

ALLERGY, GENETICS, VITAMINS

SUN + WIND + ALLERGY

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New work by Harvard colleagues shows [how sunshine hormone D constrains inflammation](#) by modulating the expression of key genes on [chr17q](#). It builds on earlier collaborative work on the vitamin D receptor in 2004 ([see their ref 5](#)) as well on my [annotation of IKZF3 \(aka aiolos aka god of winds\)](#) in 2008 and [again](#) in 2022.

While our focus on allergy development was on vitamin D supplementation of newborns, the interest of Weiss et al. was on vitamin D deficiency in pregnancy. Vitamin D deficiency may not be attributed to the rise of the [asthma and allergy epidemic](#) although this remains the never ending obsession of Weiss et al.

Nevertheless, also a wrong hypothesis may lead to new insights. IKZF3 clearly is a [key player](#) where more recently heterozygous missense/LOF variants have been found in families with B-lymphopenia and EBV-associated lymphoma while the allergy proning effect is more in the [5-prime region](#).

The new study shows (again) that cholecalciferol suppresses the activation of the IL-2 pathway. But what is the net effect of artificial cholecalciferol exposure on naive T cells? Unfortunately the new paper narrowly focuses on cytokine production in Th2 cells only and even misses the famous [Cantorna review](#) that clearly says

Since 1983 it has been described that $1,25(\text{OH})_2\text{D}$ inhibited T cell proliferation and the secretion of select cytokines after mitogen stimulation. Moreover, $1,25(\text{OH})_2\text{D}$ directly inhibited IL-2 and IFN- γ transcription [[17,18](#)]. More recently $1,25(\text{OH})_2\text{D}$ has also been shown to inhibit IL-17 secretion by Th17 cells. The effects of $1,25(\text{OH})_2\text{D}$ on Th2 cells is more controversial with evidence that $1,25(\text{OH})_2\text{D}$ inhibits IL-4 transcriptionally as well as evidence that $1,25(\text{OH})_2\text{D}$ upregulates IL-4 in mouse and human T cells.

So we need to rephrase the finding of an “immune protective effect of vitamin D in allergic lung inflammation” to an overall “immune suppressive effect of vitamin D” which is basic textbook knowledge. Unfortunately the early origin of allergy induction remains a mys-

tery.

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