The VDR Nuclear Receptor is at the heart of the human innate immunity, responsible for TLR2, TLR4, CAMP, TACO and IL2 expression [1]. During Th1 immune challenge, the VDR is activated by the endogenous secosteroid 1,25-dihydroxyvitamin-D. We have previously described how intra-phagocytic bacterial pathogens are responsible for much chronic inflammatory disease [2,3], and our phase 2 study results have confirmed this pathogenesis. In order to induce recovery from chronic inflammatory disease, it is necessary to restore VDR function by removing all exogenous sources of the secosteroid we call ‘Vitamin-D,’ and dampen down over-exuberant VDR activity, for example with the ARB Olmesartan[1]. This enables the immune system to recognize the pathogens.

RESULTS: To date we have demonstrated recovery from Hashimoto’s Thyroiditis, Rheumatoid Arthritis, Sarcoidosis, and an assortment of chronic inflammatory diagnoses. This breakthrough is the result of a collaboration between molecular scientists and a disparate group of innovative physicians, facilitated by the Internet. However, the widespread application of this pathogenic understanding will require meticulous translation of the molecular science into conventional clinical precepts.


‘Vitamin D’ is actually a seco-steroid, disables VDR, and strongly suppresses Th1 innate immunity.

25,26-D
1,25-dihydroxyvitamin-D vs 25hydroxyvitamin-D vs 24,25-dihydroxyvitamin-D vs 25,26-dihydroxyvitamin-D (docked in VDR from PDB:1DB1)
Only significant difference is 1-alpha hydroxylation

25-D
1,25 dihydroxyvitamin-D vs 25 hydroxyvitamin-D (docked in VDR from PDB:1DB1)
Only difference is 1-alpha hydroxylation

The 1-alpha oxygen hydrogen-bonds to Ser237 and Arg274 and activates VDR

Olmesartan

Arg274, Tyr143 and Ser278 stabilized by Olmesartan terminus
Robert Koch said (1890): “The bacteria must be present in every case of the disease.” Just a Chromosome? Or with what combination of the Plasmids? Chronic (decades-long) intra-cellular infection ensures that the Horizontal Transfer of DNA (between species) becomes a certainty. Research has been focusing on Polymicrobial Disease for decades, but in-vitro technologies do not replicate the in-vivo environment of Chronic Disease. Functional Genomics enables the understanding of inter-species interactions, where suppression of the immune system by one organism allows the colonization of others.

‘Vitamin D’ Supplementation Exacerbates Th1 Disease Proliferation

The 1-alpha hydroxy position is key to activation of the VDR, as it stabilizes Ser237 and Arg274. Based on the knowledge that all of these ligands 1,25-D; 25-D; 24,25-D and 25,26-D; differ only in the 1-alpha hydroxylation it becomes clear that 25-D (which is commonly tested in clinical trials), 24,25-D; 25,26-D; and even Cholecalciferol itself will displace the activating metabolite 1,25-D from the VDR, thus inactivating innate immunity. When the Ki values for each: 0.03; 0.07; 0.05; 0.1 and 0.3, are considered, it is clear that ‘Vitamin D’ supplementation which raises the 25-D assay above approx 20ng/ml is immuno-suppressive. But nutritionists have chosen this same level as indicating ‘deficiency’, a terrible mistake.

Koch’s Postulates Make No Sense in the Era of the Genome

SPECIES       SIZE (mbp)  # PLASMIDS
Staphylococcus aureus
spp. RF 122  2.74       0
spp. COL     2.81       1
spp. MRSA252 2.9        0
spp. MSSA476 2.82       1
spp. MW2     2.82       0
spp. Mu50    2.9        1
spp. N315    2.84       1
spp. USA 300 2.92       3
Staphylococcus epidermidis
spp. ATTC 12228 2.56  6
spp. RP62A   2.64       1

GPCR protein SAR0276 from the genome of MRSA252 modeled with the ARB Olmesartan docked as antagonist, Ki=0.9 nanomol.