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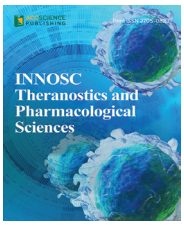

COMMENTARY

Vitamin D Deficiency as a Potential Inducer of Autoimmune Diseases in Patients with Xeroderma Pigmentosum

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This commentary aims to highlight the importance of vitamin D deficiency which was not completely addressed in a recently published paper by Saravani *et al.* [1], and also to reflect why it is important to assess the potential of vitamin D in treating autoimmune disease, especially in patients with xeroderma pigmentosum (XP) [2].

Saravani *et al.* reported in their publication the interplay of several endogenous and exogenous parameters which are involved in DNA damage and activity [1]. Among these factors, oxidative stress and smoking are believed to act as endogenous and exogenous factors respectively [3].

XP is a rare autosomal recessive genodermatosis characterized by skin hyperpigmentation, premature photoaging, and increased risk of developing skin cancer [4]. In addition to dermatological manifestations, XP patients also may present with autoimmune manifestations [4,5].

Among pathophysiological factors that trigger autoimmunity in XP patients, DNA damage has been widely shown to be involved in the development of autoimmune diseases [1]. Therefore, several studies have been conducted to identify the correlation between polymorphisms in DNA repair genes and the prevalence of the autoimmune diseases [6]. Some of the research hypotheses were discussed in the literature, especially the mechanism of autoimmune reactions in XP. Immunomodulation has been reported in some, but not in all XP patients [7]. Furthermore, downregulation of adenosine triphosphate (ATP)-dependent DNA excision repair protein genes and DNA-encoded genes implies that impaired DNA repair and ATP synthesis, or increased in apoptosis, may contribute to various manifestations of some autoimmune diseases such as systemic lupus [1,8]. In addition, ultraviolet (UV) damage is also known to modulate the immune response in the normal cells, and the presence of elevated level of unrepaired DNA damage in genodermatosis patients is likely to enhance immunosuppression in these patients [4].

On the other hand, XP patients have an increased risk of developing UV-induced skin cancer; therefore, protecting themselves from direct sun exposure is very important. Association between vitamin D deficiency and a variety of independent diseases, such as bone diseases, autoimmune diseases, hypertension, and cardiovascular disease, has clearly been shown in a number of studies [9].

Recently, there have been an increasing number of publications focusing on the effect of vitamin D on immune processes [2,10]. Vitamin D plays a key role in modulating immune function with an important impact on health maintenance and prevalence of diseases, particularly autoimmune disorders. Low serum level of 25-hydroxyvitamin D (25[OH]D) has been shown to associate with increased risk of autoimmune disease onset and/or high disease activity. The active form of vitamin D, through the interaction with its receptor, exerts different activities on the innate and adaptive immune system, among them is suppression of inflammation. Vitamin D insufficiency is linked to autoimmune disorders that commonly display significantly different symptoms between females and males due to genetic, epigenetic, hormonal, and environmental factors. Vitamin D plays a key role in the regulation of innate and adaptive immune system. It has been shown to modulate the production of several proinflammatory cytokines, such as interleukin-1 (IL-1) and tumor necrosis

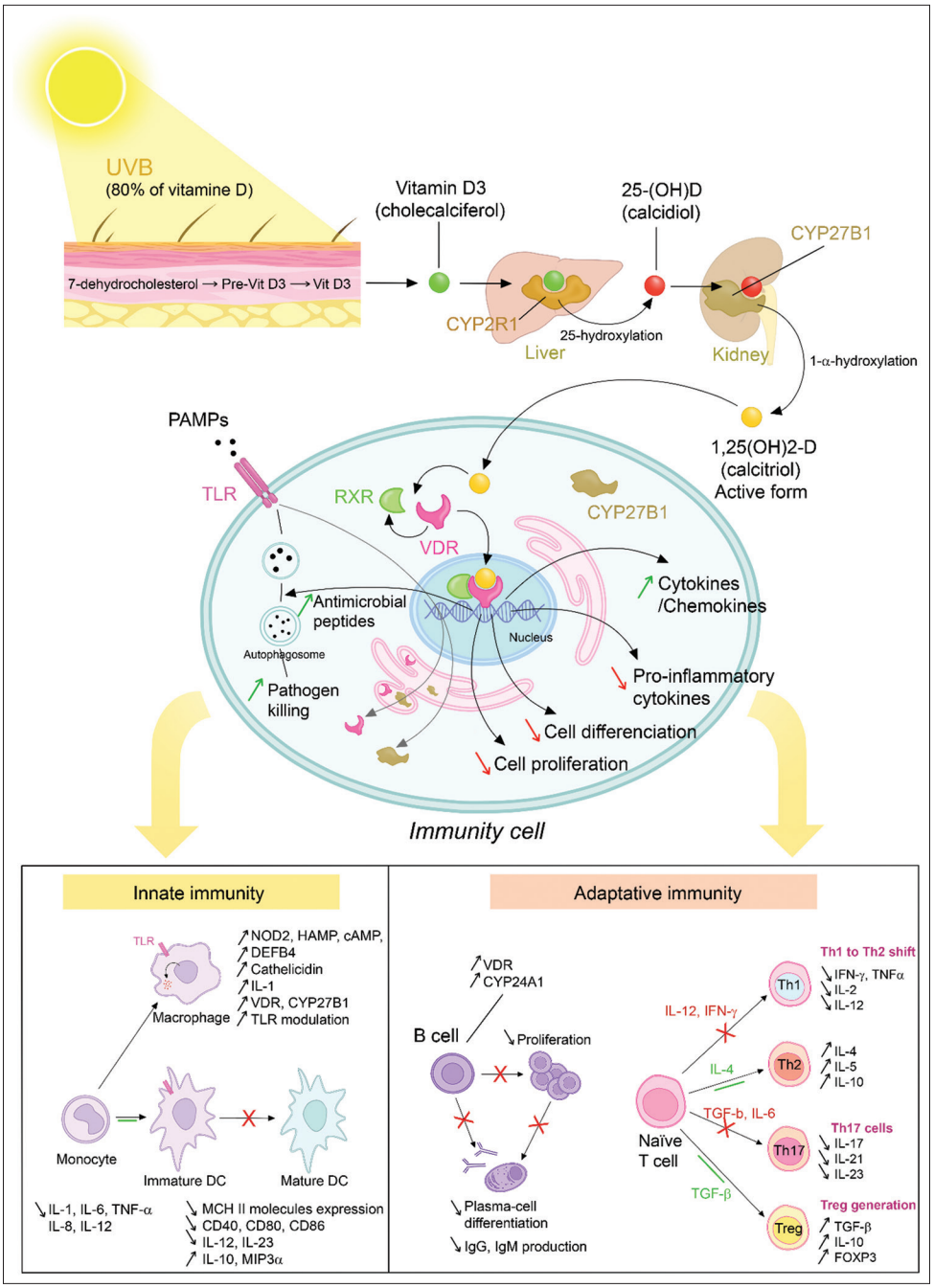

Figure 1. Numerous effects of vitamin D in cells within the immune system.

factor-alpha (TNF-α). Vitamin D also helps to regulate the production of immunoglobulins, which is triggered by the presence of antigens, helping the body to identify and respond to potentially dangerous foreign invaders. Vitamin D also helps to regulate the balance between pro-inflammatory and anti-inflammatory components of the immune system. It helps to maintain the balance of cytokines, which can either promote or inhibit inflammation. Vitamin D can also help to reduce the overproduction of proinflammatory cytokines, such as IL-1, which can lead to excessive inflammation. It inhibits B-cell proliferation and blocks B-cell differentiation and immunoglobulin secretion. Vitamin D additionally suppresses T-cell proliferation and results in a shift from a Th1 to a Th2 phenotype (**Figure 1**).

Rigorous protection from sunlight is essential in XP patients, as soon as, the disease is diagnosed or suspected, to prevent continued DNA damage or disease progression. Individuals with XP should avoid exposing their skin and eyes to UV radiation. All these measures will lead to a vitamin D deficiency and an increased autoimmune risk, as shown in our previous work [5]. It has been confirmed that vitamin D deficiency is highly prevalent in XP patients, and supplementation of vitamin D in these patients should be considered to avoid unfavorable skeletal consequences [11].

Suboptimal vitamin D status has to be addressed to protect against serious vitamin D deficiency-related health problems. These data warrant more investigation into the potential use of vitamin D in the treatment of patients with autoimmune diseases. In recent years, several clinical trials have been performed to investigate the therapeutic value of vitamin D in multiple sclerosis, type I diabetes, and systemic lupus erythematosus [2].

In summary, the data from Saravani *et al.* highlighted lupus as an autoimmune disease may be associated with XP patients, but the hypothesis of vitamin D deficiency should be underlined in view of the importance of the latest scientific data on the relationship between vitamin D deficiency and autoimmune disease.

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Conflict of interest

The author declares that there are no conflicts of interest that could be perceived as prejudicing the impartiality of the commentary.

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