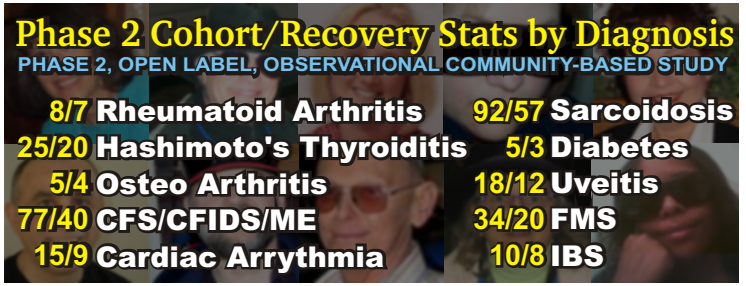
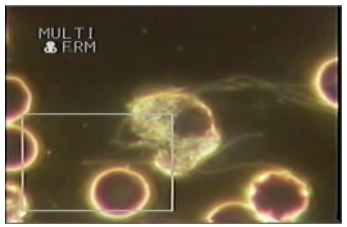
VDR Nuclear Receptor Competence is the Key to Recovery from Chronic Inflammatory and Autoimmune Disease

Author (presenter): Trevor G Marshall, PhD :: Email: Trevor@AutoimmunityResearch.org :: Director, Autoimmunity Research Foundation, Thousand Oaks, CA 91360 USA

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 1,25dihydroxyvitamin-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.





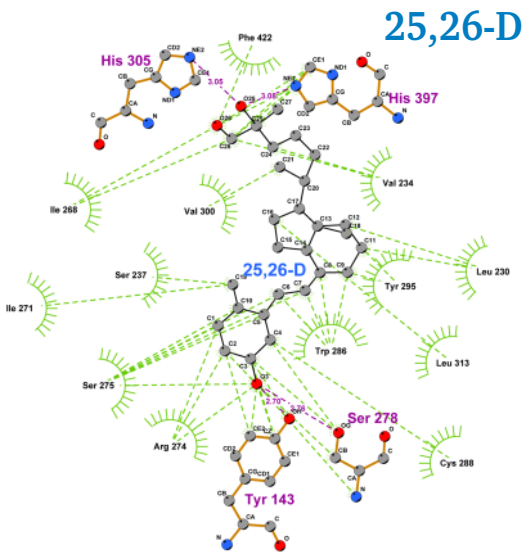
Pinprick blood from Th1 patients.
Blood left to stagnate
6-36 hours.
Picture shows L-forms in
biofilms leaving cells.

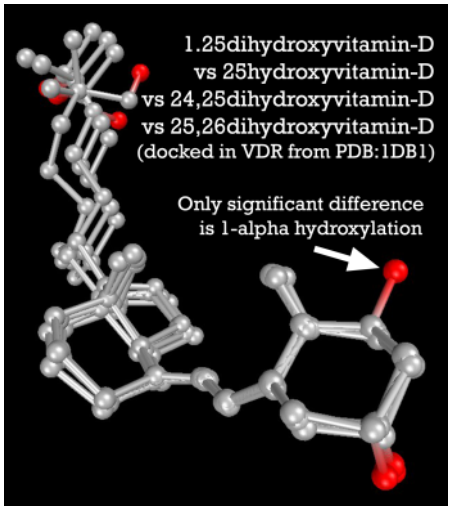
1. Marshall TG: Molecular genomics offers new insight into the exact mechanism of action of common drugs—ARBs, Statins, and Corticosteroids. FDA CDER Visiting Professor presentation, FDA Biosciences Library, Accession QH447.M27 2006.

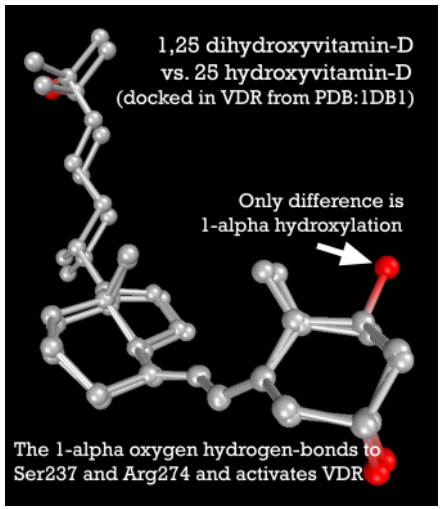
2. Marshall TG,Marshall FE: Sarcoidosis succumbs to antibiotics—implications for autoimmune disease. Autoimmunity Reviews,2004;3(4):295-3001.

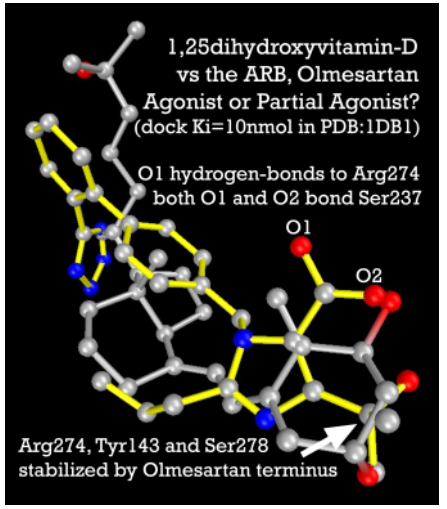
3. Marshall TG, Fenter B, Marshall FE: Antibacterial Therapy Induces Remission in Sarcoidosis. Herald MKDTS 2004g; Volume.III:Release.1. The Journal of the Interregional Clinical-Diagnostic Center, Kazan, in Russian translation. ISSN:1726-6149.

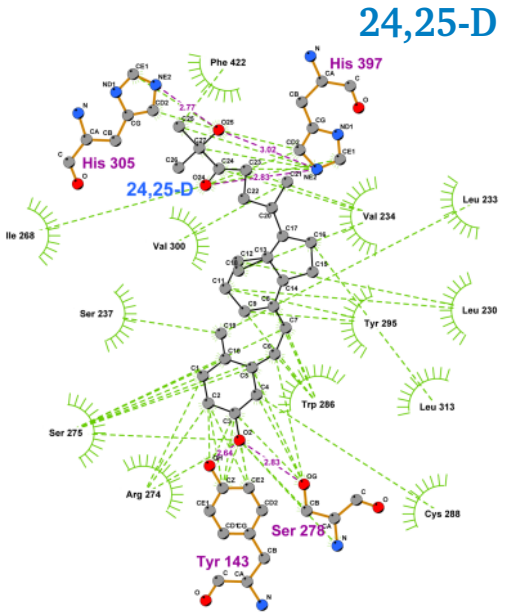
‘Vitamin D’ is actually a seco-steroid, disables VDR, and strongly supresses Th1 innate immunity

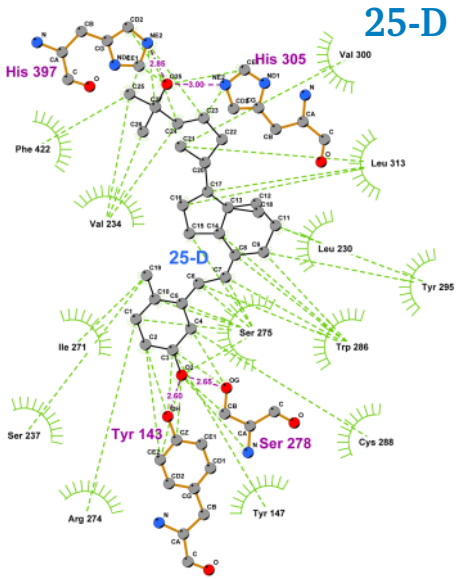


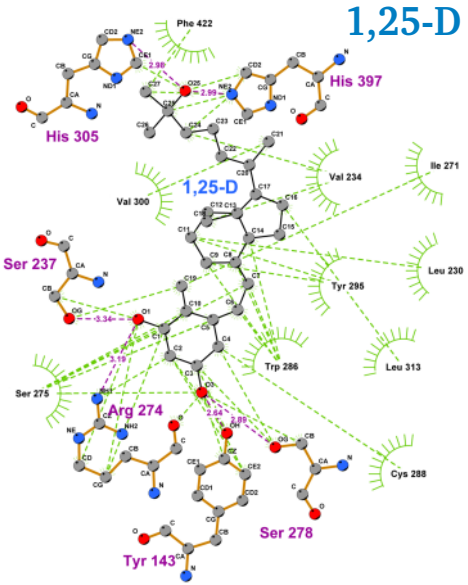


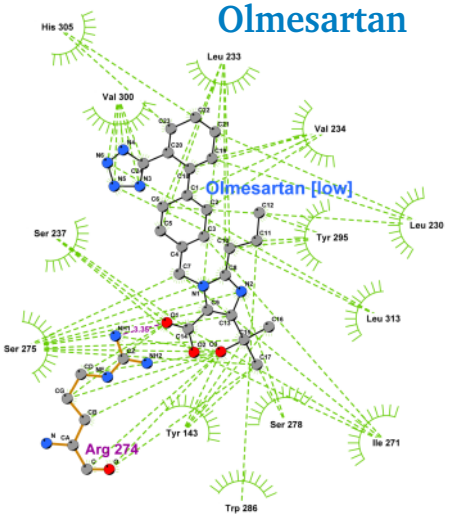






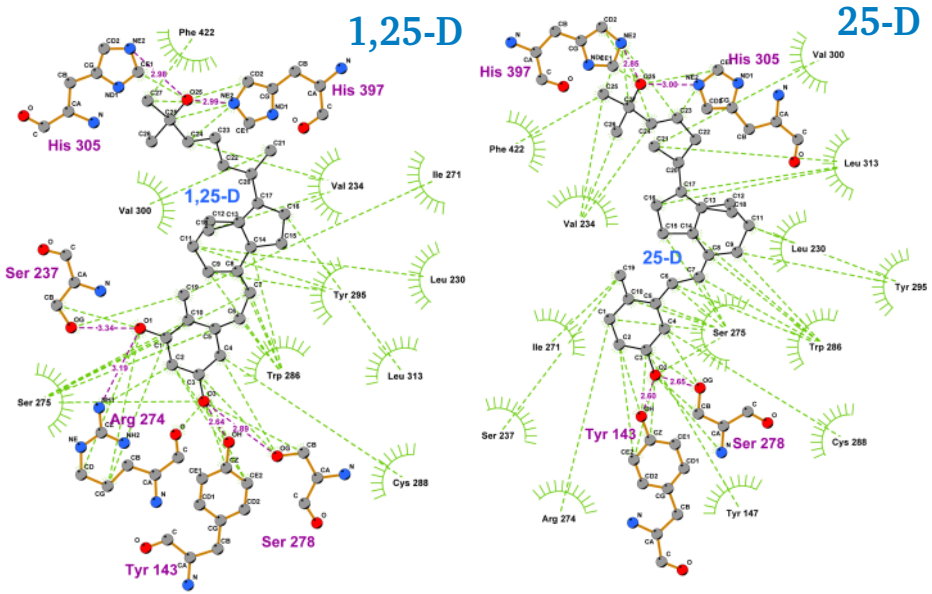






‘Vitamin D’ Supplementation Exacerbates Th1 Disease Proliferation

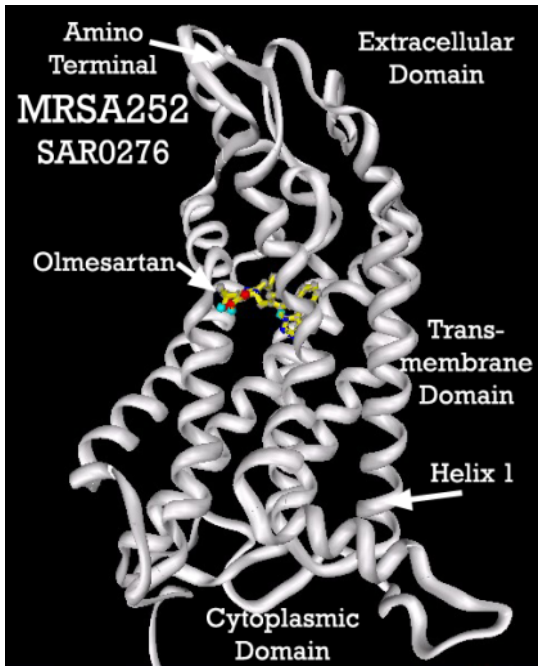
The 1-alpha hydroxy position is key to activation of the VDR, as it stabilizes Ser237 and Arg274. Based on the knowledge that all of these ligands 1,25-D; 25-D; 24,25-D and 25,26-D; differ only in the 1-alpha hydroxylation it becomes clear that 25-D (which is commonly tested in clinical trials), 24,25-D; 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

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 supression of the immune system by one organism allows the colonization of others.

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.