

Effect of Vitamin D on auto-immune diseases

Team

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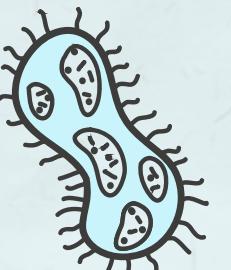
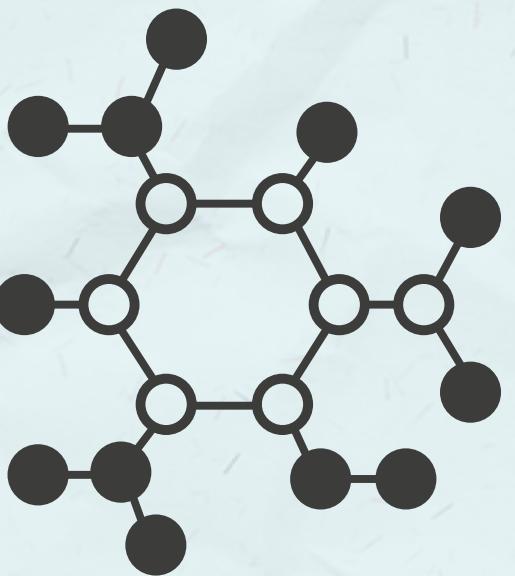
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Initial Idea

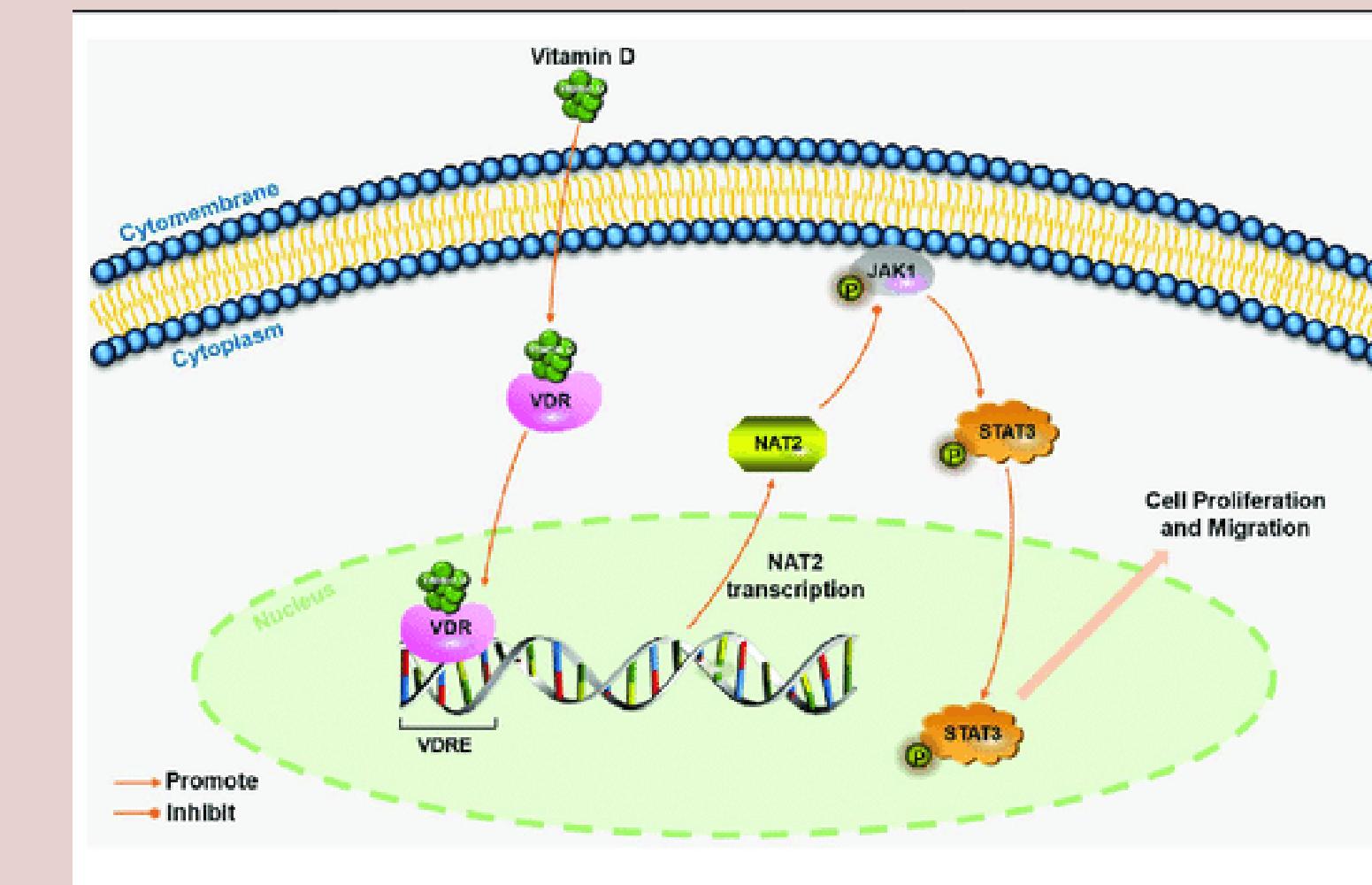
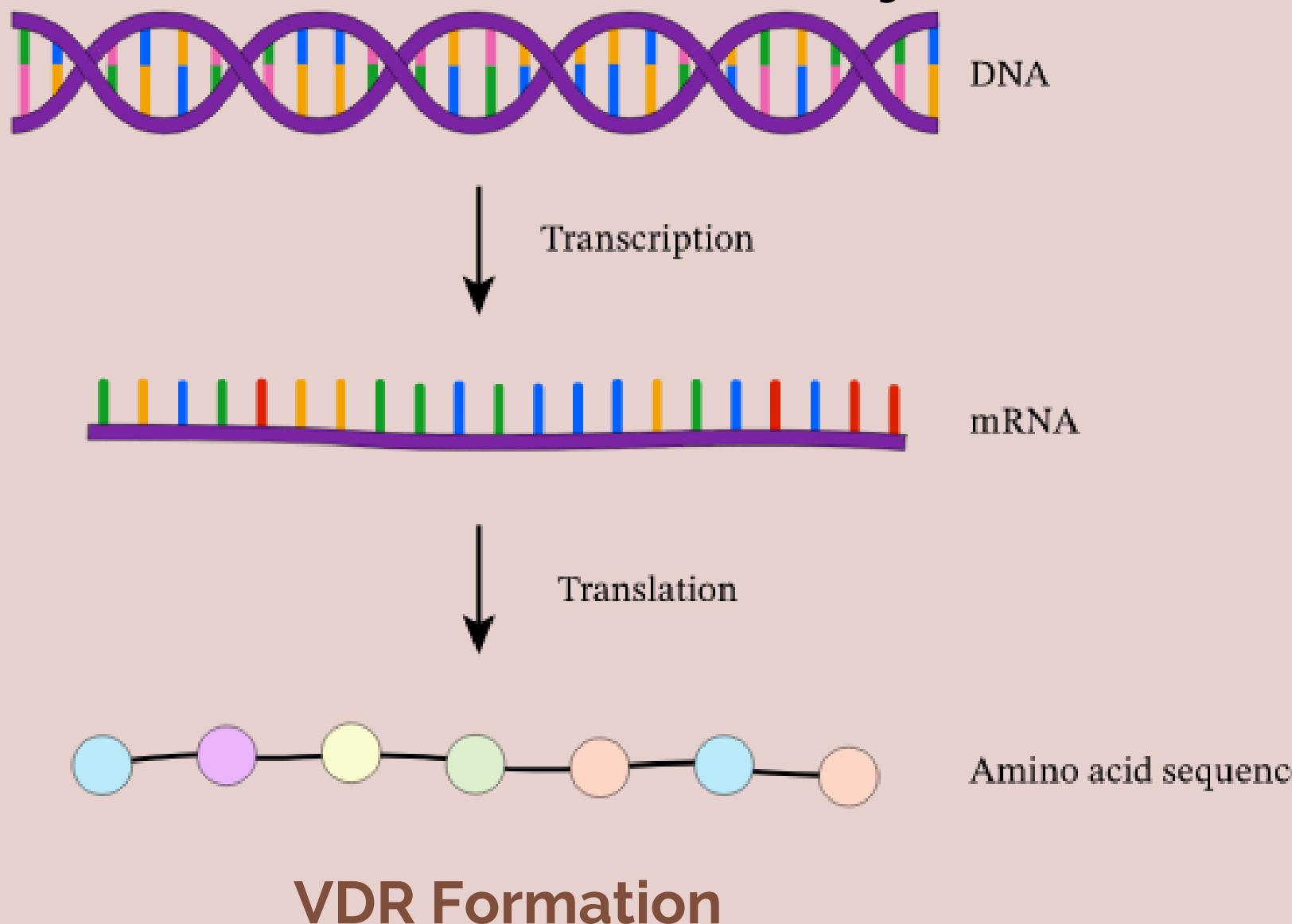
There are various causes that result in the body's immune system mistakenly attacking the body's own cells and tissues. Since this reaction is the root of autoimmune diseases, understanding such pathways can help us analyse the immune system and autoimmune diseases. We have found that Vitamin D binds to the VITAMIN-D RECEPTOR PROTEIN.

This complex regulates cell proliferation and differentiation by affecting a particular gene set. This gene set could be found by finding the genes that would be differentially expressed in our samples.

Vitamin D can effect on the pathogen as well as the immune system, can be affected through various factors.

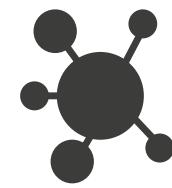
One of them could be the downregulation or upregulation of the GENE THAT SYNTHESIS VDR PROTEIN.

The other, which we will be focussing on as a part of this project, is the gene that is regulated by the VDR and Vitamin D Complex.



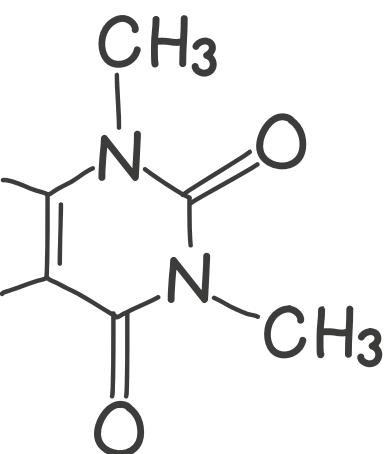
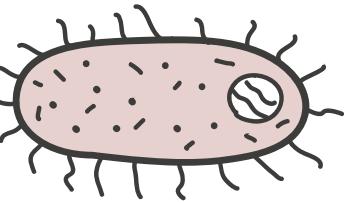
VDR Formation

VDR Vitamin-D Complex in action

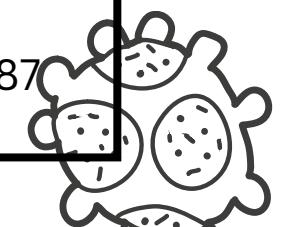
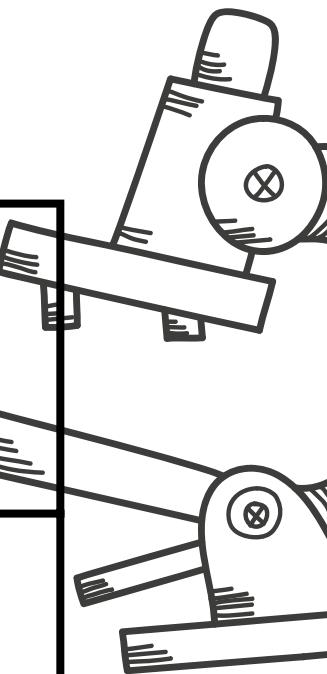


Datasets

Autoimmune



Disease	Sample Size	Experiment Type	Link
Rheumatoid arthritis	83	Microarray	https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE55457
Psoriasis	180	Microarray	https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE13355
Systemic lupus erythematosus (SLE)	129	Microarray	https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE61635
Clinically isolated syndrome (CIS)	113	Microarray	https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE13732
Alopecia	122	Microarray	https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE68801
Crohn's disease	15	Microarray	https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE24287



Datasets

Non-Autoimmune

Disease	Sample Size	Experiment Type	Link
type 2 diabetes	234	Microarray	https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE9006
osteoarthritis	33	Microarray	https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE55457
lung cancer:	192	Microarray	https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE4115
Carcinoma	575	Microarray	https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE108712
Breast cancer	121	Microarray	https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE42568

Ideal result of our experiments

We conduct a pathway analysis of the differentially expressed genes found in the samples. We would then expect those results to express a direct correlation with VDR in the case of auto-immune diseases and no such relation in cases of other diseases.

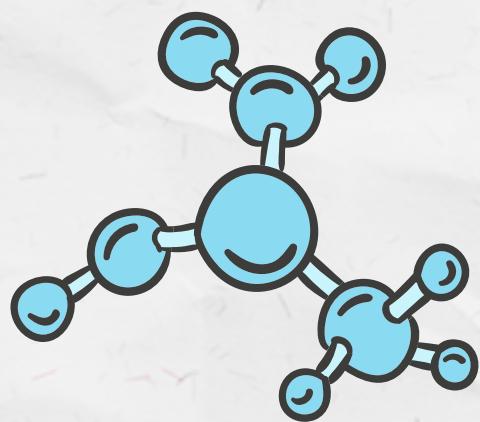
Why a direct pathway analysis was not enough

The pathway analysis revealed vitamin D pathways in three autoimmune and two non-autoimmune diseases in the differentially expressed genes. However, this conclusion was not comprehensive in accordance with our hypothesis so we decided to look into the differentially expressed genes individually.

Experimental Group

Auto-immune diseases

We found differentially expressed genes in the samples of patients having auto-immune diseases. According to our hypothesis, ideally, the presence of genes regulating the VDR Protein should have been present in these. We studied 6 such diseases, and all of them were consistent with our research: Alopecia, Rheumatoid Arthritis, Systemic lupus erythematosus(SLE), Psoriasis, Clinically Isolated Syndrome(CIS) and Crohn's Disease

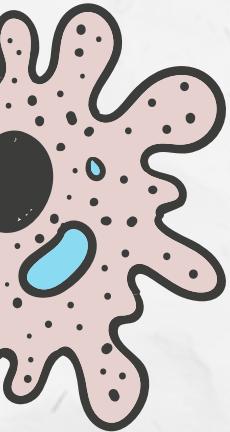




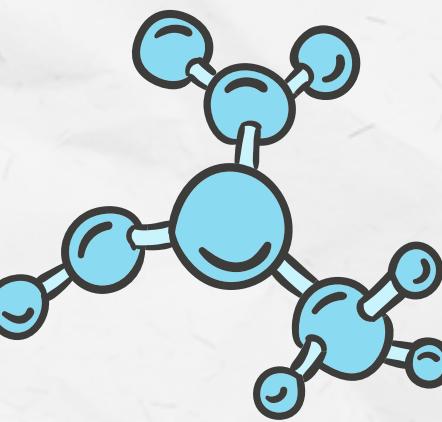
Control Group



Non-autoimmune diseases



We did the same analysis for diseases that were not auto-immune and found the differentially expressed genes. According to our hypothesis, ideally, presence of genes regulating the VDR Protein should not have been present in these. Diabetes Type-II and Carcinoma were consistent with our studies. However, we found that in Osteoarthritis, Lung Cancer and Breast Cancer, that was not the case.



The Process

- We reviewed the available literature and found the genes that transcribed for VDR Protein manufacture or regulation.
- We analyze the given microarray data and perform T-tests on them to identify differentially expressed genes.
- We find the differentially expressed genes and map these to their respective gene symbols.
- We write these symbols onto the csv file and we have marked the genes that we found to be linked to vitamin-D according to the genes that we had found earlier in the research.

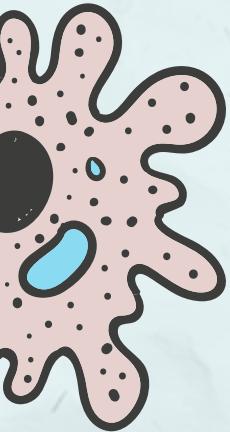


Gene Symbols in autoimmune diseases for VDR

Disease	Gene Symbols identified
Alopecia	FGF5 CD109 CD163 CD109 CD53
Clinically Isolated Syndrome	ZNF397 TGFBRAP1
Crohn's Disease	NPC1L1 MLN MLN
Psoriasis	CD24 CD47 CD24 CD274 CD24 CD24 CDH3 CYP7B1
Rheumatoid Arthritis	TGFBR2 CYP1B1 TGFBRAP1 JUN CD27 CDH1 TNFAIP8 INSIG2
Systemic lupus erythematosus (SLE)	JUNB PTP4A1

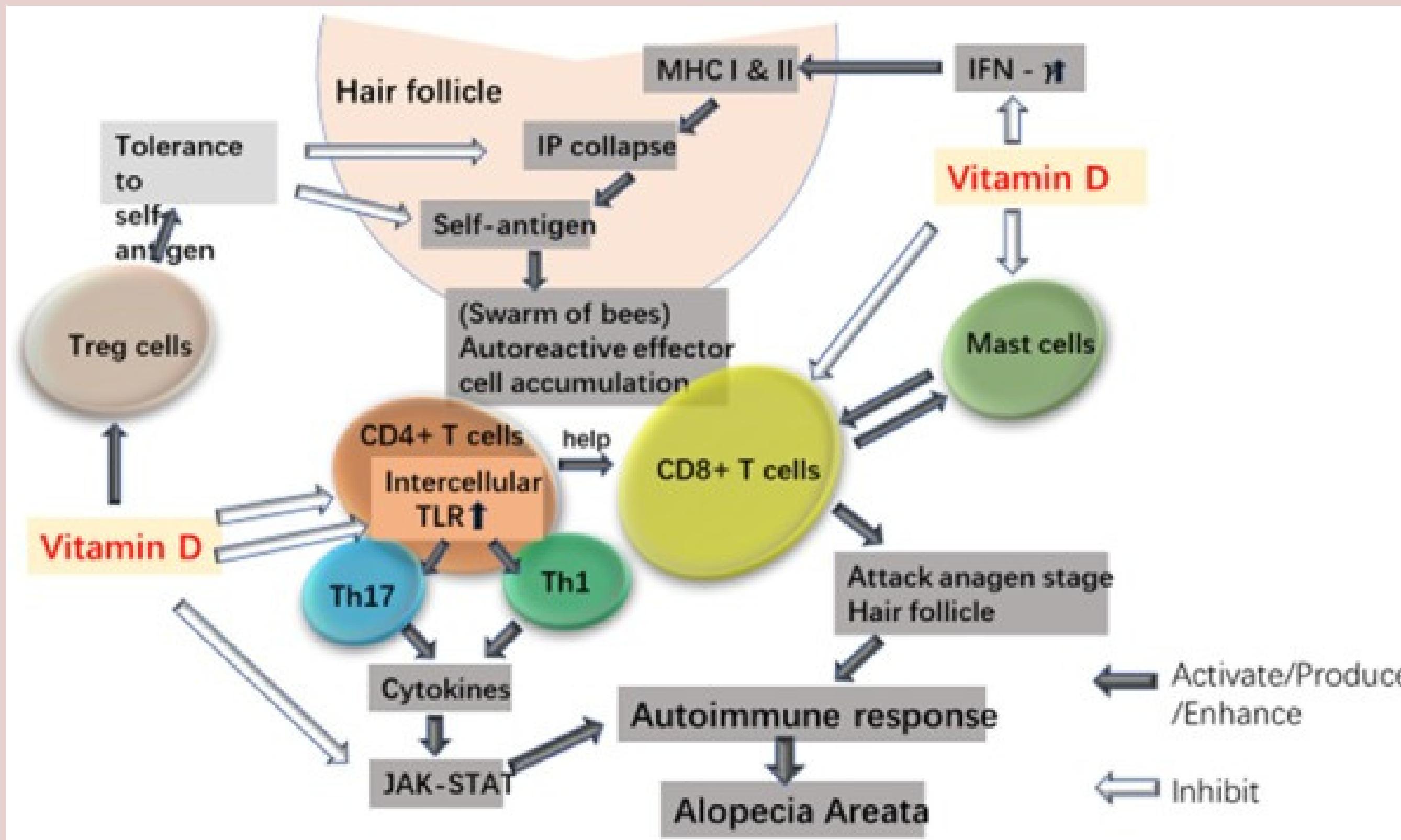


Gene Symbols in non-autoimmune diseases for VDR



Disease	Gene Symbols identified
Breast Cancer	VDR CD36
Lung Cancer	TNFAIP8L1
Osteoarthritis	TGFBFR2
Type-II Diabetes	Not Found
Carcinoma	Not Found

Vitamin D and alopecia areata: possible roles in pathogenesis and potential implications for therapy



Source link : <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6789271/>

Vitamin D and alopecia areata: possible roles in pathogenesis and potential implications for therapy

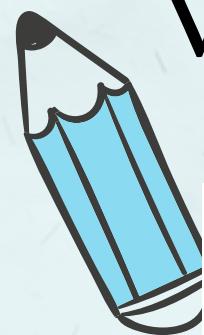
Introduction

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Alopecia areata (AA) is a common autoimmune skin disease characterized by loss of the hair on the scalp and elsewhere on the body, affecting approximately 2% of the general population at some point during their lifetime. AA may cause anxiety on patients and increases the risks of developing psychological and psychiatric complications [1]. The hair loss in AA is believed to result from an autoimmune-mediated hair follicle (HF) destruction consequent to a loss of immune privilege (IP) in the HF. Autoreactive effector T cells and mast cells, CD8-positive nature killer group 2 member D (NKG2D)-positive cytotoxic T cells (CD8⁺NKG2D⁺ cytotoxic T cells), Janus kinase/signal transducers and activators of transcriptional signaling (JAK/STAT) pathways, regulatory T cells (Tregs) and immune checkpoints and oxidative stress (OS) are involved in AA [1,2]. However, the pathogenesis of AA remains incompletely understood and AA remains incurable.

Vitamin D has been associated with various autoimmune diseases. Recently, vitamin D deficiency has been reported in AA [3]. Moreover, topical calcipotriol has been reported to be used successfully in treating AA [4-6]. These reports attracted the attention on the relationship between vitamin D and AA. The aim of this review is to summarize the current knowledge on the possible roles of vitamin D in the pathogenesis of AA and to discuss the potential implication of vitamin D in the treatment of AA.

A number of studies demonstrated significantly lower levels of vitamin D in the patients with AA than the control group [11-17]. Several studies showed significantly higher prevalence of vitamin D insufficiency in patients with AA than the control group [12,13,18,19]. But there were two reports of inconsistent results. A Turkish study found that AA patients had a deficiency of 25(OH)D, but there was no statistically significant difference in the serum vitamin D levels between AA patients and healthy controls. The authors said that this might be due to the universal tendency toward lower values of 25(OH)D in their geographical area, and they noted that the blood samples were collected only once during the late fall and winter months [20]. In a study involving 55,929 women in the Nurses' Health Study, 133 cases of AA were identified over a follow-up of 12 years. The association between estimated vitamin D status and self-reported incident AA was prospectively evaluated. No significant association between a predictive score of serum 25(OH)D levels and risk of incident AA was found [21]. Importantly, two systemic reviews and meta-analyses published in 2018 did demonstrate that, patients with AA have a higher prevalence of vitamin D deficiency and lower vitamin D levels than the control group [3,22] (Table 1). Moreover, several studies revealed that serum vitamin D levels significantly and inversely correlate with the severity of AA [12,16,17,19,23].



Vitamin D, Autoimmune Disease and Rheumatoid Arthritis

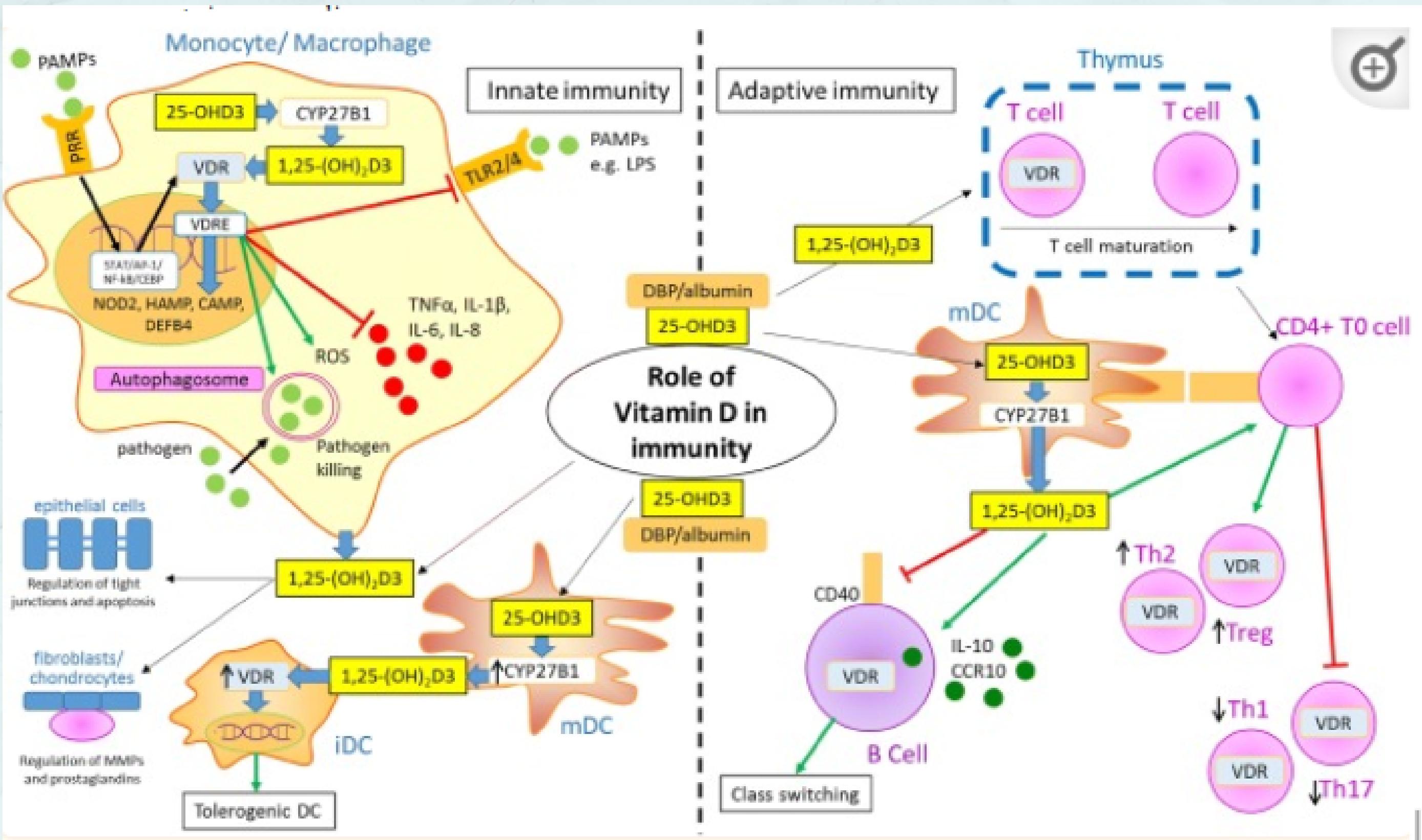
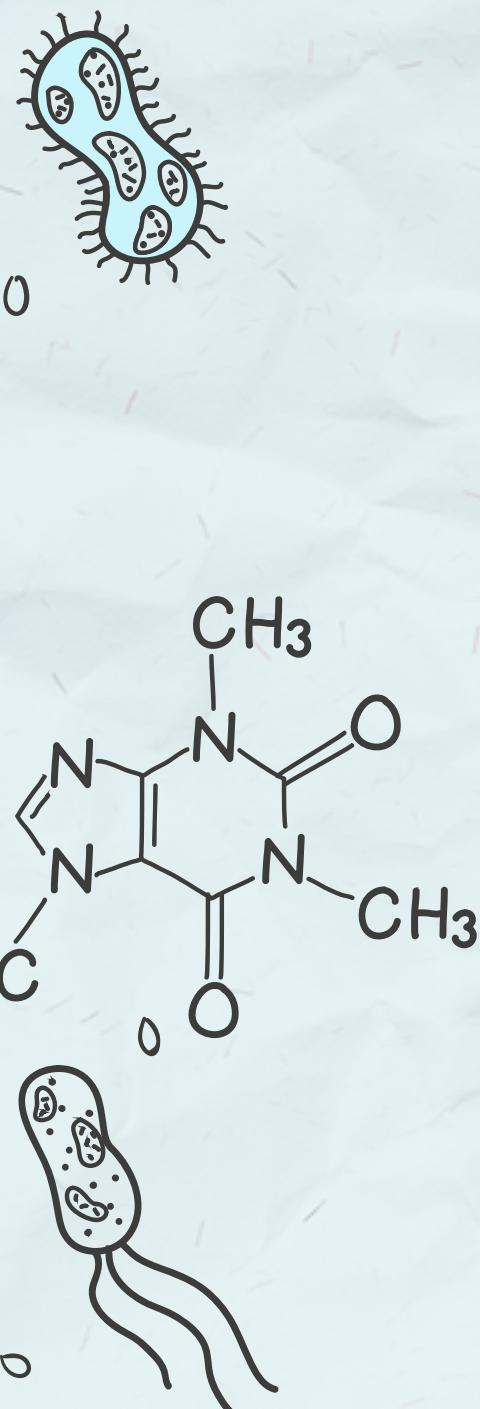
Vitamin D is a secosteroid which can be obtained from the diet (in particular from oily fish, eggs, dairy products and fortified foods). However, in humans, the majority of vitamin D is synthesised in the skin from the precursor molecule 7-dehydrocholesterol, which undergoes a series of UV light-mediated modifications to generate parental vitamin D₃ [1]. Vitamin D was first recognised for its role in bone mineralisation and calcium regulation, with vitamin D deficiency associated with the bone disease rickets [2]. More recently, vitamin D has been reported to exert many extra-skeletal effects [3] with association studies linking vitamin D status to a broad range of human health issues. Prominent amongst these is the proposed role of vitamin D in the pathophysiology of autoimmune disease, including insulin-dependent type 1 diabetes mellitus (T1D) [4], autoimmune thyroid disease [5, 6], multiple sclerosis (MS), inflammatory bowel disease (IBD) [7], systemic lupus erythematosus (SLE) [8] and rheumatoid arthritis (RA) [9]. The underlying mechanisms by which vitamin D impacts autoimmune disease remain elusive, and it is still not clear whether vitamin D deficiency contributes to autoimmune disease pathogenesis or whether it is marker of disease progression and severity. In this article, we address these issues with specific reference to the role of vitamin D in RA. We discuss the potential clinical significance, and the mechanisms of action of vitamin D in RA, and suggest areas where future research is needed.

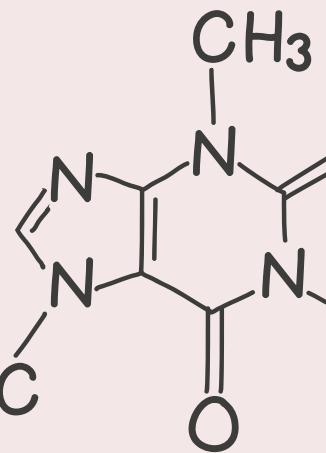
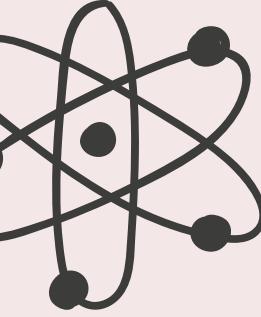


Vitamin D, Autoimmune Disease and Rheumatoid Arthritis

Vitamin D is also known to differentially regulate innate immune cell subsets, influencing cell maturation, metabolism and antigen presentation, alongside response to and production of cytokines and chemokines [13, 14, 38, 39]. Notably, mature DC express CYP27B1 but little VDR, whereas the converse is true for immature DC [13]. This has led to the hypothesis that mature DC may in fact produce vitamin D locally on activation, which then acts on immature DC to modulate immune responses [13, 40]. The principal effect of $1,25\text{-(OH)}_2\text{D}_3$ on DC is to suppress maturation markers such as CD80/CD86 [41–43] and CD83 [44], increase IL-10 production and decrease pro-inflammatory cytokines [41, 45, 46]. In this way, $1,25\text{(OH)}_2\text{D}_3$ promotes an immature, tolerogenic DC phenotype [47–49], thereby reducing antigen presentation to T cells.

Vitamin D, Autoimmune Disease and Rheumatoid Arthritis





Multiple Sclerosis and Vitamin D

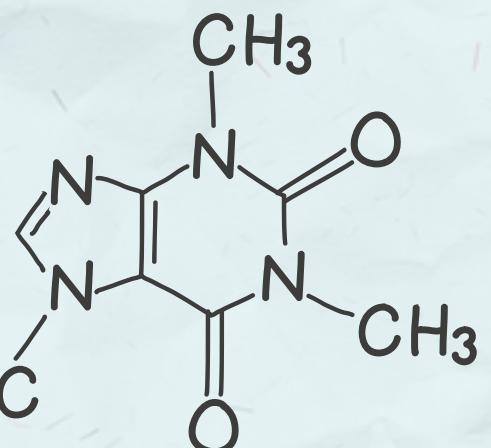
If environmental exposures are shown to cause an adverse health outcome, reducing exposure should reduce the disease risk. Links between exposures and outcomes are typically based on 'associations' derived from observational studies, and causality may not be clear. Randomized controlled trials to 'prove' causality are often not feasible or ethical. Here the history of evidence that tobacco smoking causes lung cancer—from observational studies—is compared to that of low sun exposure and/or low vitamin D status as causal risk factors for the autoimmune disease, multiple sclerosis (MS). Evidence derives from *in vitro* and animal studies, as well as ecological, case-control and cohort studies, in order of increasing strength. For smoking and lung cancer, the associations are strong, consistent, and biologically plausible—the evidence is coherent or 'in harmony'. For low sun exposure/vitamin D as risk factors for MS, the evidence is weaker, with smaller effect sizes, but coherent across a range of sources of evidence, and biologically plausible. The association is less direct—smoking is directly toxic and carcinogenic to the lung, but sun exposure/vitamin D modulate the immune system, which in turn may reduce the risk of immune attack on self-proteins in the central nervous system. Opinion about whether there is sufficient evidence to conclude that low sun exposure/vitamin D increase the risk of multiple sclerosis, is divided. General public health advice to receive sufficient sun exposure to avoid vitamin D deficiency (<50 nmol/L) should also ensure any benefits for multiple sclerosis, but must be tempered against the risk of skin cancers.

Vitamin D, Autoimmune Disease and Rheumatoid Arthritis

Conclusions

Go to: ▶

Future studies of vitamin D and RA are needed firstly to expand our current understanding of the mechanisms by which 1,25-(OH)₂D₃ is able to regulate key cells associated with RA. In particular, the observation that T cells from the inflamed joints of RA patients are insensitive to 1,25-(OH)₂D₃ [153] indicates that RA disease is associated with a corruption of vitamin D signalling that may be fundamentally important for RA disease pathology, and the therapeutic use of vitamin D. A key question that remains to be answered is whether vitamin D has greater benefits in protecting against the onset of RA as opposed to its potential application as a therapy for established RA disease. Thus, future studies to assess the effects of vitamin D supplementation on disease prevention in individuals at risk of RA, and disease development in those at early stages of RA, are required. These studies are likely to be informed by recent meta-analyses for immune effects of vitamin D. Notably, the observation from the analysis of acute respiratory infection trials that vitamin D supplementation was more beneficial in patients with low baseline serum vitamin D, and was more effective when supplementation was used as lower daily or weekly dosing [159], provides some important pointers for future studies of vitamin D and RA. Repeated lower doses of vitamin D supplementation would also help to avoid potential adverse effects of higher doses of vitamin D, in particular the reported increased risk of falls in elderly patients receiving a single bolus of higher-dose vitamin D [160]. Future studies also need to take into consideration clinical subgroups of patients, including distinguishing between ethnic groups and disease of different durations. The potential for a simple, low-risk and low-cost intervention such as vitamin D as a plausible adjunctive treatment for RA is an exciting notion. Robust evidence to support wider routine use of vitamin D supplementation in RA has the potential to significantly enhance treatment for RA and other



List of biological functions of the 291 genes whose expression was influenced by vitamin D₃ supplementation.

Biological functions	Gene symbol
Apoptosis and immune response	OSM, AXUD1, CD83, PHLPP, TNFAIP3, NFKBIA, ZNF287, PTRH2, XIAP, TTNFAIP8L2, ZDHHC16, TIA1, NUDCD1, KLF11, RASA1, EGR1
Mineralization and bone development	JUND, SBDS, ZNRD1, MINPP1
Transcriptional regulation	ORC2L, KLF10, TRIM27, EGR1, NFIL3, JUN, NR4A2, ZNF225, ZNF607, ZNF780B, ZNF616, RASA1, ZNF397, ZNF284, ZFP62, HOMEZ, ZNF701, GTF2E1, ZNF232, ZNF473, TAF1A, ZNF587, MIZF, ZNF223, ZNF175, MED7, ZNF320, ZNF17, ZNF45, ZFP3, ZNF283, EGR1, MED17, ZNF235, NF780A, ZNF322A, KLF11, SUV420H1, ZNF852, HCFC2, NAPC3, TRIP11, JRKL, ZNF234, ZNF260, JUNB, KLF10, TRIM27
Metabolic processes	TGDS, NAPEPLD, KIAA0859, ARSK, TMEM68, INSIG2, GALK2, FPGT, HMGCL, HSD17B7P2, HSD17B7
Response to stress and DNA repair	FANCF, MSH5, PXDNL, ATF4, STIP1, HSPA4, HSPH1, POLA2, SOS1
RNA processing	CCDC76, MTO1, C1orf25, PUS3, RBM5, CSTF3, ZFP36, RNASEL, NUP107, ZCCHC8, POP1, INTS7, GEMIN6
Ion and protein transporter	SLC39A7, SLC30A6, SLC30A5, COPB2, NUP43, GOPC, SLC35B3, BET1, USO1, PIGM, TRAPPC6B
Biological process	TGDS, NAPEPLD, KIAA0859, ARSK, TMEM68, INSIG2, GALK2, FPGT, HMGCL, HSD17B7P2, HSD17B7
Epigenetic modification	HIST1H1E, H1FX, ALKBH1, UTP3, N6AMT1, METTL4
Cell cycle and DNA replication	FGF5, IRS2, MIS12, C10orf2, ORC2L, HELB, CUZD1, KIAA1009, POLA2, CETN3, CEP110, POLA2, PTP4A1
Signal transduction	GRASP, GNRH1, TAS2R4, TAS2R3, CXCR7, RIC8B, SOS1, BBS10
Protein modification	PIM3, PTP4A1, RNF139, PDP2, GGCX, PPID, TTC9C, SIK1, STK38
Development and cell differentiation	PDE4DIP, TUBD1, KEAP1, BBS7, UTP3, C11orf73, MKKS, BPNT1, NOC3L

Influence of Vitamin D Status and Vitamin D3 Supplementation on Genome Wide Expression of White Blood Cells

Source link: <https://www.genecards.org/cgi-bin/carddisp.pl?gene=IL1RN>

Polarization of Human Monocyte-Derived Cells With Vitamin D Promotes Control of *Mycobacterium tuberculosis* Infection

Human lung tissue biopsies (TB lesion and distal sites), obtained from patients with non-cavitory TB ($n = 5$) as previously described (25, 26), were freeze-fixed in OCT (Tissue-TEK, Sakura) before cutting two 50 μ m cryosections that were homogenized in 1 ml of TRI-reagent and processed for mRNA extraction. Similarly, RNA was extracted from uninfected or Mtb-infected monocyte-derived cells 24 h post-infection using Ribopure RNA extraction kit as described by the manufacturer (Ambion, Thermo Fisher Scientific, Waltham, MA). cDNA was synthesized using Super Script ViloTM cDNA Synthesis Kit (Applied Biosystems, Foster City, CA). Transcripts of Arg1, Arg2, CAMP, NOS2A, CCL2, CCL22, TNF α , TGF β , IL-10, TLR2, IL-6, IL-1 β , IL-1RA, and IDO (Indoleamine 2,3-dioxygenase) (Applied Biosystems) were measured in duplicates relative to the reference gene, housekeeping 18S rRNA (18S rRNA-housekeeping gene kit, Applied Biosystems), using quantitative real-time PCR (RT-PCR) (QuantStudio 5 Real-Time PCR System, Thermo Fisher Scientific, MA, USA). The results were analyzed by using the relative standard method. Briefly, the relative expression of the target genes was calculated by relating the Ct-value for Mtb-infected to uninfected M0 monocyte-derived cells. Data are presented as fold change of mRNA.

Abstract

For a long time, orally ingested vitamin D was assumed to enter the body exclusively via simple passive diffusion. Recent data from *in vitro* experiments have described Niemann-Pick C1-like protein 1 (Npc1l1) as an important sterol transporter for vitamin D absorption. However, short-term applications of ezetimibe, which inhibits Npc1l1, were not associated with reduced vitamin D uptake in animals and humans. The current study aimed to elucidate the effect of long-term inhibition of Npc1l1 by ezetimibe on the uptake and storage of orally administered triple deuterated vitamin D₃ (vitamin D_{3-d₃}). Therefore, 30 male wild-type mice were randomly assigned into three groups and received diets with 25 µg/kg of vitamin D_{3-d₃} that contained 0 (control group), 50 or 100 mg/kg ezetimibe for six weeks. Mice fed diets with 50 or 100 mg/kg ezetimibe had lower circulating levels of cholesterol than control mice (-12 %, -15 %, P < 0.01). In contrast, the concentrations of 7-dehydrocholesterol in serum (P < 0.001) and liver (P < 0.05) were higher in mice treated with ezetimibe than in control mice, indicating an increased sterol synthesis to compensate for cholesterol reduction. Long-term application of ezetimibe significantly reduced the concentrations of vitamin D_{3-d₃} in the serum and tissues of mice. The magnitude of vitamin D₃ reduction was comparable between the two ezetimibe groups. In comparison to the control group, mice treated with ezetimibe had lower concentrations of deuterated vitamin D₃ compared with the control group in serum (62 %, P < 0.001), liver (79 %, P < 0.001), kidney (54 %, P < 0.001), adipose tissues (55 %, P < 0.001) and muscle (41 %, P < 0.001). Surprisingly, the serum concentration of deuterated 25-hydroxyvitamin D₃ was higher in the group fed 100 mg/kg ezetimibe than in the control group (P < 0.05). The protein expression of the vitamin D hydroxylases Cyp2r1, Cyp27a1, Cyp3a11, Cyp24a1 and Cyp2j3 in liver and Cyp27b1 and Cyp24a1 in kidney remained largely unaffected by ezetimibe. To conclude, Npc1l1 appears to be crucial for the uptake of orally ingested vitamin D because long-term inhibition of Npc1l1 by ezetimibe strongly reduced the levels of deuterium-labeled vitamin D in the body; the observed rise in deuterated 25-hydroxyvitamin D₃ in serum of these mice can not be explained by the expression levels of the key enzymes involved in vitamin D hydroxylation.

Inhibition of Niemann-Pick C1-like protein 1 by ezetimibe reduces uptake of deuterium-labeled vitamin D in mice

Source link:

<https://pubmed.ncbi.nlm.nih.gov/316829>

Aliases for IL1RN Gene

Aliases for IL1RN Gene

GeneCards Symbol: *IL1RN* ²

Interleukin 1 Receptor Antagonist ^{2 3 5}

ICIL-1RA ^{2 3 4 5}

IL-1RN ^{2 3 4 5}

IL1RA ^{2 3 4 5}

IL1F3 ^{2 3 4 5}

IRAP ^{2 3 4 5}

Interleukin-1 Receptor Antagonist Protein ^{2 3 4}

IL1 Inhibitor ^{3 4}

MGC10430 ^{2 5}

IL-1ra ^{3 4}

Intracellular Interleukin-1 Receptor Antagonist (IcIL-1ra) ³

Intracellular Interleukin-1 Receptor Antagonist ²

Intracellular IL-1 Receptor Antagonist Type II ³

Type II Interleukin-1 Receptor Antagonist ³

Anakinra ⁴

IL-1ra3 ³

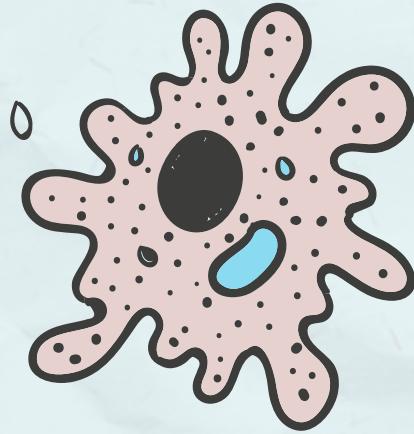
MVCD4 ³

DIRA ³

External Ids for IL1RN Gene

HGNC: 6000 NCBI Entrez Gene: 3557 Ensembl: ENSG00000136689 OMIM®: 147679 UniProtKB/Swiss-Prot: P18510

Source link: <https://www.genecards.org/cgi-bin/carddisp.pl?gene=IL1RN>



GENE

Was this helpful?



JUN – Jun proto-oncogene, AP-1 transcription factor subunit

Homo sapiens (human)

Also known as: AP-1, AP1, c-Jun, cJUN, p39

Gene ID: 3725

[RefSeq transcripts \(1\)](#) [RefSeq proteins \(1\)](#) [RefSeqGene \(2\)](#) [PubMed \(1,274\)](#)

[Orthologs](#)

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GENE

Was this helpful?



JUNB – JunB proto-oncogene, AP-1 transcription factor subunit

Homo sapiens (human)

Also known as: AP-1

Gene ID: 3726

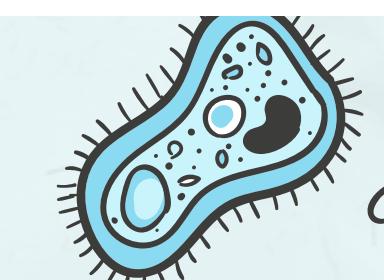
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[Orthologs](#)

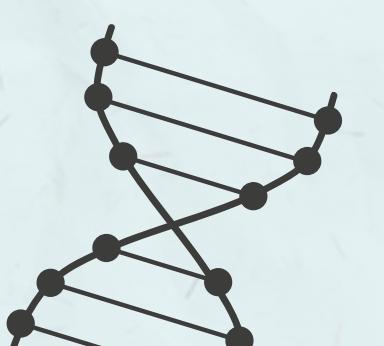
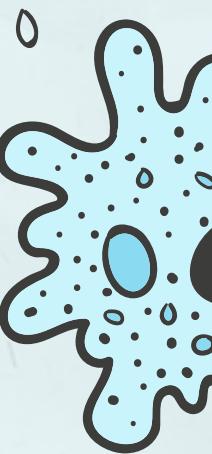
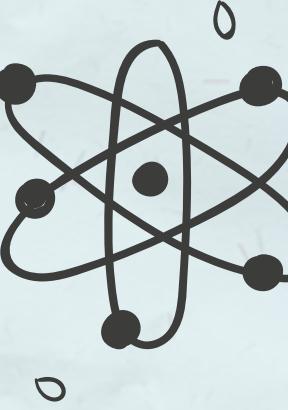
[Genome Data Viewer](#)

[BLAST](#)

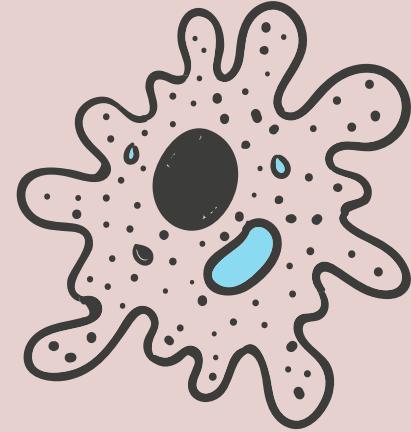
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Source: NCBI



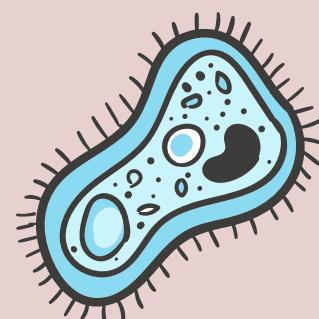
CONCLUSION



We have found that for autoimmune diseases there were significant differentially expressed genes which were affected due to vitamin D.

However, for non autoimmune disease also, we found significant differentially expressed pathways and genes like VDR also.

Thus we cannot conclude that vitamin D is
That we're trying to find if the differentially expressed genes of all the auto
immune disorders, that are listed have a distinct pathway directly affected
by the deficiency of Vitamin-D. But that was not the case.



Finding significant gene symbols in autoimmune diseases

	A	B	C	D	E	F	
1	alopecia	rhematoid (vitamin d)	sle	psoriasis (vitamin)	cis (vitamin)	crohns	
2	KRTAP1-3	PER2	TBC1D22B	PI3	HBA1	FOLH1B	
3	KRTAP8-1	GSN	BAG1	PI3	HBA2	FOLH1	
4	KRT33A	SKAP2	TRPM7	S100A7A	MXD1	NPC1L1	
5	GPRC5D	TGFBR2	FLACC1	DEFB4A	ALAS1	FOLH1	
6	KRTAP5-8	SH2D1A	BAG1	DEFB4B	HBB	MLN	
7	LY6G6D	NA	GUK1	AKR1B10	SRP72	SORD	
8	HOXC13	KRTAP5-8	EPB41	S100A12	NA		
9	CHAC1	NUMA1	VWCE	KYNU	PLAUR	KIF19	
10	KRTAP10-12	SLC7A8	NA	TCN1	HBB	FPR1	
11	KRT83	APP	EPB41	IL36G	PLAUR	NFE2	
12	PSORS1C2	TMEM259	NA	KYNU		ZNF439	
13	KRTAP7-1	ZBTB7C	UBXN6	SPRR2C	USP31	MLN	
14	S100A3	DENND1B	RIOK3	SERPINB4	OSBPL8	APPL1	
15	LOC101928881	GABARAPL1	USP7-AS1	SERPINB3	AAK1	FOXD1	
16	LOC100505782	ADAM15	TRPM7	SERPINB4	ITK	HOXA5	
17	KRT81	NAB2	FLACC1	SERPINB3	IQGAP1		
18	KRTAP4-4	PI4K2A	NA	ADAMDEC1	UBAP1		
19	KRTAP4-11	PCDHGA11	NEMF	GPR15LG	CEP68		
20	KRTAP2-3	SRPRA	ALDH5A1	HPSE	KIF5C		
21	KRTAP4-2	TMEM259	NA	ZC3H12A	CST3		
22	DSG4	SLC7A8	GUCD1	KYNU	AKT3		
23	PARM1	RAP2C	USP12	GPR15LG	CEP350		
24	KRTAP19-3	NA	NA	SPRR2D	GAS7		
25	KRTAP9-3	UNC45A	UBXN6	SPRR2B	HBB		

Finding significant gene symbols in non-autoimmune diseases

1					
2	Diabetes	osteoarthritis	lung	carcinoma	breast cancer (vitamin d)
3					
4	HNRNPD	TGFBR2	NA	COL4A1	SOX4
5	U2AF2	APP	ZNF160	PDPN	NA
6	EGR2	TOP1	TNFAIP8L1	COL5A2	ZNF692
7	REX1BD	MCL1	ZC3H7B	POSTN	PAQR4
8	EGR3	RAB35	ATP8B1	COL3A1	TRIM11
9	PTGS2	GRB10	TOB1	TNC	WDR90
10	CCR1	NA	RPL37A	PLOD2	DYNC2I2
11	IL1B	SMC3		SERPINE2	SMARCA4
12	CCL2	DUSP1		CXCL1	PRKCZ
13	TSPAN14	SLC7A8		GAPDH	SUGP2
14	MPDZ	GSN			FOXP2
15	RGS2	TMEM259			CENPF
16		NA			LRRN3
17		COL6A1			SNRNP200
18		MYO9B			TCF3
19		RBM25			MORC2
20		NUMA1			ACVR1C
21		NA			PAFAH1B3
22		STX16			LLGL2
23		SFSWAP			SDC1
24		KRTAP5-8			NA
25		CAMKK2			CCDC178
26		-----			---

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