



## Author Response to “In Defense of the UVB-Vitamin D-Cancer Hypothesis.”

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### To the Editor:

In his letter criticizing my article on *Vitamin D, cancer, and dysregulated phosphate metabolism*, William B. Grant, Ph. D., declares a conflict of interest, writing that he receives funding from a well-known vitamin supplement firm. In researching my article, my main focus was purposively not placed on the plethora of research studies from the past showing mixed findings of vitamin D supplementation and cancer prevention—a body of research which Dr Grant referred to as supporting the UVB-vitamin D-cancer hypothesis. Rather, my objectives included briefly summarizing findings from the most recent large clinical trials of vitamin D supplementation and cancer, such as the Vitamin D and Omega 3 Trial (VITAL) [1] and the Vitamin D Assessment study (ViDA) [2]. Although these major studies do not support cancer prevention with vitamin D supplementation, nevertheless, my article stressed that vitamin D supplementation and cancer prevention remains an unsettled issue due to variable findings.

There is a need to introduce new hypotheses and insights into the problem with the hope of stimulating a new perspective for further research. I discussed implications of the endocrine regulation of vitamin D and serum phosphate, and how dysregulated serum phosphate triggers the endocrine lowering of vitamin D levels, and is also associated with increased risk of tumorigenesis. Therefore, I proposed the vitamin D-hyperphosphatemia-cancer hypothesis in which hyperphosphatemia is a mediating factor in the association of tumorigenesis with lowered levels of bioactive vitamin D.

Regarding the UVB-vitamin D-cancer hypothesis to which Dr Grant referred, this hypothesis was proposed by Garland and Garland in 1980 [3] and attributes the association of lower colon cancer incidence at lower latitudes with higher vitamin D levels from greater UVB exposure, without mentioning vitamin D supplementation. Curiously, Dr Grant accused me of selectively ignoring papers that supported the UVB-vitamin D-cancer hypothesis, even though I cited Grant’s 2012 ecological study in my article in support of this hypothesis. Apparently, Dr Grant considers vitamin D supplementation an established part of the UVB-vitamin D-cancer hypothesis, but our opinions diverge on that matter. In any event, my objective was not to refute the UVB-vitamin D-cancer hypothesis in its original form as proposed by Garland and Garland, but to offer an alternative hypothesis in line with updated research evidence involving the endocrine relationship between vitamin D and cancer that I had previously discussed in my vitamin D-hyperphosphatemia-cancer hypothesis.

Regardless if higher vitamin D levels at lower latitudes are derived from UVB exposure or supplementation, the evidence in the vitamin D-hyperphosphatemia-cancer hypothesis suggests that dysregulated phosphate metabolism is the mediating factor that is associated with both increased cancer risk and reduced vitamin D levels. Therefore, I challenged whether vitamin D levels were a causative factor in reducing cancer at lower latitudes, and I proposed instead that reduced phosphate intake from crops grown in tropical and semi-tropical soil with low phosphate content and bioavailability could provide an alternative explanation: thus, my latitude-phosphorus-cancer hypothesis.

Dr Grant, unfortunately, did not have much to say about either of my hypotheses, which was the central point of my article; therefore, in my opinion his criticisms of the article are misdirected. Furthermore, if lower cancer rates in the tropics are linked to lower animal-based product consumption, as Dr Grant suggests, and since

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animal foods are high in phosphorus, his remarks provide additional support for my latitude-phosphorus-cancer hypothesis in which reduced dietary phosphate consumption at lower latitudes is a potential preventive factor in reduced cancer incidence.

### Compliance with ethical standards

**Conflict of interest** The author declares no conflict of interest.

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