

STUDY OF MICRORNA 22 LEVEL IN PSORIASIS PATIENTS

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Abstract

Objectives: The analysis of psoriasis patients' blood levels of micro-RNA 22 (MiR-22). Context: While MiR-22 has been implicated in the development of other autoimmune disorders, nothing is known about its function in psoriasis and its therapeutic or diagnostic potential. Data Sources: Studies that investigated the potential function of MiR-22 in psoriasis patients up to the year 2023 were located by searching and examining the Medline databases (Pub Med and Medscape). Study Selection: Each study was carefully reviewed by experts in the field to ensure its inclusion. They were considered for inclusion if they met the following requirements: Language used: English for both writing and publication. Second, they are published in publications that undergo a peer review process. Thirdly, describe the possible relationship between psoriasis patients and serum MiR-22 levels. When extracting data, studies were discarded if they did not meet the inclusion criteria. Ethical permission, clear eligibility criteria, suitable controls, sufficient information, and well-defined evaluation measures were all variables in determining the study's quality. For our concerned research outcomes, data were independently extracted from all qualifying studies utilising a data collecting form. Results: psoriasis patients' levels of MiR-22 expression are much lower than those of the control group.

Keywords: Psoriasis, MiR-22, Psoriasis, MiR-22.

Introduction

Psoriasis is a prevalent inflammatory illness. Worldwide, it affects around 2% of the population. Changes in keratinocyte differentiation and inflammatory cell infiltration into the epidermis are hallmarks of this condition. The pathophysiology of this condition is influenced by three key factors: genes, immunological dysregulations, and environmental stimuli (1).

Noncoding RNAs of 18–24 nucleotides in length are known as microRNAs (miRNAs) (2). Messenger RNAs (miRNAs) regulate gene expression after transcription and RNA silencing is their job (3).

The development of psoriasis is influenced by microRNAs. MicroRNAs regulate a large number of genes that regulate several biological processes, including cell proliferation, cellular differentiation, and cell death (apoptosis) (4)

Pathogenesis in psoriasis may include an inhibitor of miR-22, which is regulated by signal transducer and transcription factor 3 (STAT3). A new role for STAT3 in the development of inflammatory diseases similar to psoriasis has been identified. Almost all cell types implicated in illness initiation exhibit STAT3 hyperactivity, which is believed to mediate the signalling of most cytokines, including interleukin IL-23/IL-17 (5).

The tools and techniques

Data Origins: A search of the Medline databases was conducted to source the literature on the probable association between serum MiR-22 level and psoriasis, as well as its connection to severity of disease decline up to 2022. (Pub Med and Medscape).

Research Question Selection: Research was selected via an open, honest, and thorough

evaluation procedure. They were considered for inclusion if they met the following requirements:

1. First published in an English-language work. 2. Having an appearance in journals that have a rigorous peer-review procedure. Describe the link between psoriasis vulgaris and serum miR-22.

Extracting Data: Studies were not considered for inclusion unless they fulfilled all of the requirements. The study's quality was determined by its adherence to ethical guidelines, which included establishing clear eligibility criteria, controls, information, and assessment methods. To ensure that our research results were accurately represented, data were independently extracted from all eligible and qualifying studies utilising a data collecting form.

Literature review:

Psoriasis

Psoriasis is an inflammatory skin disorder characterised by continuous protocell proliferation. The extensor surfaces, scalp, and lumbosacral area are the most common sites where you may see red plaques coated with silvery scales (6). Joints are not immune to the illness. Flare ups are the one and only way to manage psoriasis, since the condition itself has no known treatment. The low quality of life experienced by many psoriasis sufferers leads to the development of depression. The prevalence of psoriasis ranges from 0.2% to 4.8%. (7).

Any age might be the onset of psoriasis. It has been recognised that there is a bimodal age of onset. The average age at which psoriasis initially appears may be anywhere from fifteen to twenty years old, with a second peak somewhere between the ages of fifty and sixty (8).

A variety of morphologies, including plaque, guttate, rupioid, erythrodermic, pustular, inverted,

elephantine, and psoriatic arthritis, may be seen in psoriasis. Scalp, palmoplantar, vaginal, and nail involvement can lead to site variation. The Koebner phenomenon occurs whenever a psoriasis patient has a skin damage, whether it be from mechanical, chemical, or radiation-based harm. The level of disease activity is shown by it (9).

How Psoriasis Develops

Although the precise cause of psoriasis remains a mystery, it is widely believed to be an autoimmune condition triggered by T cells. Many psoriatic patients, especially those of different racial and cultural backgrounds, share HLA antigens. There may be a hereditary component if it runs in families. The skin may develop psoriasis lesions as a result of exposure to radiation, chemicals, or mechanical stress (10).

Psoriasis may be exacerbated by beta-blockers, chloroquine, lithium, steroids, and nonsteroidal anti-inflammatory medications (NSAIDs). Psoriasis tends to become better in the summer and worse in the winter. Other than the ones already mentioned, psoriasis may be brought on by infections, mental stress, alcohol, tobacco, obesity, and low calcium levels in the blood (11).

The inflammatory and autoantibodies processes overlap and even amplify each other in psoriasis, which displays characteristics of an autoimmune disease (12).

The maintenance phase of psoriatic inflammation is driven by the activation of the adaptive immune response via various T cell subsets. The production of new keratinocytes in the skin is stimulated by Th17 cytokines, such as IL-17, IL-21, and IL-22 (13). Psoriasis is characterised by chronic inflammation, which in turn causes abnormal differentiation of keratinocytes and unchecked proliferation of these cells (13).

The maturation of myeloid dendritic cells (MDCs) and the generation of inflammatory cytokines including TNF- α , IL-17, IL-21, and IL-22 are facilitated by the activation of plasmacytoid dendritic cells (PDCs). This in turn activates T helper 1 and Th17. These cytokines, particularly IL-17, stimulate keratinocytes, which subsequently create chemokines, antimicrobial peptides, and cytokines, all of which amplify inflammation (14).

Differentiating Psoriasis Clinically

A variety of morphologies, including plaque, guttate, rupioid, erythrodermic, pustular, inverted, elephantine, and psoriatic arthritis, may be seen in psoriasis. Scalp, palmoplantar, vaginal, and nail involvement can lead to site variation. The Koebner phenomenon occurs whenever a psoriasis patient has a skin damage, whether it be from mechanical, chemical, or radiation-based harm. The level of disease activity is shown by it (15).

Psoriasis plaque

This particular variety often manifests as red, scaly plaques that are adorned with silvery scales. It

tends to manifest most frequently on the back, scalp, elbows, and knees. It affects 85 to 90% of persons with psoriasis and is the most frequent kind. It is possible to identify specific areas of bleeding during repeated excision of psoriatic scales. The Auspitz sign is a clinical diagnostic tool that confirms a patient's condition (15).

Guttate psoriasis syndrome

In children, a streptococcal infection of the upper respiratory tract may cause a skin condition known as eruptive psoriasis. Lesions like raindrops, which are red and scaly, often appear on the trunk and back of the affected person. It is the most promising kind of psoriasis (15).

Pemphigoid pustulosis

It manifests as tiny, non-infectious lesions filled with pus and encircled by redness. There are two kinds: localised and generalised. A sterile pustule on an erythematous plaque covering the whole body is the hallmark of generalised pustular psoriasis, which is characterised by hypocalcaemia (15).

Psoriasis caused by erythrodermic factors

Redness, swelling, and flaking skin across 90% of the body's surface area characterise this condition. Itchy, swollen, and painful symptoms are common. The sudden discontinuation of systemic steroids causes an aggravation of unstable plaque psoriasis. Erythroderma may lead to cardiac failure and other complications such as impaired skin barrier functions, abnormal basal metabolic rate, and increased cutaneous circulation (15).

Interaction with nails

Psoriasis may cause changes in the nails, such as pitting, oil patches, subungual hyperkeratosis, dystrophies, and anchyloses of the nails (16).

A skin condition that affects the mouth

The most prevalent symptom of oral psoriasis is a fissured tongue, which may be seen in 6.5% to 20% of those with psoriasis of the skin (17).

Opposite psoriasis

Also known as intertriginous psoriasis or flexural psoriasis. In intertriginous locations such as the groynes, armpits, inter gluteal region, and infra mammary region, it manifests as smooth, red, and strongly delineated patches. There could be wetness, maceration, and the presence of cracks that smell bad or itch. A dermatophyte infection, which may manifest at these locations with symptoms including a central clearing and an active border characterised by scales, vesicles, and pustules, must be distinguished from this (17).

Scabies psoriasis

Red plaques covered in oily scales are the classic symptoms of this kind of psoriasis. Areas including the scalp, forehead, nasolabial folds, sternum, and retro-auricular folds are often affected because of the increased production of sebum there (18).

Arthritis Due to Psoriasis

Thirty percent of psoriasis patients also suffer from this kind of chronic inflammatory arthritis. Psoriasis of the nails and skin often coexist with it. Inflammation of the connective tissues and joints, especially those of the little limbs (the fingers and toes), may be rather painful. The result is dactylitis, an enlargement of the toes and fingers that resembles a sausage. Hips, knees, and the spine (spondylitis) and sacroiliac joints (sacroiliitis) are all potential sites of psoriatic arthritis (18).

Pimples on the eye

Trichiasis, ectropion, conjunctivitis, and corneal dryness are all symptoms of psoriasis, which also affects the eyelid and conjunctiva. Blepharitis is the most prevalent eye symptom, followed by cicatricial ectropion, madarosis, and trichiasis. Anterior uveitis may be seen in certain instances (18).

MiR-22

MicroRNAs (miRNAs) regulate tumour formation among their many other physiological and pathological roles. Out of all 20 human normal tissues (brain, lung, liver, heart, kidney, spleen, smooth muscle, bladder, prostate, testis, ovary, oesophagus, cervix, trachea, thymus, placenta, smooth intestine, colon, thyroid, and adipose tissue), the expression of miR-22 is relatively higher in heart, smooth muscle, as well as adipose tissue (19).

The miR-22 gene is linked to an exon of the C17orf91 gene and is situated in a fragile cancer-relevant genomic region on chromosome 17 (17p13.3) (20).

The Role of microRNAs

Through their involvement in regulating cellular-level biological processes as development, metabolism, proliferation, apoptosis, viral infection, and tumorigenesis, miRNAs are linked to the underlying molecular mechanisms of several disorders (21).

MicroRNA-22 in illness

An important factor in cancer cell motility, invasion, and metastasis, MiR-22 expression varies between cancer types and is reflected in cancer monitoring, prognosis, and diagnosis. One potential independent early diagnostic biomarker for ICC (intrahepatic cholangio-carcinoma), hepatocellular cancer with hepatitis C virus, and lung adenocarcinoma is the low expression of miR-22 in serum from these individuals (22).

There is substantial evidence linking MiR-22 to neurodegenerative illnesses as well. Patients with HD, AD, and PD have downregulated levels of MiR-22 in their brains. Furthermore, overexpression of MiR-22 protects primary hippocampus neurons from senescence, and MiR-22 has been associated with neurodegeneration and ageing. Although the exact process by which MiR-22 protects neurons from damage has not been determined, there is mounting evidence that it plays a role in both HD and AD (23).

MicroRNAs in relation to several skin disorders:

When using microRNAs (miRNAs) to treat illness, it is common practise to boost downregulated miRNAs using miRNA mimics and complement elevated miRNAs with miRNA inhibitors. Therefore, microRNAs are essential for understanding the disease's pathophysiology, making a diagnosis, and developing a therapy plan. MiR-22 in psoriasis is one of the illnesses impacted by microRNAs, which include vitiligo, bullous disease, sclerosis, and more (24)

Recently, it has been evident that microRNAs have the ability to control keratinocyte differentiation, proliferation, and cytokine responses; T cell activation and survival; and the communication between immunocytes and keratinocytes. Despite describing a distinct expression profile of miRNAs in psoriasis relative to healthy skin, objective biomarkers reflecting diagnosis and disease activity have not yet found practical use. Research on the function of microRNAs (miRNAs) in psoriasis has the potential to provide light on the causes, symptoms, and potential treatments for this skin condition (25).

The results of this research provide light on MiR-22's function in psoriasis and its promise as a treatment target, which is an important conclusion. Considering MiR-22's dysregulation, it might be a biomarker for psoriasis or a target for future treatments.

References

- [1] Huang YW, Tsai TF (2021): HLA-Cw1 and Psoriasis. *Am J Dermatol.* ; 22(3):339-347.
- [2] Singhvi, G., Manchanda, P., Rapalli, V. K., Dubey, S. K., Gupta, G., & Dua, K. (2018). MicroRNAs as biological regulators in skin disorders. *Biomedicine & Pharmacotherapy*, 108, 996-1004..
- [3] Dua, K., Hansbro, N. G., Foster, P. S., & Hansbro, P. M. (2016). MicroRNAs as therapeutics for future drug delivery systems in treatment of lung diseases. *Drug Delivery and Translational Research*, 7(1), 168–178..
- [4] Soltanzadeh-Yamchi, M., Shahbazi, M., Aslani, S., & Mohammadnia-Afrouzi, M. (2018). MicroRNA signature of regulatory T cells in health and autoimmunity. *Biomedicine & Pharmacotherapy*, 100, 316–323. -.
- [5] Wang, L., Qiu, R., Zhang, Z., Han, Z., Yao, C., Hou, G., ... & Shen, N. (2020). The microRNA miR-22 represses Th17 cell pathogenicity by targeting PTEN-regulated pathways. *Immunohorizons*, 4(6), 308-318.
- [6] Segaert S, Calzavara-Pinton P, de la Cueva P, Jalili A, Lons Danic D (2022): Long-term topical management of psoriasis: the road ahead. *Journal of Dermatological Treatment*, 33(1), pp.111-120.

- [7] 7-. Tirmizi, S. S. (2022). Efficacy of Secukinumab in Moderate to Severe Psoriasis Vulgaris: A Prospective Study. *Pakistan Journal of Medical & Health Sciences*, 16(09), 983-983.
- [8] 8- Yamanaka, K., Yamamoto, O., & Honda, T. (2021). Pathophysiology of psoriasis: a review. *The Journal of Dermatology*, 48(6), 722-731.
- [9] Eder, L., Widdifield, J., Rosen, C. F., Cook, R., Lee, K., Alhusayen, R., Paterson, M. J., Cheng, S. Y., et al. (2019). Trends in the Prevalence and Incidence of Psoriasis and Psoriatic Arthritis in Ontario, Canada: A Population-Based Study. *Arthritis Care & Research*, 71(8), 1084-1091.
- [10] 10- Armstrong, A. W., Mehta, M. D., Schupp, C. W., Gondo, G. C., Bell, S. J., & Griffiths, C. E. M. (2021). Psoriasis prevalence in adults in the United States. *JAMA Dermatology*, 157(8), 940-946.
- [11] Thomas, J., Kumar, P., & Balaji, S. R. (2016). *Textbook of Psoriasis*.
- [12] 12-. Yamanaka, K., Yamamoto, O., & Honda, T. (2021). Pathophysiology of psoriasis: a review. *The Journal of Dermatology*, 48(6), 722-731
- [13] Kahn, J., Deverapalli, S. C., & Rosmarin, D. (2018). JAK-STAT signaling pathway inhibition: a role for treatment of various dermatologic diseases. *Seminars in Cutaneous Medicine and Surgery*, 37(3), 198-208.
- [14] Larsabal, M., Ly, S., Sbidian, E., Moyal-Barracco, M., Dauendorffer, J. - N., Dupin, N., et al(2019). Prevalence and impact of genital psoriasis. *British Journal of Dermatology*, 180(3).
- [15] Caiazzo, G., Fabbrocini, G., Di Caprio, R., Raimondo, A., Scala, E., Balato, N., & Balato, A. (2018). Psoriasis, Cardiovascular Events, and Biologics: Lights and Shadows. *Frontiers in Immunology*, 9, 1668.
- [16] Louden, B. A., Pearce, D. J., Lang, W., & Feldman, S. R. (2004). A simplified psoriasis area severity index (SPASI) for rating psoriasis severity in clinic patients. *Dermatology Online Journal*, 10(2).
- [17] Dauden, E., Blasco, A. J., Bonanad, C., Botella, R., Carrascosa, J. M., González-Parra, E., Jodar, E., Joven, B., Lázaro, P., Oliveira, A., Quintero, J., & Rivera, R. (2018). Position statement for the management of comorbidities in psoriasis. *Journal of the European Academy of Dermatology and Venereology*, 32(12), 2058-2073
- [18] Yang, E. J., Beck, K. M., Sanchez, I. M., Koo, J., & Liao, W. (2018). The impact of genital psoriasis on quality of life: a systematic review. *Psoriasis (Auckland, N.Z.)*, 8, 41-47.
- [19] Neely, L. A., Patel, S., Garver, J., Gallo, M., Hackett, M., McLaughlin, S., Nadel, M., Harris, J., Gullans, S., & Rooke, J. (2005). A single-molecule method for the quantitation of microRNA gene expression. *Nature Methods*, 3(1), 41-46.
- [20] Ji, J., Shi, J., Budhu, A., Yu, Z., Forgues, M., Roessler, S., et al. (2009). MicroRNA expression, survival, and response to interferon in liver cancer. *The New England Journal of Medicine*, 361(15), 1437-1447.
- [21] Su, F., Jin, L., & Liu, W. (2021). MicroRNA-125a correlates with decreased psoriasis severity and inflammation and represses keratinocyte proliferation. *Dermatology*, 237(4), 568-578.
- [22] Shin, Y. M., Yun, J., Lee, O. J., Han, H. S., Lim, S. Net al (2014). Diagnostic value of circulating extracellular miR-134, miR-185, and miR-22 levels in lung adenocarcinoma-associated malignant pleural effusion. *Cancer research and treatment: official journal of Korean Cancer Association*, 46(2), 178-185
- [23] Jovicic, A., Zaldivar Jolissaint, J. F., Moser, R., Silva Santos, M. D. F., and Luthi-Carter, R. (2013). MicroRNA-22 (miR-22) overexpression is neuroprotective via general anti-apoptotic effects and may also target specific Huntington's disease-related mechanisms. *PloS one*, 8(1), e54222.
- [24] Ross, K. (2018). Towards topical microRNA-directed therapy for epidermal disorders. *Journal of Controlled Release*, 269, 136-147.
- [25] Xu, N., Meisgen, F., Butler, L. M., Han, G., Wang, X. J., Söderberg-Nauclér, C., & Sonkoly, E. (2013). MicroRNA-31 is overexpressed in psoriasis and modulates inflammatory cytokine and chemokine production in keratinocytes via targeting serine/threonine kinase 40. *The Journal of Immunology*, 190(2), 678-688.