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Chapter 1

Psoriasis and Genetics

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Abstract

Psoriasis is an erythematous, scaly chronic inflammatory dermatosis and occurs due to altered epidermal differentiation and hyperproliferation due to faulty signals that speed up the growth cycle of skin cells. Psoriasis reduces quality of life, and psoriatic patients generally have higher risk for metabolic disease. Psoriasis is associated with many burdening comorbidities, which often share similar pathogenic features and follow a progressive pattern. Genetic variation in human genome causes specific kind of disease, and nowadays, research is focused on metabolic pathways that trigger psoriasis and related comorbidities. In addition, genetic variations are also important for psoriasis treatment regime and response. The purpose of this section is to shown to genetic epidemiology, pharmacogenetics, immune genetics of psoriasis and related comorbidities.

Keywords: psoriasis, genetics, variations, SNP

1. Introduction

Psoriasis was first thought to originate from a biochemical imbalance due to excessive proliferation of keratinocytes; yet recent researches focused on the investigation of the genetic basis of this immunological condition.

Psoriasis, a chronic inflammatory disease, is thought to be closely related to metabolic and cardiovascular diseases; however, mortality rate of the disease is rare. Genetic and epidemiologic studies have also pointed out that cardiovascular and metabolic diseases are more prevalent in the community than psoriasis cases in psoriasis cases. Thus, determination of genetic variation on genome that triggers both psoriasis and related comorbidities is crucial.

In addition, personal genomic variations are important for diagnosis and treatment of the psoriasis and related comorbidities effectively.

2. Epidemiology of psoriasis

Psoriasis can affect people of all ages, ethnic origins and genders around the world. There are very literatures showing the incidence of the disease, since there is no compulsory retention of psoriasis case recordings and reliable source constraints. On the other hand, prevalence varies among different countries in Europe [1]. Although psoriasis may affect 2% of the world population, the incidence of disease varies 0.09–11.4% between different countries and races [1–4]. The reasons for the variability of prevalence are that the epidemiological methods and limitations of the studies differ [2]. Psoriasis is not evident among Latin American indigenous, people of Samoa and New Zealand, and in contrast, the prevalence is increasing up to 12% in Kasachy [5]. The prevalence of psoriasis in Asian countries or Asians common countries is 0.4% in China, 0.3–1% in Japan, and 0.8% in India, while the prevalence of West African and American black population was reported as 0.3–0.7% and 0.7%, respectively [6].

The results have shown that there is a very weak correlation between geographical latitude and psoriasis [2, 7]. In contrast, psoriasis is more commonly seen in places where the upper latitudes of that are colder and Caucasians are more frequent[5, 8–10]. For example, in twin studies carried out in Australia, it has a higher prevalence of psoriasis in southern region of cold than the northern region where is warmer [8, 9]. When investigating the regional distribution of psoriasis cases in Norway, the incidence of disease has been found to increase inversely proportional to the temperature rise in the country [10].

According to the global disease burden study conducted in 2010 [11], it has been reported that the disability-adjusted life year increases with age, especially the highest burden of disease shown between the ages of 50–69 [2, 11]. Psoriasis is associated with many burdening comorbidities, which often share similar pathogenic features and follow a progressive pattern, and thus, direct and indirect cost of psoriasis has significant effects on both patients and health care systems.

3. Psoriasis as a genetic disease

Genetic factors play a role in psoriasis development; yet, the exact mechanism that triggers psoriasis is still unknown. Twin studies, familial aggregation studies, linkage studies, and population-based association studies are all important to understand the effect of the genes in heritability of the disease. Nowadays, genome-wide association studies and linkage studies are also frequently used to identify disease mechanism and risk-related genes. Association studies on genome-wide and a meta-analysis aim to reveal the potential risk genes and loci of genome that emerged comorbidities as a result of these diseases such as s psoriasis.

Psoriasis is a complex disease that not simply explained by Mendelian inheritance rules. Lomholt's study that performed (1954) in an island has determined that 91% of psoriatic patients have a previous family history [12]. Earlier studies speculated psoriasis as autosomal dominant disease, but the truth is so different [13]. This speculation relies on the fact that human lymphocyte antigen gene located in a single locus thus its effects as dominant. That is why psoriasis is accepted as a dominant disease [13]. Although dominant inheritance firstly goes to foreground in studies to investigate the pattern of inheritance of psoriasis, it has been focused on the disease transition by heterogeneous or polygenic in broader studies.

The twin studies rely on the fact, if the disease occurs in monozygotic twins because of phenotypical differences between monozygotic twins. This means that environmental factors affect the disease because they have identical genetic background. In contrast, dizygotic twins have genetic background like brothers or sisters, and thus, phenotypical differences occur as a result of genetic or environmental factors or both.

The concordance of psoriasis has greater rates in monozygotic twins than dizygotic twins'; thus, genetic factors are important for disease development. In contrast, the rate is never reaching to 100% in monozygotic twins so environmental influences for disease development. Duffy et al. [8] have reported concordance for psoriasis higher in monozygotic twins (35%) when compared to dizygotic twins (12%) in Australian population. The data from National Twin Registry System of Denmark had been shown that the concordance of psoriasis in dizygotic twins was 15–30%; yet, the rates rises up to 65–72% in monozygotic twins [14]. The Danish Twin Registry System records have shown that monozygotic twins increased risk of psoriasis than in dizygotic twins [15]. A twin study has been shown that psoriasis risk has been rise up to 3 times in monozygotic twins when compared to fraternal twins [16]. Although twin studies have shown strongest genetic background of psoriasis, heritability rate of psoriasis never reaches to 100% among monozygotic twins. This missing heritability means environmental factors [15, 16] and epigenetic alterations [17] have effects on psoriasis development.

Psoriasis was diagnosed 6% in first-degree relatives of patients with psoriasis [18, 19] generations, settlement in geographical regions and ethnic group studies related to population showed that psoriasis is a complex genetic-based, multifactorial disease [6]. All these data showed why psoriasis was accepted as a heritable disease but not 100% as a genetic disease. Psoriasis was first associated with the major histocompatibility complex (MHC) region in the short arm of the 6th chromosome in 1972 [20–22]. MHC is an intense region of the genome and contains HLA-I and HLA-class human leukocyte antigens. In fact, the 80–200 kb long region in the HLA-C gene region has been accepted as the Psoriasis susceptibility gene region (PSOR1) [23]. HLA-Cw6 in PSOR1 region was associated with psoriasis in many ethnic groups and geographical regions [24–27]. However, the risk zones related to subclinical forms of the disease vary in patients with psoriasis. For example, HLA-Cw6 positivity is associated with early onset and familial transition of psoriasis [28]. HLA-CW6 gene region affects the response of ustekinumab using in the treatment of psoriasis [29]. Other gene regions (PSORS2 (17q25), PSORS3 (4q34), PSORS4 (1q), PSORS5 (3q21, PSORS6 (19p13), PSORS7 (1p) PSORS8 (16q12-13), PSORS11 (5q31.1-q33.1), PSORS12 (20q13), and PSORS13 (6q21)) related to psoriasis distribute to different chromosomes [13, 30–37].

4. Immunogenetics of psoriasis

Psoriasis is an immune-mediated disease and, for that reason, immune-mediated mechanism has been extensively studied. Genetic studies focus on identification reasons that trigger uncontrolled proliferation of keratinocytes and recruitment of T cells into the skin. In healthy individuals, T cells are originated from embryonal pluripotent cells by cytokine induction. Immature thymocytes are transferred to thymus for proliferation through clonal expansion. T cells are specified to helper T cells or cytoxic T cells by adding specific surface antigens ($CD4^+$ or $CD8^+$) and differentiating to give response for antigenic signals. In psoriatic skin samples, Th1 cell differentiation is up-regulated and that cause impaired Th1/Th2 balanced [38, 39]. Evidence indicates that Th1-delivered cytokines IL-1, IL-2, IL-6, IL-8, tumor necrosis factor-α (TNF- α), transforming growth factor (TGF) and Granulocyte-macrophage colony-stimulating factor are upregulated, while Th2-delivered cytokines IL-4, IL-5, and IL-10 are downregulated [40–44]. The cytokines IL-12 is critical for both T-cell activation and differentiation also contributes to DC/T cell interactions [45]. TNIP1, NFKBIA, IL12B and LCE3D–LCE3E are known susceptibility loci for psoriasis [46], and the variation of IL-12 is associated with psoriasis in different populations [47–49]. Meta analyses have shown that IL-12B variation (rs3212227, rs6887695) has been associated both psoriasis and psoriatic arthritis [50]. IL-12 and IL-23 are heterodynamic cytokines; both of them share same p40 subunit. IL-12 consists of p35 and p40 subunit and IL-23 consist of p19 and p40 subunits. The metabolic model for psoriasis suggests that dermal dendritic cells are secreted IL-23 by that way trigger Th17 cell line activation. IL-23 is crucial for naive T cell differentiation to Th17. Activated Th17 cells are secreted IL-17A, IL-17F, IL-22 and IL-26 and that proinflammatory cytokines effects epidermal and dermal cells gene expression and keratinocyte maturation. For that reason, IL12/IL 23 pathway seems important for psoriasis treatment and different studies are performed in that metabolic pathway [51–54].

5. Immunohistochemical parameters

The demonstration of specific markers by immunohistochemical methods in histopathological tissue specimens diagnosed as psoriasis is important in terms of supporting and confirming the diagnosis. We have evaluated most of the cytokines referred to in the pathophysiology in immunogenetic section which can be used for immunohistochemical methods. In psoriatic tissue, sample Th1-mediated cytokines IL-1, IL-2, IL-6, IL-8, tumor necrosis factor-α (TNF-α), transforming growth factor (TGF) and granulocyte-macrophage colony-stimulating factor increase and Th2-mediated cytokines IL-4, IL-5, and IL-10 decrease [40–44].

IL-17 plays an important role in psoriasis, and recently, both IL-17 inhibitors and IL-17receptor type A blockers are new monoclonal antibodies which are approved by US FDA [55]. Lee and colleagues have immunohistochemically evaluated IL-17A expressions in different types of psoriasis, and the results have shown that samples from palmoplantar and pustular type psoriasis samples were stained with IL-17A strongly, while plaque type samples were stained with IL-17A intermittently [56].

Macrophage migration inhibitory factor (MIF) is directly related to the severity of clinical symptoms, and serum MIF levels are usually high in patients with psoriasis [57]. In contrast, immunohistochemical staining by anti-MIF antibody in psoriatic lesions showed that MIF levels are very low [58]. Toll-like receptors (TLRs) are a group of molecules that play a crucial role in innate immunity and also regulate antimicrobial defense. TLR2 is immunohistochemically staining uniformly in all the layers of the normal deep epidermis that does not lose its nuclei, yet TLR2 staining differs in psoriatic skin samples [59, 60]. Panzer and colleagues have shown that TLR2 staining is lower in granular and upper spinous, whereas it was strongly observed in the lower spinous and basal strata [59]. TLR4 is normally found in all the nuclear layers, while it is more pronounced in the upper layers of the basal layer. In psoriatic skin lesions, TLR4 was stained weak in the basal layer, yet TLR4 was stained strongly in the upper spinous and granular layers [59]. IL-8 is produced in psoriatic lesions and immunohistochemical demonstration supports disease diagnosis [61]. In a study, evaluating the relationship between geographic tongue (GT) and psoriasis has been shown that anti-CD4, CD8, CD20, CD68, S100, and Ki-67 antibodies results were similar in tissue samples from both diseases, and according to that result, geographic tongue is speculates as an oral psoriasis lesion [62].

6. Pharmacokinetics of psoriasis in genetic aspect

Psoriasis is a chronic, non-curative disease, and thus, effective psoriasis treatment is important for long-term cure and inhibition of disease manifestation. Psoriasis can be treated by topical, photo(chemo)therapy, classic systemic drug(methotrexate, cyclosporine, acitretin) and biologic agents (infliximab, adalimumab, etanercept). The psoriasis treatment is affected by psoriasis type, severity, presence of comorbidities, previous response to other treatments and patients.

Ustekinumab is an anti-p40 monoclonal antibody which is effective for psoriasis treatment via its inhibitor effect of interleukin-12/23 pathway. By that way, ustekinumab inhibits T helper (Th)1 and Th17 pathway and inhibits immune cell activation. In addition, HLA-Cw+ patients have better clinical response to ustekinumab than HLACw- ones [29]. Talamonti et al. state that HLACw+ patients response to ustekinumab is 9.8 times more efficient than mutant genotype. In contrast, TNFAIP3 polymorphism and LCE3B/3C gene deletions have no effect on ustekinumab response [29].

TNF-inhibitors infliximab and adalimumab and the fusion protein, etanercept are used widely for psoriasis treatment. Nishikawa and colleagues [63] have shown that JAG2, ADRA2A and TLR10 polymorphisms are associated with TNFα response. Prieto-Pérez and colleagues [64] have shown that PGLYR4, ZNF816A, CTNNA2, IL12B, MAP3K1, and HLA-C genes are associated with anti-TNF response at 3 months, while FCGR2A, HTR2A, and CDKAL1 are related anti-TNF response at 6 months. TNF gene polymorphism is also associated with psoriasis and psoriatic arthritis due to its effects on TNF production. Murdaca and colleagues have demonstrated TNF-α polymorphism on +489 position of the gene effects efficiency of etanercept treatment on psoriatic arthritis patients (PsA) [65]. In fact, the idea simply relies on the fact that gene polymorphism affects the biological properties of encoded proteins. TNF blockers

are widely used for regulation of inflammatory cascade and by that way treatment of the immune-related disease. If polymorphic product of the gene is your pharmaceutical target and has different molecular structure, then wild type its means pharmacodynamics of the drug varies due to personal variation.

Both IL-17 antagonists and IL-17 receptor blockers are accepted as effective and safe for psoriasis treatment [66]. Brodalumab is a human monoclonal antibody that binds to interleukin-17 receptor and waits for US-FDA approval for psoriasis treatment [55, 67]. IL-17 expression is upregulated in psoriatic skin samples. Both secukinumab and ixekizumab are the cytokine antagonists used for psoriasis treatment [68]. Nowadays, recent studies are focused on the relationship between IL-17 family cytokines (IL-17A, IL-17B, IL-17C, IL-17D, IL-17E, and IL-17F) and IL-17 receptor polymorphisms with psoriasis susceptibility and treatment response [69–71].

7. The link between psoriasis and comorbidities in view of genetics

Nowadays, psoriasis is accepted as a systemic disease because of higher rates of obesity, depression, psychiatric disorders, diabetes, hyperlipidemia, cardiovascular diseases, arthritis, uveitis, ulcerative colitis, Crohn's disease, and metabolic syndrome among psoriatic patients. Even if, the mortality rate of the psoriasis is low, psoriatic patients over 65 have at least two comorbidities [72]. Thus, interdisciplinary approach should be an integral part of the routine, and also the dermatologist should be careful with psoriasis and related disorders. Although the systemic inflammation process during psoriasis development is still unclear, the chronic inflammatory process may trigger development of many burden comorbidities in psoriatic patients. Many epidemiological studies revealed relationship between psoriasis and diabetes [72, 73]. Aside, the studies have shown that cardiovascular risk increases among patient with psoriasis and psoriatic arthritis [74]. In that point, dermatologist should be careful about systemic drug usage for psoriasis treatment because medications can sometime trigger maintenance factor in the pathogenesis of psoriasis [75–78].

In that section, we would like to evaluate the common mechanism between psoriasis and psoriatic comorbidities in molecular and genetic basis. For example, psoriatic patients are more prone to develop Crohn's disease more than general population [79]. The molecular basis of Crohn's disease is activation of CD4+ T cells by intestinal epithelial cells (IECs) and lamina propria immune cells and that activate both Th1 and Th17cells and cause elevated level of TNFα and Th17-related cytokine. Th1 and Th17 differentiation is common both in psoriasis and Crohn's disease; for that reason, TNF inhibitors are effective for treatment of Crohn's disease as psoriasis [80].

7.1. Psoriatic arthritis

Joint involvements in patients with psoriasis were put forward for the first time by Alibert in 1818 [81, 82]. Psoriatic arthritis is a negative spondyloarthropathy [71–83]. Important radiological findings of the psoriatic arthritis are peripheral joint involvement, destructive

and proliferative changes, spinal involvement, interphalangeal joint ledge, fibroosteitis and acroostelolysis [84, 85]. Strong genetic relationship is remarkable between positive family history [81, 86] and human leukocyte antigen (HLA) class II alleles for psoriatic arthritis [87–89].

Psoriatic arthritis (PsA) is diagnosed in 25–34% of psoriatic patients [90]. Psoriasis without joint involvement (PsO) and psoriatic arthritis (PsA) occur as a result of autoimmune responses that are triggered by genetic and environmental factors. The pathogenesis of psoriasis only (PsO) and psoriatic arthritis (PsA) may be explained impaired cytokine levels [91].

To clarify immungenetics mechanism of psoriatic arthritis has been focused on human leukocyte antigen (HLA). HLA gene region is located on the short arm of chromosome 6. This region is highly polymorphic depending on mutation and recombination [92]. Psoriatic arthritis associates with various HLA risk haplotype such as HLA-B7 B57 B13, B16, B17, DR7, B38, B39, CW6, and B27 [89, 93, 94]. While CW6 HLA-alleles were associated with early onset of the disease [95], HLA-B38 and HLA-B39 were associated with polyarthritis [87], and HLA-B27 was associated with dorsal involvement. Positivity of human leukocyte antigen "HLA-B27" in psoriatic arthritis patients makes a higher risk of arthritis compared to other HLA alleles [90, 96]. In Turkish population, we have found that HLA-B27 positivity increased the risk of psoriasis and psoriatic arthritis 5 to 10 times more, respectively [97]. There are various molecular-based hypotheses such as molecular mimicry, defective immunity, heavy chain folding incorrectly, and deterioration of HLA-B27 allele for relationship between HLA-B27 and psoriatic arthritis (PsA) [97].

7.2. Obesity

Storing energy in the form of triacylglycerols is considered to be the primary task of adipocytes; but adipocytes have physically some additional functions such as preservation of internal organs, regulating temperature, storage of lipid-soluble vitamins, steroid metabolism, immunity, and being assigned in inflammatory processes [98, 99]. Adipose tissue runs like as an endocrine tissue as the sympathetic system regulators with hormone and cytokine production during the regulation of energy metabolism [100]. Adipose tissue plays also an important role in homeostasis besides production, secretion such as TNF-alpha, IL-8, monocyte chemoattractant protein 1, cytokines and chemokines and storing energy in the form of fatty acids, together with the adipokines, leptin, adiponectin, resistin, such as pro-inflammatory and anti–inflammatory factors [98, 101].

The risk of diseases such as a high rate of insulin resistance, type 2 diabetes, dyslipidemia, gout, hypertension, and cardiovascular involvement is higher in obese individuals [102–107, 110]. Adipokine tissue secretes cytokines thus increasing volume or amount of adipokine tissue cause increasing the amount of circulating cytokines. Then, elevated amount of cytokines causes arteriosclerosis and insulin resistance and to induce hypertension and type 2 diabetes [108].

In a study that investigated the risk of obesity in patients with psoriasis, same sex siblings and 88 psoriasis outpatients were compared by calculating the BMI. The result of this study has obtained a significant relationship between the severity of psoriasis and BMI [109]. Duarte et al. have found that it was a statistically significant relationship between obesity and psoriasis severity on patients with psoriasis by using different parameters, such as BMI and waist/hip ratio [110]. It was shown

to be positive commensurate with psoriasis risk of weight gain and high BMI in another study performed in the United States with 809 psoriasis patients followed for 12 years [111]. Obesity was determined to be more than psoriasis only (PSO) patients [112–114], and it was determined that obesity increases the risk of psoriatic arthritis in individuals under 18 years of age [115].

7.3. The impaired glucose tolerance and diabetes

Glucose intolerance, diabetes, and obesity are more frequent in patients with psoriasis [74, 75, 116–119]. The study conducted by Onsun et al. has found that diabetes was significantly more frequent in patients with psoriasis when compared to the incidence of psoriasis in patients with diabetes [120]. Azfar and his colleagues have found that patients with severe psoriasis involvement have more risk of with diabetes; in contrast, they concluded that psoriasis was an independent risk factor for type 2 diabetes [121]. Armesto and colleagues have found that occurrence of risk of type 2 diabetes was found to have higher, late-onset, nonfamilial transmission, but in patients with joint involvement [122]. Finley et al. have shown that expression of IL-17 and IL-20 is elevated in diabetic wounds, and they emphasized the psoriasis and diabetes link via cytokines [123]. Granata et al. have demonstrated that IL-23/IL-17, and IL-18 are main cytokines that has central role for obesity, type 1 diabetes, and psoriasis [124]. Eirís et al. have demonstrated that IL12B rs6887695 and rs3212227 increase the type 2 diabetes risk approximately 3 and 6 times, respectively [125]. In addition, IL23 receptor polymorphism was also found significantly associated with diabetes in psoriatic patients [125]. Presta et al. have found that polymorphism in the 3′untranslated region of IL-18 gene increases the insulin sensitivity risk [126]. In addition to literature, we have evaluated the diabetes risk among psoriasis patients; yet, we could not find any significant relation between TNF-α-238 G/A and TNF-α-308 G/A polymorphisms with diabetes [127].

7.4. Cardiovascular diseases

The epidemiological studies have shown that cardiovascular morbidity and mortality increased in patients with psoriasis in Refs. [77, 78, 128, 129]. Inflammation located in pathogenesis of psoriasis is known to cause metabolic and cardiovascular disease. The molecular relationship between psoriasis and cardiovascular disease may be explained by T cell activation and enhance of Th1 cytokine production (TNF-α, IL-1β, IL-10, and IFN). The TNF-α and IL-1 trigger oxidative stress causes migration of leukocytes into atherosclerotic plaques [101], so TNF inhibitors have beneficial effects on prevention of cardiovascular events both in psoriasis and psoriatic arthritis [130]. Our study group has evaluated hypertension risk and psoriasis. eNOS Glu298Asp single-nucleotide polymorphism has found to be increased in hypertensive psoriatic patients when compared with healthy volunteers [131]. In contrast, we could not find relationship between TNF-α-298 and TNF-α-308 polymorphisms with hypertension and cardiovascular disease [127].

7.5. Metabolic syndrome

Metabolic syndrome is associated with conditions such as physical inactivity and improper diet, occurring nutrition changes, and daily lifestyle. It is characterized as a disease of civilization by high mortality and morbidity [132].

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It is a fact that metabolic syndrome and its components are often seen in patients with psoriasis. Also, polymorphism may be triggering both psoriasis and metabolic syndrome together. Abdel Hay and Rashed have shown that leptin gene 2548G/A polymorphism increases risk of both psoriasis and metabolic syndrome [133].

7.6. Psychological trauma and addiction

Psoriasis is a chronic skin disease that negatively affects the quality of life in many ways. Patients with psoriasis reduce quality of life with comorbidities like arthritis. Psoriasis can lead not only to physical health problems, but also to mental and social health problems. Psoriatic lesions that occur especially in hands, face, and on the scalp cause shame, embarrassment, and social inhibition in social life and by that way increase the risk of depression, anxiety, lack of self-confidence, smoking and alcohol addiction, and trend of suicidal thoughts in patients with psoriasis [134].

Kurd et al. have shown that depression, anxiety, and suicidality risk increases 1.39, 1.31, and 1.44 times more in psoriatic patients than healthy people, respectively [135]. Psoriatic patients are more prone to psychiatric comorbidities and suicidal ideation than other dermatological diseases [136]. Deveci and et al. have found significantly higher depression rate and suicide attempts in cases with psoriasis when compared to patients with other dermatological problems [137].

Use of alcohol and tobacco makes difficult the therapeutic harmony and also increases the toxicity of the drug besides reducing the effectiveness of systemic anti-psoriatic drug. Excessive alcohol intake can induce production of proinflammatory cytokine in various cell types and increase the cell lymphocyte proliferation and activation [138]. Serotonin may be triggered psoriasis as a growth factor that promotes keratinocyte proliferation [139]. The serotonin transporter gene promoter region and serotonin2A receptor gene have been found associated with psoriasis in Thai population [140, 141].

8. Conclusions

What would cause the metabolic alteration among psoriatic patients? Does systemic drug usage in long term causes comorbidities in patients with psoriasis? or Is it the domino effect of impaired metabolism? It has not reached a consensus about it.

Advances in understanding the immune-mediated pathological mechanisms of psoriasis will be highlighted with the relationship between psoriasis and psoriasis-related comorbidities. Much psoriatic comorbidity may be triggered by the cytokines and chemokines, which were secreted by T-cells, keratinocytes, and antigens presenting cells after keratinocyte hyper proliferation. Hence, molecular approaches are important to identify the link immunogenic mechanism with psoriasis-related comorbidities in view of molecular pathways.

Determinations of genomic risk profile of the psoriatic patients allow diagnosing of psoriasis and its related comorbidities at an early stage; hence, the life quality can be increased by treating them earlier. In addition, evidence-based information helps physicians to make clear decision

and help to minimize medical errors as well as unnecessary drug usage. As a sum, this information allows to increase treatment cost and work loss. In addition, pharmacogenomics of drugs among psoriatic patients is tightly related to personal variations on genome, and thus, complex genetic heterogeneity affects the treatment power.

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