The influence of methylmercury on vitamin D3-induced transcriptomic effects within skin of the Atlantic bottlenose dolphin (*Tursiops truncatus*)

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The Atlantic bottlenose dolphin has attracted attention as a potential sentinel for human health. Greater knowledge of how the dolphin responds to environmental stress is needed, but such studies are limited by its status as a protected species. As a consequence, we established cell strains and an SV40-transformed cell line to be used as *in vitro* tools for measuring the molecular-level effect of the environment on this marine mammal. Specifically, we are investigating the vitamin D3 pathway within these cells. Vitamin D is of interest because of its acknowledged chemopreventative and immunomodulatory properties within terrestrial animals. Whether aquatic mammals also possess this pathway and gain the same immune benefits from vitamin D3 as terrestrial mammals is unknown. Our question is whether the pathway exists in dolphin skin and whether environmental stressors interfere with the downstream effects of vitamin D, proposing a potential mechanism for the detrimental impact of environmental fluctuations on marine mammal health. The bioactive and hormonal form of vitamin D3, 1,25-dihydroxyvitamin D3 (1,25D3), interacts with the vitamin D receptor (VDR) which is a potent regulator of gene transcription. We have previously detected within dolphin skin a 1,25D3-induced upregulation of VDR levels and expression of several genes, as identified by cDNA microarray analysis. One stressor of interest relevant to the dolphin's environment is methylmercury, which has been detected at levels considered toxic within various tissues of the animal, including skin. We show here that sublethal concentrations of methylmercury compromise 1,25D3's ability to upregulate both VDR and the expression of those target genes identified by microarray analysis. This suggests that stressors such as mercury interfere with the downstream transcriptional responses induced by vitamin D3. Such findings may help elucidate the role of vitamin D on innate immunity in dolphin skin and the role that stressors play at the molecular level.

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