced psoriatic lesions [25]. Therefore, a thorough exploration of the mechanism linking apop-

tosis in psoriasis holds significant potential for guiding the identification of drug targets in psoriasis treatment. Investigating keratinocyte apoptosis to explore microscopic indicators for the diagnosis of psoriasis will become a key direction in psoriasis treatment.

The research on psoriasis and apoptosis has revealed the important role of apoptosis in the pathogenesis of psoriasis. Upregulation of genes that inhibit apoptosis and resistance to apoptosis are the main mechanisms. However, some researchers believe that the expression of pro-apoptotic genes also plays a role in the occurrence and development of psoriasis. For example, the presence of cysteinyl aspartate specific protease (caspases) in tissue cells regulates the entire dynamic process of apoptosis, determining the direction and final destination of apoptosis [27]. Recently, caspases have been implicated in psoriasis. Johansen *et al.* [28] reported significantly elevated expression of caspase-1 in lesional biopsies from psoriasis patients. Sun *et al*. [29] identified caspase-1 as an upstream factor of IL-1β in human normal keratinocytes, inducing IL-1β maturation and participating in inflammatory responses in psoriatic lesions. The pathogenesis of psoriasis is complex and involves multiple factors. The role of apoptosis in the development and progression of psoriasis is not yet fully understood. Apoptosis can influence the onset and progression of the disease through its occurrence in different cells and at various stages of the disease. In-depth research into the apoptotic signalling pathways and their regulatory mechanisms in psoriasis can provide a theoretical basis for developing new therapeutic strategies. Future research will continue to explore the specific role of apoptosis in psoriasis and seek effective interventions to improve treatment outcomes for the disease.

Psoriasis and ferroptosis

In 2012, Dixon *et al.* identified the oncogenic RAS-selective lethal small molecule, erastin, which induces a distinctive iron-dependent form of programmed cell death termed ferroptosis [30]. Ferroptosis is morphologically, biochemically, and genetically distinct from apoptosis, necrosis, and autophagy [30, 31]. In ferroptosis, an excessive accumulation of ferrous iron within cells via the Fenton reaction promotes the generation of reactive oxygen species (ROS), leading to the destruction of antioxidant system and subsequent lipid peroxidation [32]. Currently, the mechanism of ferroptosis is closely linked to the disturbed balance of iron homeostasis, inhibition of cystine/glutamate antiporter (system x_c^-), glutathione (GSH) depletion and degradation of glutathione peroxidase 4 (GPX4) activity [33–36]. Recent studies have shown that ferroptosis may represent a novel mechanism in the development of psoriasis, with differentially expressed ferroptosis related genes identified in psoriasis [36, 37]. Therefore, we explored the relationship between ferroptosis and psoriasis to provide novel clues to elucidate the pathogenesis of psoriasis.

Iron metabolism is closely related to psoriasis. Numerous studies have demonstrated statistically lower levels of serum Fe, transferring receptor (TRF) and total iron binding capacity (TIBC) in patients with psoriasis compared to normal controls. Additionally, higher hepcidin levels were observed in psoriasis patients [38–40]. In the majority of cases, the hypoferremia observed in skin disease is attributed to a metabolic abnormality in iron metabolism [41]. Therefore, the disrupted iron metabolism in psoriasis patients provides the basis for the occurrence of ferroptosis. Leveque *et al.* observed elevated iron in the dermis of psoriatic patients [42]. Substantial evidence suggests that psoriasis is mediated by oxidative stress, and iron can catalyse the synthesis of reactive oxygen species (ROS). Iron, which is trapped in the dermis, promotes oxidative stress and further promotes the development of psoriasis. Recently, researchers have increasingly identified a connection between ferroptosis and psoriasis, suggesting that the activation of ferroptosis can contribute to the formation of skin lesions in psoriasis [36]. In a bioinformatics analysis illustrating functions of ferroptosis-related genes (FRGs) in psoriasis, Wu *et al.* proposed that PEBP1, PRKAA2 and ACSF2 are associated with ferroptosis and participate in regulating immune microenvironment in psoriasis cases [37]. In the work of Li *et al*., they observed increased levels of lipid ROS and ferrous iron in the epidermis of psoriasis vulgaris (PV) patients and confirmed the activation of ferroptosis in both PV patients and psoriasis-like mice models [36]. Liu *et al*. had shown that erastin, a ferroptosis inducer, significantly inhibited keratinocyte viability, promoted the accumulation of MDA, ROS and Fe^{2+}, and enhanced the expression of ferroptosis related genes expression, such as ACSL4, TNF-α, IL-6 and IL-8 [43]. Recently Li *et al.* confirmed that ferroptosis activation owing to iron overload underlies the pathogenesis of psoriasis [36]. Altogether, iron metabolism disorders and iron overload in the dermis leading to ferroptosis may be one of the pathogenic mechanisms of psoriasis. Ferroptosis directly affects cells, such as inhibiting the vitality of keratinocytes and disrupting the cellular microenvironment. On the other hand, the occurrence of ferroptosis is accompanied by oxidative stress and the accumulation of lipid peroxides, both of which promote the occurrence and development of psoriasis. Therefore, ferroptosis may be one of the therapeutic targets for psoriasis.

The ongoing improvement in understanding ferroptosis has led to extensive research on various drugs and compounds for the treatment of psoriasis induced by iron overload. Shou *et al.* revealed an expression pattern of ferroptosis wherein specific molecules enhance inflammatory reactions in psoriasis [44]. Ferrostatin-1 (Fer-1), a potent inhibitor of lipid peroxidation, suppressed ferroptosis in erastin-treated keratinocytes and exhibited

a positive effect on the treatment of psoriatic lesions by inhibiting inflammatory responses [10]. Additionally, inhibiting ACSL4, a gene related to ferroptosis, could attenuate the pro-inflammatory effect of ferroptosis inducer erastin in keratinocyte [43]. Lu *et al*. showed that biomimetic iron single-atom catalysts (FeN4O2-SACs) with ROS scavenging capability can be utilized for the treatment and relapse prevention of psoriasis via the restoration of the related gene [45]. However, the role of ferroptosis in the occurrence and development of psoriasis is not yet fully understood, such as whether ferroptosis is mainly related to the occurrence of early psoriasis. Therefore, a new therapeutic target for the prevention and treatment of psoriasis has emerged, which is to inhibit the occurrence of ferroptosis, but the obstacles are many and still more clinical trials are required.

Psoriasis and pyroptosis

Pyroptosis, an inflammatory form of programmed cell death, distinguishes itself from traditional apoptosis and necrosis. Typically instigated by the activation of the distinct inflammatory caspase family [46, 47], pyroptosis is characterized by cellular swelling, rupture, and a cascade of robust inflammatory responses. Moreover, the occurrence of pyroptosis relies on pivotal executor molecules in the gasdermin protein family, comprising GSDMA, GSDMB, GSDMC, GSDMD, and GSDME [48]. Upon cellular stimulation, proteins within the gasdermin family undergo cleavage activation, releasing N-terminal domains with pore-forming activity. These domains bind to cell membrane phospholipids, inducing oligomerization and forming stable membrane pores, ultimately leading to the release of a plethora of pro-inflammatory cytokines and the generation of danger signals [49, 50]. Research has already highlighted the predominant role of pyroptosis in immune regulation, inflammatory diseases, and antimicrobial defence [51–53]. The relationship between pyroptosis and psoriasis, a chronic autoimmune inflammatory skin disease, has undoubtedly become a focal point for scientists. In recent years, researchers have extensively and comprehensively explored the intricate mechanisms and relationship between these two phenomena, revealing the potential pivotal role of pyroptosis in the onset and progression of psoriasis.

Keratinocytes are the predominant cells implicated in psoriasis [54]. Deng *et al*. identified a virulence factor, Streptococcus pyogenes cysteine protease (SpeB), in their study, revealing its ability to induce relaxation in cornification cells by cleaving GSDMA. GSDMA, a key executor of inflammatory cell death or pyroptosis and a prominent member of the gasdermin protein family, releases an active N-terminal domain upon cleavage, triggering keratinocyte pyroptosis, is considered a major contributor to the relaxation of keratinocytes [55]. This finding implies a close association between keratinocytes and pyroptosis. In a recent single-cell transcriptome study, cells from stratum corneum in psoriatic skin exhibited high expression of GSDMA and GSDMC compared to control skin cells, while cells in stratum basal exhibited elevated expression of GSDMB. Notably, in this experiment, pyroptosis-related genes expression was downregulated in stratum corneum cells, while genes such as CASP1, CASP8, GSDMA, GSDMB, and GSDMD associated with pyroptosis were upregulated in stratum basal cells. This indicates a close connection between pyroptosis and psoriasis [9]. In addition, recently, in psoriasis lesions, GSDME was also found to be significantly up-regulated, and GSDME$^{-/-}$ could reduce the progress of psoriasis by reducing the inflammation of keratinocytes [56, 57], which further indicated that cell apoptosis was involved in the progress of psoriasis. However, further in-depth research is needed to understand how pyroptosis exerts its biological effects in psoriasis. In a study by Bharadwaj *et al*., methotrexate, a commonly used treatment for psoriasis, was found to inhibit skin inflammation in psoriasis primarily through the SLC46A2-NOD1 signalling axis. The specific mechanism involves SLC46A2 activating NOD1/2 to deliver DAP-muropeptides to keratinocytes, subsequently triggering pyroptosis through caspase-1 and GSDMD [58]. Beyond skin keratinocytes, the functions of macrophages and other immune cells are equally critical in the progression of psoriasis. Zhang *et al*. utilized bioinformatics methods to identify a significant upregulation of the pyroptosis-related gene NLRP3 in skin lesions of psoriasis patients. Subsequent validations using imiquimod-induced psoriasis mouse models and LPS-induced macrophages confirmed this finding. Treating mice with a specific inhibitor of NLRP3, MCC950, resulted in a reduced psoriatic lesion area, severity index score, hyperplasia, and inflammation in mice [59]. This suggests that macrophage pyroptosis is involved in the progression of psoriasis. Similarly, in an imiquimod-induced psoriasis mouse model, treatment with cycloartenol (CAG) inhibited NLRP3-mediated macrophage pyroptosis and improved IMQ-induced psoriasis by reducing the expression of caspase-1 and GSDMD [60]. Additionally, in the same psoriasis mouse model, chloroquine diphosphate (CQD), a historically used topical antimicrobial for skin and vaginal infections, was found to reduce the severity of psoriatic reactions by inhibiting the activation of NLRP3 inflammasomes in macrophages [61]. This suggests that, aside from regulating pyroptosis in keratinocytes, modulating immune pyroptosis may be a crucial strategy for treating psoriasis. However, the development of specific treatment methods requires further experimental validation. NLRP1, another member of the NLRP family, was found to increase its expression in psoriasis, and it can affect the secretion of IL-1β and IL-18 in keratinocytes, suggesting that NLRP1 can affect the progression of psoriasis by affecting the pyroptosis of keratinocytes [62, 63]. However, the specific mechanism

needs to be further explored by designing corresponding gene knockout mice.

In summary, through a comprehensive analysis and deeper understanding of the role of pyroptosis in the onset and progression of psoriasis, we can enhance our comprehension of the pathophysiological processes of this chronic skin disease. Furthermore, this association not only provides a new perspective for the study of psoriasis but also furnishes valuable insights for potential future therapeutic strategies. Delving into the relationship between pyroptosis and psoriasis holds promise for uncovering novel directions in the development of more effective treatment modalities and interventions.

Psoriasis and autophagy

Autophagy is a process that maintains intracellular homeostasis by eliminating defective proteins and damaged organelles [64]. It is categorized into three types: macroautophagy, microautophagy, and molecular chaperone-mediated autophagy. Among them, the most classical type is macroautophagy, commonly known as "autophagy" [65]. The process of autophagy encompasses the induction of autophagy, the generation of autophagosomes, the fusion of autophagosomes within lysosomes, and the enzymatic degradation and recirculation of autophagosome contents within lysosomes. Autophagy initiation begins with the induction of autophagy by a complex composed of UNC51-like kinase (ULK1), FAK family kinase-interacting protein 200 (FIP200), and autophagy-associated protein 13 (Atg13). Mammalian target of rapamycin (mTOR) is a highly conserved kinase that interacts with a variety of proteins to form two distinct complexes, rapamycin complex 1 (mTORC1) and rapamycin complex 2 (mTORC2), involved in the regulation of autophagy [66, 67]. Under nutrient-rich conditions, mTORC1 binds to the ULK1 kinase complex and phosphorylates ULK1 to inhibit autophagy. Conversely, it induces autophagy [68, 69]. Phosphatidylinositol 3 kinase (PI3K), a member of the lipid kinase family, produces phosphatidylinositol 3,4,5-trisphosphate in the plasma membrane to recruit and activate downstream signalling molecules [70]. In turn, PI3K and its product PI(3,4,5)P3 can activate Akt/PKB, which activates mTOR to inhibit autophagy [71].

Growing evidence suggests a strong association between autophagy and psoriasis. Studies have reported a significant decrease in expression of autophagy markers, including LC3 protein and ULK1 in psoriatic lesions compared to normal skin [72, 73]. Several studies on the role of autophagy in psoriasis have revealed that aberrant autophagy leads to production of inflammatory cytokines and hyperproliferation of keratinocytes [69, 74–76]. IL-17A is a well-known key effector in psoriasis [77]. Varshney *et al.* study also found that IL-17A-induced activation of the PI3K/Akt/mTOR signalling pathway by KC to inhibit autophagosome formation and enhancement of autophagic flux to inhibit autophagy. Meanwhile, the role of autophagy in psoriasis was further confirmed by the reduced expression of LC3-II in psoriatic lesional skin compared with non-lesional skin, and the induction of autophagy in keratinocytes by the anti-psoriasis drug methotrexate [78]. In addition, there is growing evidence that dysfunctional autophagy-induced inflammation leads to increased skin inflammation in psoriasis [74, 79]. For example, the gene AP1S3, involved in autophagosome formation, is mutated in psoriasis patients, and keratinocytes deficient in AP1S3 exhibit defective autophagy, promoting skin inflammation [79]. This also suggests that autophagy is involved in the pathogenesis of psoriasis. Said *et al.* also found that the autophagy inhibitor chloroquine exacerbates psoriasis progression by promoting the secretion of the pro-inflammatory cytokine IL-23 by Langerhans-like cells, which in turn promotes the production of IL-17 by CD4+ T-cells [80]. Tang *et al.* discovered that overexpression of the lncRNA MEG3 blocks the PI3K/AKT/ mTOR signalling activation, promotes autophagy and inhibits inflammation in TNF-α-treated keratinocytes and psoriatic mice, and provides a potential therapeutic target for psoriasis [81]. These results reflect that the induction of autophagy disorders exacerbates psoriasis and reveal a potential role for autophagic mechanisms in psoriasis. In short, autophagy serves as a protective mechanism in psoriasis.

Rapamycin is an inhibitor of mTOR (mechanistic target of rapamycin) complex 1 (mTORC1). mTORC1 signalling is implicated in the control of autophagy [68]. Rapamycin is commonly used as an autophagy inducer in *in vitro* studies [82]. Kim *et al.* found that rapamycin increased the expression of autophagy-associated proteins, inducing autophagy and thereby alleviating IMQ-induced inflammation in psoriasis mice [83]. Similarly, topical application of a selective ULK1 inhibitor, SBI0206965, significantly attenuates epidermal hyperplasia, neutrophil infiltration, and psoriasis-associated marker transcription in IMQ-induced psoriasiform dermatitis by modulating keratinocytes and its interaction with neutrophils [73]. In an IMQ-induced mouse model of psoriasis, Roy *et al.* demonstrated that administration of fenofibrate effectively inhibited the IL-17A and Akt/mTOR pathways. This promoted keratinocytes differentiation and autophagy, leading to a reduction in epidermal thickness and alleviation of skin inflammation in mice [84]. Similarly, fenofibrate, a small molecule drug targeting IL-17a, controls inflammation in psoriasis by modulating downstream signalling pathways (NF-κB and MAPK pathways) and inducing ULK1-mediated autophagy to regulate cytokine secretion [85]. In addition to conventional medications, a number of herbal medicines including matrine, PSORI-CM02 (an empirical herbal formula consisting of turmeric, red peony, comfrey, poria, and umeboshi), and Jueyin granules, have all been shown to ameliorate psoriasis by inducing the autophagic path-

way [86–88]. All of these studies showed that increased autophagy significantly inhibited skin inflammation and improved psoriasis-like symptoms. Conversely, inhibition or impairment of autophagy exacerbated the inflammatory response. Overall, autophagy serves as a protective mechanism against inflammation in psoriatic skin, and is a potential target for the treatment of psoriasis.

Summary and outlook

Given the intricate nature of the disease, diverse forms of cell death manifest in specific or multiple cell types at various stages of psoriasis. Previous studies suggest pivotal roles of pyroptosis and apoptosis in fostering inflammation and psoriasis pathogenesis [7, 59, 89]. The autoimmune milieu hints at the potential involvement of ferroptosis in modulating cellular metabolism [9, 44]. Conversely, some studies indicate a positive association between autophagy and psoriasis [76, 90, 91].

The interplay between psoriasis and cell death represents a multifaceted domain, warranting further exploration to unravel the intricate molecular mechanisms and interactions underlying the correlation with psoriasis. Large-scale genome association studies stand to unveil common genetic variants intricately linked with the intrinsic cell death machinery implicated in psoriasis. Additionally, the exploration of inhibitors targeting cell death pathways shows promise in ameliorating psoriasis progression. However, substantial strides are needed before the clinical application of these strategies in psoriasis.

In conclusion, comprehending the intricate association between psoriasis and cell death holds promise for fostering novel therapeutic approaches and preventive strategies for managing and preventing chronic diseases linked with psoriasis. This understanding promises to enhance the management and prevention of chronic diseases entwined with psoriasis.

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Ethical approval

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Conflict of interest

The authors declare no conflict of interest.

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