Original Research

Journal of Advanced Veterinary Research
(2025) Volume 15, Issue 4, 487-491

The expression pattern of the vitamin D receptor gene (VDR) and the related cytokine response in horses with allergic dermatitis

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ARTICLE INFO

Recieved: 16 September 2025

Accepted: 28 September 2025

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Keywords:

Skin atopy, Equine, IL-1β, TNF-α, Vitamin D

ABSTRACT

Allergic dermatitis in horses is a prevalent clinical issue due to food allergy or insect bites and stings. The purpose of this research was to assess the correlation of the Vitamin D Receptor (VDR) gene and cytokines in horses suffering from allergic dermatitis. Forty horses diagnosed with allergic dermatitis and five clinically healthy horses were investigated. Serum concentration of tumor necrosis factor alpha (TNF-α) and interleukin-1β (IL-1β) was evaluated, and real-time PCR was conducted for relative quantitation of the mRNA expression level of the VDR gene in the blood samples of the horses. The horses with allergic dermatitis presented with pruritus, scabbing, alopecia confined to the lesion site, anxiety, and redness of the skin clinically. There was considerable elevation in IL-1β ($p < 0.01$) and TNF ($p < 0.01$) levels in horses with allergic dermatitis relative to clinically healthy horses. However, expression of the VDR gene was reduced ($p < 0.001$) considerably in horses with allergic dermatitis relative to controls. There was considerable correlation of IL-1β with TNF-α levels ($p < 0.001$). Conversely, a negative correlation was noted between VDR expression and levels of IL-1β and TNF-α. In conclusion, the findings in this study show that the VDR gene has a critical role to play in the context of allergic dermatitis in horses. More research needs to be conducted on the possibility of vitamin D as a preventative treatment for allergic dermatitis in clinical practice.

Introduction

Horses' health and well-being can be negatively affected by skin diseases; the disease can be exacerbated by delays in diagnosis and initiation of effective treatment regimens, and clinical signs sometimes do not help the similarity despite different causes (contagious versus non-infectious) (Scott and Miller, 2011). Horses are exposed to a large variety of potential allergens in the environment. Therefore, when a horse develops skin hypersensitivity, it is often difficult to determine the allergen responsible (Lorch *et al*., 2001)

Skin hypersensitivity has important effects on horses and their owners, such as hypersensitivity to Culicoides and atopic dermatitis (sweet itch, summer eczema). Itching, alopecia, and discomfort are the characteristic symptoms of these diseases. Clinical symptoms can become so severe that animals can injure their skin and become unable to function (Haegen *et al*., 2001; Wilson *et al*., 2001).

The pathogenesis of Hypersensitivity Dermatitis is dictated by the disappointment of T helper cell differentiation (Th) and cytokine emission profiles. Several proinflammatory cytokines and chemokines, such as IL-1 and tumor necrosis factor (TNF) (Nassif *et al*., 2004; Caproni *et al*., 2006; Nomura *et al*., 2011).

In acute or chronic dermatitis, cytokines are among the first mediators to be released and are implicated in various dermatological diseases (Stamatas *et al*., 2013; Akdis *et al*., 2016). Recent studies have also implicated inflammatory cytokines in allergic diseases such as contact dermatitis, atopic dermatitis, and some forms of urticaria (Abramovits *et al*., 2013; Yamanaka and Mizutani, 2015). Recent findings indicate that IL-1β not only causes skin rashes in autoimmune inflammatory diseases (Nakamura *et al*., 2009) but also plays a role in other allergy-related diseases such as bronchial asthma (Birrell and Eltom, 2011), atopic dermatitis (AD), and contact hypersensitivity (Watanabe *et al*., 2007).

Interleukin-1β is the primary secreted form of IL-1 and was initially identified as a lymphocyte activation agent that promotes B cell activation. This cytokine is mainly produced by activated macrophages, dendritic cells, and monocytes and mediates the inflammatory response through various cell activities such as cell proliferation, differentiation, and apoptosis (Nakae, 2003). TNF-α is the most frequently investigated multidirectional cytokine of the TNF family. Under pathological conditions, high TNF-α levels lead to characteristic inflammatory reactions in many diseases (Mukhopadhyay *et al*., 2006).

Vitamin D plays a major role in growth, differentiation of multiple cells, and calcium homeostasis (Adams and Hewison, 2008). It activates cells responsible for both innate immunity and adaptation, with gene expression of the vitamin D receptor (VDR) in response to 1,25-dehydroxycholecalciferol (Adorini and Penna, 2008). Vitamin D3, the active form of Vitamin D, not only controls calcium and bone metabolism but also plays a role in immune modulation in monocytes, macrophages, and activated lymphocytes mediated via their receptor binding (VDR) (Lương and Nguyễn, 2012). VDR is present in many immune cells, such as macrophages, dendritic cells, and T and B lymphocytes (Toubi and Shoenfeld, 2010) and plays a complex role in the host immune response after stimulation (Hewison, 2010).

To the best of our knowledge, there are limited studies on the impact of Vitamin D on horses with skin diseases. This study aimed to clarify the association between VDR gene expression and related cytokines in horse allergic dermatitis.

Materials and methods

Horses and management

Forty-five horses were aged between 1 and 10 years old. Forty of these horses presented with the clinical presentation of skin disorders due to allergic reactions. Five apparently healthy horses were selected

ISSN: 2090-6277/2090-6269/

for this study's control group based on clinical evaluation. The study was conducted in Egypt's Dakahlia Province between December 2017 and November 2018. All the donkeys used in the study were given a balanced ratio of ground maize supplemented with trace elements and mineral mix, 2.0 to 5.0 kg of mixed bran, and wheat straw chop. The Medical Research Ethics Committee, College of Veterinary Medicine, Mansoura University, Mansoura, Egypt, and all other institutional requirements for use and animal care were followed. Thorough information regarding the medical records, clinical observations, and full case history was gathered.

Clinical presentation

Detailed clinical examination was performed on the surveyed horses (Constable *et al*., 2017). The examination involved the identification of signs of allergic dermatitis (itching, scaling, scaly lesions, hair loss, dandruff, redness, inflammation, and flaking of the skin).

Blood samples

A pair of blood samples (5 ml each) was drawn by puncturing the jugular vein of each horse. The first sample was collected into an anticoagulant-containing tube (EDTA) to detect the mRNA level of the VDR gene. The second was drawn in a plain tube to separate the serum, which was kept at -80°C till analysis.

Cytokines

Serum levels of IL-Iβ and TNF-α were quantified using equine ELISA kits (CUSABIO, USA). Both tests were performed in two versions and the optical density was determined using the standard chromatography method.

Extraction of RNA and reverse transcription

Total RNA was extracted from whole blood samples using a QIAamp® RNA Blood Mini Kit (QIAGEN, Germany) according to the manufacturer's instructions. The purity was measured using a nanoparticle spectrophotometer (UV-Vis Spectrophotometer Q5000, Thermo Fisher Scientific, USA). cDNA was synthesized from each sample according to the manufacturer's protocol using (HiSenScript TM RH [-] cDNA synthesis kit (iNtRON Biotechnology, Korea). A total of 20 µl of reaction mixture was prepared (total RNA of up to 5 µl and 10 µl of 2x RT Reaction). The solution, 1 µl of the enzyme mixture solution, and DNase/RNase-free water up to 20 µl; the final reaction mixture was put into a thermal cycle and the following program was carried out: reverse transcription at 45°C for 1h, then RTase inhibition at 85°C for 10 min. Finally, cDNA samples were stored at -20°C.

Primer design

Primers were designed to express the vitamin D receptor gene through alignment of the following sequences of the vitamin D receptor in several species of equine (*Equus caballus* XM_005611070.3, *Equus asinus* XM_014850058.1, *Equus przewalskii* XM_008513615.1). The PCR product was 514 bp long (Table 1).

Table 1. Set of primer sequence for evaluation of genetic expression of vitamin D receptor (VDR) gene in horses.

Gene	Accession No#	Strand	Primer sequence 5′3′
VDR	NM_001163959.1	F	ATCCTGACAGATGAGGAGGTG
		R	GAGACAAGGCAGGGATCTGA
β-actin	XM_014834961	F	GGAGTAAACGGATTTGGCC
		R	CATGGGTGGAATCATACTGAAA

Real-time PCR

The mRNA level of the VDR gene in horse blood samples was quantified using real-time PCR with a Master Mix (SYBR Green with low ROX, Enzynomics, Korea). β-actin was used as the housekeeping gene with the following primer pair sequence (R: CATGGGTGGAATCATACTGAAA, F: GGAGTAAACGGATTTGGCC) (accession number XM_014834961).

Twenty microliters of reaction mixture were made of 10 µl TOPrealTM Qpcr 2x PreMIX, 1 µl of cDNA template, and 1 µl of 10 µl for each VDR forward and reverse primer (Equus cabalus) was used (F: ATCCTGACAGATGAGGAGGTG, R: GAGACAAGGCAGGGATCTGA) No. Inlet NM_001163959.1) surrounding exons 3 and 4 from the coding region of the VDR, and 7 µl of sterile ultra-pure DNase-free water was added to bring the total volume up to 20 µl. The PCR conditions were as follows: initial denaturation at 95°C for 10 min, followed by 40 cycles of denaturation at 95°C for 10 s, annealing at 59.2°C for 15s, and elongation at 72°C for 30s. At the end of the amplification phase, a melt curve analysis was performed to confirm the specificity of the PCR product. Relative mRNA expression was evaluated using the 2-ΔΔCt method (Livak and Schmittgen, 2001). Quantitative real-time PCR was performed to evaluate the VDR expression profile.

Statistical analysis

Data analysis was performed using commercial software (SPSS for windows V.20, SPSS, Chicago, USA). The data were checked for normal distribution patterns using the D'Agostino-Pearson test. The data were found to be normally distributed; consequently, the mean and standard deviation were calculated for each parameter. Data were analyzed using an independent samples t-test to determine which groups were statistically different. The correlation between the VDR expression pattern and the levels of the selected cytokines was determined using Pearson's correlation. The correlation between the coefficient and the p-value was recorded. For the statistics given, the results were considered significant at $p < 0.05$.

Results

The current study aimed to investigate the expression pattern of the vitamin D receptor gene in horses with allergic skin diseases. Allergic dermatitis was diagnosed based on the patient's history, clinical investigation, and biochemical analyses. The recorded clinical signs included itching, biting at his side, scab over, loss of hair, dandruff, redness, inflammation, and scaling of the skin.

Concerning the serum level of IL-1β, Figure 1 shows a significant increase ($p < 0.001$) of IL-1β in horses with allergic dermatitis compared to control horses (443.40±27.62 pg/ml vs 141.20±4.56 pg/ml).

Concerning the serum level of TNF-α, Figure 1 shows also a significant increase ($p < 0.001$) of TNF-α in horses with allergic dermatitis compared to control horses (645.10±22.86 pg/ml vs 272.10±13.21 pg/ml).

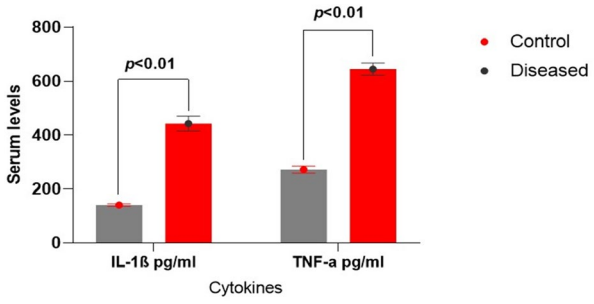

Figure 1. Serum level of TNF-α and IL-1β in healthy horses and in those with allergic dermatitis.

Regarding the gene expression of VDR in horses with allergic derma-

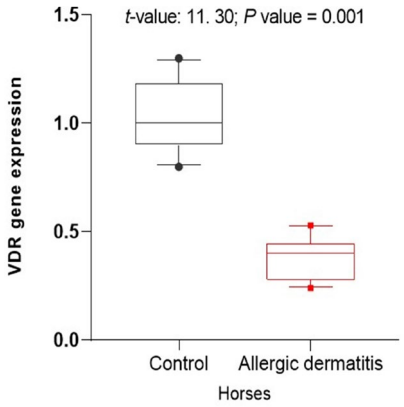

Figure 2. Vitamin D receptor (VDR) gene expression pattern in healthy horses and in those with allergic dermatitis.

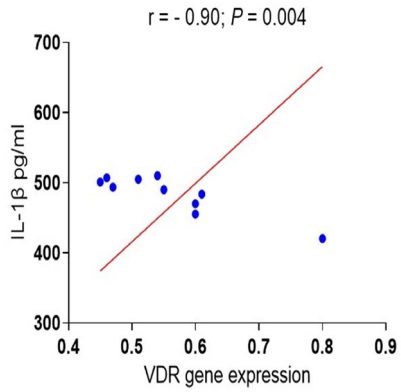

Figure 3. Correlation between serum of IL-1β level and VDR gene expression in horses with allergic dermatitis.

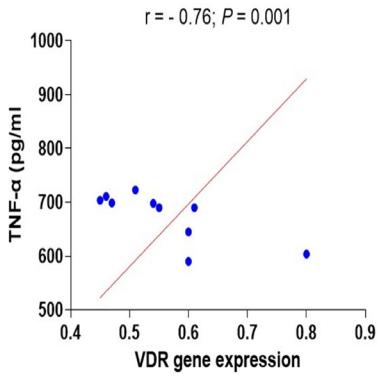

Figure 4. Correlation between serum level of TNF-α and VDR gene expression in horses with allergic dermatitis.

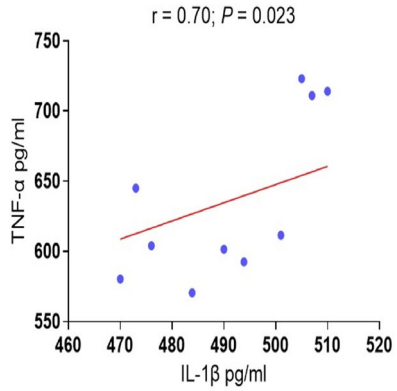

Figure 5. Correlation between serum levels of IL-1β and TNF-α in horses with allergic dermatitis.

titis, there was a significant downregulation ($p < 0.001$) compared with the control group (Figure 2).

Investigating the correlations among the measured parameters indicated that there was a negative correlation between the VDR gene and IL1β and TNFα in horses with allergic dermatitis (Figures 3-4). However, there was a positive correlation between IL1β and TNFα levels (Figure 5).

Discussion

Allergy is a multifaceted condition influenced by both genetic and environmental factors that play a role in disease development (Ahmad *et al.*, 2018). This study examined the relationship between VDR expression and cytokine levels in horses with allergic dermatitis.

Clinically, horses with allergic dermatitis exhibit pruritus, redness of the skin, anxiety, scab formation, and regional alopecia. Among all clinical findings, pruritus was recorded in 100% of the affected horses (Table 2). These findings were in accordance with those previously described (Marsella, 2024). Insect bite hypersensitivity (IBH) is initially characterized by papules, followed by severe itching, which are the most common clinical symptoms (van den Boom and Ducro, 2008). Itching leads to self-trauma, causing hair loss, flaking, and thickening of the skin (Björnsdóttir *et al.*, 2006; van den Boom and Ducro, 2008).

Table 2. Clinical findings in 40 horses with allergic dermatitis.

Clinical signs	Horses (n=40)	%
Pruritus	40	100
Scab	31	77.5
Regional loss of hair	30	75
Dandruff	31	77.5
Redness	33	82.5
Inflammation	35	87.5

In pruritus, various cells and pathogens can interact with nerve endings and contribute to the itching (Steinhoff *et al.*, 2006).. Histamine is the primary trigger of pruritus, as it activates cutaneous sensory nerves (Gould *et al.*, 2003; Ohsawa and Hirasawa, 2014), although it has also been shown that mast cell tryptase can have itching effects (Kawakami *et al.*, 2009). Furthermore, substance P (SP) found in mast cells acts as a mediator of itching. When receptors or ion channels are stimulated, sensory nerve endings release nerve mediators that convey itch signals to the spinal cord and the brain (Steinhoff *et al.*, 2006). VDR was significantly downregulated in the present study. In comparison to the healthy skin of the control group, Darwish *et al.* (2013) established a significant decrease in the expression of VDR in atopic dermatitis lesions. This signifies that the increased susceptibility of patients to skin infections was caused by the decreased expression of an antimicrobial peptide.

Active vitamin D metabolites reduce the production and expression of pro-inflammatory cytokines, such as TNF-α and IL-1β, by exerting anti-inflammatory effects on the inflammatory monocyte profile (Giulietti *et al.*, 2007; Neve *et al.*, 2013; Pilz *et al.*, 2013). Cells expressing membrane vitamin D receptors have some direct actions on vitamin D (Vuolo *et al.*, 2012). However, gene expression regulation accounts for most of the physiological effects of vitamin D. 1, 25 dihydroxyvitamin D (1, 25 $(OH)_2D_3$, the active form of vitamin D) interacts with high specificity and affinity to its nuclear receptor (nVDR).

The current study showed a considerable increase in IL1β. According to Hay *et al.* (2013), atopic dermatitis patients had a statistically significant ($P<0.001$) higher level of IL1β than controls. Its function as an inflammatory starter in AD can be explained by the fact that IL-1β is responsible for acute-phase reactions to inflammation (O'Neill, 2008).. Furthermore, in a rat model of cervical spondylosis, Yin *et al.* (2018) reported that the level of tumor necrosis factor α and the serum level of interleukin IL-1β were considerably higher than those in the control group, and non-immune

cells, such as keratinocytes, also secrete IL-1β, in addition to immune cells, such as dendritic cells, neutrophils, B lymphocytes, NK cells, and monocytes/macrophages (Dinarello, 2009; Feldmeyer *et al*., 2010). A wide variety of cell types can be affected by IL-1β (Dinarello, 2009; Dinarello, 2011). It is an important mediator of the acute phase of inflammation that triggers both systemic and local reactions. The release of downstream pro-inflammatory mediators, such as TNF-α and IL-1, is one of its many impacts (Weber *et al*., 2010).

In the present study, TNF-α was significantly elevated in horses with allergic dermatitis, which is supported by the findings of Kordulewska *et al*. (2018), who found that 30 individuals diagnosed with allergies had elevated serum levels of TNF-α and IL-1β. The pathophysiology of several inflammatory skin conditions, including psoriasis, cutaneous lupus, allergic and irritant contact dermatitis, and chronic photosensitive diseases, is linked to TNF, which is thought to be a significant mediator of cutaneous inflammation (LaDuca and Gaspari, 2001; Trent and Kerdel, 2005).

According to Grzanka *et al*. (2019), participants with moderate-to-severe chronic urticaria and chronic spontaneous urticaria (CSU) had considerably higher TNF-α concentrations than controls, although subjects with mild symptoms did not differ significantly in TNF-α concentrations. According to previous reports, TNF is a key player in the pathophysiology of allergies. Epithelial barriers and sensitive immune cells release TNF-in response to allergen exposure (Choi *et al*., 2012; Lee *et al*., 2016).

The present results revealed that the level of VDR expression was negatively correlated with the levels of pro-inflammatory agents; in other words, VDR expression could influence the inflammatory response in the body. VDR gene expression was negatively correlated with TNF-α and IL-1β levels. This finding may reflect a role for vitamin D in the inflammatory process. It has been found that VDR expression in alveolar macrophages is age related in horses (Berghaus *et al*., 2023). In Rhodococcus equi infected horses, there was a significant decrease in VDR expression and a significant increase in TNF and IL-1β levels in alveolar macrophages (Berghaus *et al*., 2024). However, in ponies, the upregulation of VDR protein expression may be affected by many factors (Puangthong *et al*., 2021). These findings are consistent with those of studies in human (Chen and Xu, 2018), where TNF-α was negatively correlated with the expression of the VDR gene ($P<0.05$) but positively correlated with the levels of pro-inflammatory factors. Serum 25 (OH) D and TNF-α levels in normal women are inversely related in humans (Peterson and Heffernan, 2008). TNF and IL-6 levels are inversely correlated with vitamin D level in COVID-19 patients (Jain *et al*., 2020), while vitamin D levels are inversely correlated with the level of IL-1β (Ebadi and Montano-Loza, 2020). VDR signaling and TNF-α levels were inversely related in a model of rheumatic arthritis of the mouth (Zwerina *et al*., 2011). Vitamin D is linked to immunological disorders because it is a determinant regulator of the immune system (Cantorna *et al*., 2012).

Conclusion

Vitamin D receptor gene plays an important role in the occurrence of skin diseases in horses, especially allergic dermatitis. Further studies on the role of vitamin D as a preventive agent for skin diseases are required in clinical practice.

Acknowledgments

Acknowledgement to Deanship of Scientific Research, Vice Presidency for Graduate Studies and Scientific Research, King Faisal University for financial support (Grant number: KFU253267).

Conflict of interest

The authors have no conflict of interest to declare.

References

Abramovits, W., Rivas Bejarano, J.J., Valdecantos, W.C., 2013. Role of Interleukin 1 in Atopic Dermatitis. Dermatologic Clinics 31, 437-444.

Adams, J.S., Hewison, M., 2008. Unexpected actions of vitamin D: new perspectives on the regulation of innate and adaptive immunity. Nature Clinical Practice Endocrinology and Metabolism 4, 80-90.

Adorini, L., Penna, G., 2008. Control of autoimmune diseases by the vitamin D endocrine system. Nature Clinical Practice Rheumatology 4, 404-412.

Ahmad, S., Azid, N.A., Boer, J.C., Lim, J., Chen, X., Plebanski, M., Mohamud, R., 2018. The key role of TNF-TNFR2 interactions in the modulation of allergic inflammation: a review. Frontiers in immunology 9, 1-10.

Akdis, M., Aab, A., Altunbulakli, C., Azkur, K., Costa, R.A., Crameri, R., Duan, S., Eiwegger, T., Eljaszewicz, A., Ferstl, R., Frei, R., Garbani, M., Globinska, A., Hess, L., Huitema, C., Kubo, T., Komlosi, Z., Konieczna, P., Kovacs, N., Kucuksezer, U.C., Meyer, N., Morita, H., Olzhausen, J., O'Mahony, L., Pezer, M., Prati, M., Rebane, A., Rhyner, C., Rinaldi, A., Sokolowska, M., Stanic, B., Sugita, K., Treis, A., van de Veen, W., Wanke, K., Wawrzyniak, M., Wawrzyniak, P., Wirz, O.F., Zakzuk, J.S., Akdis, C.A., 2016. Interleukins (from IL-1 to IL-38), interferons, transforming growth factor β, and TNF-α: Receptors, functions, and roles in diseases. Journal of Allergy and Clinical Immunology 138, 984-1010.

Berghaus, L., Cathcart, J., Berghaus, R., Hart, K., 2023. Age-related changes in vitamin D metabolism and vitamin D receptor expression in equine alveolar macrophages: A preliminary study. Veterinary Immunology and Immunopathology 259, 110593.

Berghaus, L., Cathcart, J., Berghaus, R., Ryan, C., Toribio, R., Hart, K., 2024. The impact of age on vitamin D receptor expression, vitamin D metabolism and cytokine production in ex vivo Rhodococcus equi infection of equine alveolar macrophages. Veterinary Immunology and Immunopathology, 110707.

Birrell, M.A., Eltom, S., 2011. The role of the NLRP3 Inflammasome in the pathogenesis of airway disease. Pharmacology and Therapeutics 130, 364-370.

Björnsdóttir, S., Sigvaldadóttir, J., Broström, H., Langvad, B., Sigurðsson, Á., 2006. Summer eczema in exported Icelandic horses: influence of environmental and genetic factors. Acta Veterinaria Scandinavica 48, 1-4.

Cantorna, M.T., Zhao, J., Yang, L., 2012. Vitamin D, invariant natural killer T-cells and experimental autoimmune disease. Proceedings of the Nutrition Society 71, 62-66.

Caproni, M., Torchia, D., Schincaglia, E., Volpi, W., Frezzolini, A., Schena, D., Marzano, A., Quaglino, P., De Simone, C., Parodi, A., Barletta, E., Fabbri, P., 2006. Expression of cytokines and chemokine receptors in the cutaneous lesions of erythema multiforme and Stevens-Johnson syndrome/toxic epidermal necrolysis. British Journal of Dermatology 155, 722-728.

Chen, Y., Xu, T., 2018. Association of vitamin D receptor expression with inflammatory changes and prognosis of asthma. Experimental and therapeutic medicine 16, 5096-5102.

Choi, J.P., Kim, Y.S., Kim, O.Y., Kim, Y.M., Jeon, S.G., Roh, T.Y., Park, J.S., Gho, Y.S., Kim, Y.K., 2012. TNF-alpha is a key mediator in the development of Th2 cell response to inhaled allergens induced by a viral PAMP double-stranded RNA. Allergy 67, 1138-1148.

Constable, P., Hinchcliff, K., Done, S., Grünberg, W., 2017. Preface to the Eleventh Edition, In: Veterinary Medicine. Elsevier, Saunders Ltd.

Darwish, H.M., Ghoneim, N.M., Hassan, D.A., Farag, A.S., Rashed, L., 2013. Vitamin D receptor and cathelicidin expressions in children with atopic dermatitis. Egyptian Journal of Dermatology Venerology 33, 1.

Dinarello, C.A., 2009. Immunological and Inflammatory Functions of the Interleukin-1 Family. Annual Review of Immunology 27, 519-550.

Dinarello, C.A., 2011. Blocking interleukin-1β in acute and chronic autoinflammatory diseases. Journal of Internal Medicine 269, 16-28.

Ebadi, M., Montano-Loza, A.J., 2020. Perspective: improving vitamin D status in the management of COVID-19. European journal of clinical nutrition 74, 856-859.

Feldmeyer, L., Werner, S., French, L.E., Beer, H.-D., 2010. Interleukin-1, inflammasomes and the skin. European Journal of Cell Biology 89, 638-644.

Giulietti, A., van Etten, E., Overbergh, L., Stoffels, K., Bouillon, R., Mathieu, C., 2007. Monocytes from type 2 diabetic patients have a pro-inflammatory profile. Diabetes Research and Clinical Practice 77, 47-57.

Gould, H.J., Sutton, B.J., Beavil, A.J., Beavil, R.L., McCloskey, N., Coker, H.A., Fear, D., Smurthwaite, L., 2003. Thebiology Ofigeand Thebasis of allergic disease. Annual Review of Immunology 21, 579-628.

Grzanka, R., Damasiewicz-Bodzek, A., Kasperska-Zajac, A., 2019. Tumor necrosis factor-alpha and Fas/Fas ligand signaling pathways in chronic spontaneous urticaria. Allergy, Asthma & Clinical Immunology 15, 1-9.

Haegen, A.V.D., Griot-Wenk, M., Welle, M., Busato, A., Tscharner, C.V., Zurbriggen, A., Marti, E., 2001. Immunoglobulin-E-bearing cells in skin biopsies of horses with insect bite hypersensitivity. Equine veterinary journal 33, 699-706.

Hay, R.M.A., Ibrahim, N.F., Metwally, D., Rashed, L.A., 2013. The role of interleukin-1ß and interleukin-33 in atopic dermatitis. Our Dermatology Online 4, 11.

Hewison, M., 2010. Vitamin D and the Immune System: New Perspectives on an Old Theme. Endocrinology and Metabolism Clinics of North America 39, 365-379.

Jain, A., Chaurasia, R., Sengar, N.S. Singh, M., Mahor, S., Narain, S., 2020. Analysis of vitamin D level among asymptomatic and critically ill COVID-19 patients and its correlation with inflammatory markers. Sci. Rep. 10, 20191.

Kawakami, T., Ando, T., Kimura, M., Wilson, B.S., Kawakami, Y., 2009. Mast cells in atopic dermatitis. Current Opinion in Immunology 21, 666-678.

Kordulewska, N.K., Cieślińska, A., Fiedorowicz, E., Jarmołowska, B., Piskorz-Ogórek, K., Kostyra, E., 2018. Cytokines concentrations in serum samples from allergic children—Multiple analysis to define biomarkers for better diagnosis of allergic inflammatory process. Immunobiology 223, 648-657.

LaDuca, J.R., Gaspari, A.A., 2001. Targeting Tumour Necrosis Factor Alpha. Dermatologic Clinics 19, 617-635.

Lee, H.S., Park, H.-W., Song, W.-J., Jeon, E.Y., Bang, B., Shim, E.-j., Moon, H.-G., Kim, Y.-K., Kang, H.-R., Min, K.-U., Cho, S.-H., 2016. TNF-α enhance Th2 and Th17

immune responses regulating by IL23 during sensitization in asthma model. Cytokine 79, 23-30.
Livak, K.J., Schmittgen, T.D., 2001. Analysis of Relative Gene Expression Data Using Real-Time Quantitative PCR and the 2−ΔΔCT Method. Methods 25, 402-408.
Lorch, G., Hillier, A., Kwochka, K.W., Saville, W.J., Kohn, C.W., LeRoy, B.E., 2001. Comparison of immediate intradermal test reactivity with serum IgE quantitation by use of a radioallergosorbent test and two ELISA in horses with and without atopy. Journal of the American Veterinary Medical Association 218, 1314-1322.
Lương, K., Nguyễn, L., 2012. Role of Vitamin D in Parkinson's Disease. ISRN Neurology 2012, 1-11.
Marsella, R., 2024. Pruritic Horse: Approach to Allergic Skin Diseases in Horses. Veterinary Clinic North American Equine Practice 40, 219-235.
Mukhopadhyay, S., Hoidal, J.R., Mukherjee, T.K., 2006. Role of TNFα in pulmonary pathophysiology. Respiratory Research 7, 1-9.
Nakae, S., 2003. IL-1 is required for allergen-specific Th2 cell activation and the development of airway hypersensitivity response. International Immunology 15, 483-490.
Nakamura, Y., Kambe, N., Saito, M., Nishikomori, R., Kim, Y.-G., Murakami, M., Núñez, G., Matsue, H., 2009. Mast cells mediate neutrophil recruitment and vascular leakage through the NLRP3 inflammasome in histamine-independent urticaria. Journal of Experimental Medicine 206, 1037-1046.
Nassif, A., Moslehi, H., Le Gouvello, S., Bagot, M., Lyonnet, L., Michel, L., Boumsell, L., Bensussan, A., Roujeau, J.-C., 2004. Evaluation of the Potential Role of Cytokines in Toxic Epidermal Necrolysis. Journal of Investigative Dermatology 123, 850-855.
Neve, A., Corrado, A., Cantatore, F.P., 2013. Immunomodulatory effects of vitamin D in peripheral blood monocyte-derived macrophages from patients with rheumatoid arthritis. Clinical and Experimental Medicine 14, 275-283.
Nomura, Y., Aihara, M., Matsukura, S., Ikezawa, Y., Kambara, T., Aihara, Y., Takahashi, Y., Ikezawa, Z., 2011. Evaluation of serum cytokine levels in toxic epidermal necrolysis and Stevens-Johnson syndrome compared with other delayed-type adverse drug reactions. The Journal of Dermatology 38, 1076-1079.
O'Neill, L.A.J., 2008. The interleukin-1 receptor/Toll-like receptor superfamily: 10 years of progress. Immunological Reviews 226, 10-18.
Ohsawa, Y., Hirasawa, N., 2014. The Role of Histamine H1 and H4 Receptors in Atopic Dermatitis: From Basic Research to Clinical Study. Allergology International 63, 533-542.
Peterson, C.A., Heffernan, M.E., 2008. Serum tumor necrosis factor-alpha concentrations are negatively correlated with serum 25 (OH) D concentrations in healthy women. Journal of Inflammation 5, 1-9.
Pilz, S., Kienreich, K., Rutters, F., de Jongh, R., van Ballegooijen, A.J., Grübler, M., Tomaschitz, A., Dekker, J.M., 2013. Role of vitamin D in the development of insulin resistance and type 2 diabetes. Current Diabetes Reports 13, 261-270.
Puangthong, C., Sukhong, P., Saengnual, P., Srikuea, R., Chanda, M., 2021. A single bout of high-intensity exercise modulates the expression of vitamin D receptor and vitamin D-metabolising enzymes in horse skeletal muscle. Equine Veterinary Journal 53, 796-805.
Scott, D.W., Miller, W.H., 2011. Neoplasms, Cysts, Hamartomas, and Keratoses, In: Equine Dermatology. Elsevier, pp. 468-516.
Stamatas, G., Morello, A., Mays, D., 2013. Early Inflammatory Processes in the Skin. Current Molecular Medicine 13, 1250-1269.
Steinhoff, M., Bienenstock, J., Schmelz, M., Maurer, M., Wei, E., Bíró, T., 2006. Neurophysiological, Neuroimmunological, and Neuroendocrine Basis of Pruritus. Journal of Investigative Dermatology 126, 1705-1718.
Toubi, E., Shoenfeld, Y., 2010. The role of vitamin D in regulating immune responses. Israel Medical Association J 12, 174-175.
Trent, J.T., Kerdel, F.A., 2005. Tumor necrosis factor alpha inhibitors for the treatment of dermatologic diseases. Dermatology Nursing 17, 97-107.
van den Boom, R., Ducro, B., 2008. Identification of factors associated with the development of insect bite hypersensitivity in horses in the Netherlands. Tijdschrift voor diergeneeskunde 133, 554-559.
Vuolo, L., Di Somma, C., Faggiano, A., Colao, A., 2012. Vitamin D and Cancer. Frontiers in Endocrinology 3, 1-13.
Watanabe, H., Gaide, O., Pétrilli, V., Martinon, F., Contassot, E., Roques, S., Kummer, J.A., Tschopp, J., French, L.E., 2007. Activation of the IL-1β-Processing Inflammasome Is Involved in Contact Hypersensitivity. Journal of Investigative Dermatology 127, 1956-1963.
Weber, A., Wasiliew, P., Kracht, M., 2010. Interleukin-1 (IL-1) Pathway. Science Signaling 3, 1-6.
Wilson, A., Harwood, L., Björnsdottir, S., Marti, E., Day, M., 2001. Detection of IgG and IgE serum antibodies to Culicoides salivary gland antigens in horses with insect dermal hypersensitivity (sweet itch). Equine Veterinary Journal 33, 707-713.
Yamanaka, K., Mizutani, H., 2015. Inflammatory skin march: IL-1–mediated skin inflammation, atopic dermatitis, and psoriasis to cardiovascular events. Journal of Allergy and Clinical Immunology 136, 823-824.
Yin, J., Huang, Y., Gao, G., Nong, L., Xu, N., Zhou, D., 2018. Changes and significance of inflammatory cytokines in a rat model of cervical spondylosis. Experimental Therapeutic Medicine 15, 400-406.
Zwerina, K., Baum, W., Axmann, R., Heiland, G.R., Distler, J.H., Smolen, J., Hayer, S., Zwerina, J., Schett, G., 2011. Vitamin D receptor regulates TNF-mediated arthritis. Annals of the Rheumatic Diseases, Annrheumdis142331.