VDR Receptor Competence Induces Recovery from Diseases of the Aging

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The VDR nuclear receptor is at the heart of human innate immunity, being responsible for expression of a majority of the body's antimicrobial peptides[1]. Chronic inflammatory disease causes VDR dysfunction, with ripple-down effects on the Thyroid, Glucocorticoid, Androgen and Progesterone nuclear receptors[1]. This VDR dysfunction inhibits the innate immune system from expressing most of its antimicrobial peptides, allowing viral and bacterial metagenomic communities to evade phagocytosis, and become persistent pathogens. We have identified at least one bacterial sulfonolipid[2], Capnine, which is a strong VDR antagonist. It is produced by biofilm-dwelling gliding bacteria, including spp. *Flavobacter*. The VDR dysfunction is clearly no accident, but is a result of the survival mechanism of these persistent intraphagocytic pathogens. Further, in silico analysis has shown that the murine environment is incapable of accurately modeling human chronic disease, due to differing human and rodent VDR homology. The VDR controls the homeostasis of myriad complex feedback metabolic pathways[1]. Key to these pathways is the Pregnane Xenobiotic Receptor (PXR), which transcribes key P450 enzymes, vital to the processes which allow the body to detoxify. In 2002 we commenced an open-label, adaptive, Phase 2 study[3,4] using a novel VDR agonist, Olmesartan Medoxomil (which was initially developed as an Angiotensin Receptor Blocker), together with (biofilm-targeted) sub-inhibitory concentrations of antibiotics which function by inhibiting 70S ribosomal protein synthesis. This study has routinely induced recovery from a wide variety of chronic diseases including many which are considered to be 'diseases of the aging.' We have now confirmed the molecular biology underlying our pathogenic description of chronic disease, and a therapy evolved, which, over the course of 3-6 years, induces full recovery. Symptomatic exacerbation resulting from immunopathology limits the rate at which bacterial killing can be induced, emphasizing the advantages of using this therapy in a preventative, rather then curative, modality.

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