

## Issues and Perspectives in Psoriasis Management

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### Perspective

Psoriasis is recognized as a chronic inflammatory autoimmune disease caused by genetics, the immune system and environmental factors with inherent aberrations in the skin in the form of either consistently excess proliferation of cellular constituents, particularly the epidermis, keratinocytes to hyperproliferate and perpetuate the disease process. Psoriasis varies in severity from small, localized patches to complete body coverage. These skin patches are typically red, dry, itchy and scaly.

Humans lose five thousand million skin cells every day. How this colossal shedding process can occur without there being a break in the skin barrier is unraveled by the discovery of the unique shape (tetrakaidecahedron) and binding capability of epidermal cells providing a very tight, cohesive bond, explaining how skin maintains a barrier even when it is shedding [1]. It could also help us to understand what happens when it forms incorrectly, which could lead to conditions like psoriasis. Failure in the interlocking barrier between cells (the tight junctions), may partly explain why in psoriasis there is an overproduction of epidermal cells, causing thick patches of skin on the surface.

The psoriasis connection has been suggested with leaky gut in the literature. The intestinal barrier is a single layer of cells lining the gut that mainly consists of enterocyte membranes and tight junctions between enterocytes, and its integrity is essential for the digestion and absorption of nutrients, both in humans and animals [2]. When proteins/toxins leak from the gut, the body recognizes them as foreign. The body then attacks them by triggering an autoimmune, inflammatory response and one of the manifestations is in the form of psoriasis. Because of this, it's within the realm of possibility that the two conditions i.e. leaky gut and psoriasis are related. Zonula occludens (ZO-1), claudin-1, and occludin are intestinal tight junction proteins, essential to maintain tight junction stability, and barrier function [3]. There are various treatments which may help heal leaky gut like antioxidant supplements, zinc supplementation with nutrients that support healthy intestinal mucosa. Several polymers are also cited in the literature to maintain the intestinal integrity like chitosan, alginate, gum acacia etc. This manages the psoriasis in the interior situation i.e. leaky gut and helping in the reduced

manifestation on the skin. It has been shown in mice; the integrity of the intestinal barrier is compromised by low doses of dietary chitosan supplementation [4,5]. In a study, alginate supplementation exerted beneficial effects in improving the intestinal integrity of weaned pigs [2]. This behavior was closely related to the enhanced antioxidant capacity and decreased mast cell degranulation, as well as prevention of mast cell pro-inflammatory cytokines release, via restraining the TLR4/NF- $\kappa$ B and NOD1/NF- $\kappa$ B signalling pathways [6]. Research has demonstrated that acacia gum helped in restoring gut impermeability at a cellular level. Polymeric metal composite formulations containing components like chitosan/alginate/gum acacia along with Zn salts or oxides would be beneficial to maintain the intestinal integrity and thereby helpful in managing psoriasis.

Literature also suggests the use of equine milk helps in the management of psoriasis. Equine milk stimulates the increase of good bacteria species like *Lactobacillus delbrueckii* ssp. *bulgaricus*, *Lactococcus lactis* ssp. *lactis*, *Kluyveromyces fragilis* and *Saccharomyces unisporus* in the bowel flora [7]; this will help in decreasing the absorption of toxic substances in the bloodstream. The equine milk possessing high levels of albumin and globulin (building materials for antibodies), minerals and high quality unsaturated fat acids and thus offers a good opportunity for regulating and strengthening the immune system [8]. Among the functional proteins detected in donkey milk, there are molecules active in antimicrobial protection such as lysozyme and lactoferrin. Lactoferrin inhibits the growth of iron-dependent bacteria in the gastrointestinal tract. This inhibits certain organisms, such as coliforms and yeast that require iron. Lysozyme in donkey milk is present in large amounts, indeed ranges from 1.0 mg/mL to 4 mg/mL [8]; this substance is present also in human (0.12 mg/ml) but only in trace amounts in cow and goat milk. Lysozyme in donkey milk is extremely thermo-stable. Owing to its resistance to acid and protease, it may play a considerable task in the intestinal immune response.

Scientists have also identified about genetic variants that make a person more likely to develop psoriatic disease. The genes involved in the development of psoriasis are primarily related to

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Received: August 4, 2019; Accepted: August 14, 2019; Published: August 23, 2019

Citation: Manuja A, Kumar B, Tripathi BN (2019) Issues and Perspectives in Psoriasis Management. Immunome Res 15:168. DOI: 10.35248/1745-7580.19.15.168

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the immune system. Researchers are continuing to look into each of the genes and their connection to psoriasis. However, there are scattered reports where an autosomal dominant and autosomal recessive pattern of inheritance for psoriasis has been proposed. While a family history of psoriasis can't be ignored, genes are just one aspect of this complicated condition. A new perspective arises from study to investigate the difference in the shape of the cells in the patients suffering from the disease and persons not suffering in family with the history of psoriasis. This also warrants the research front in the area of unraveling of the genes responsible for the specific shape of skin cells i.e. tetrakaidecahedron or any deviation in the structure/shape of the cells avoiding the tight junctions. Any lacunae in producing glue like structure required for the tight junctions in skin is another area to look for. Personalized medicine has also enormous prospective with both diagnosis and treatment opportunities being motivated by various factors associated with an individual including genetic information in view of revolutionized next-generation sequencing technologies and may provide targeted therapeutics.

These perspectives focused on the molecular crosstalk between intestinal epithelial cells to regulate the tight junctions present the significance of sealing the seeps using polymers, zinc supplements, equine milk for enhancing barrier integrity. Thus prevent paracellular diffusion of unwanted microorganisms and other antigens across the epithelium which may lead to systemic inflammatory response in the whole body. Although many queries are still left to answer yet these perspectives offer insights into challenges being faced to manage psoriasis and present a future outlook at how to best combat this skin disease.

## CONFLICTS OF INTEREST

Authors declare no conflict of interest.

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