

# Integral Relationship Between Vitamin B1 and Hypoxia Inducible Factor-1alpha

June 1

Tuesday, 12:30pm

Online Webinar

Researchers



**Speaker:**

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**Host: Gary E. Gibson, Ph.D.**

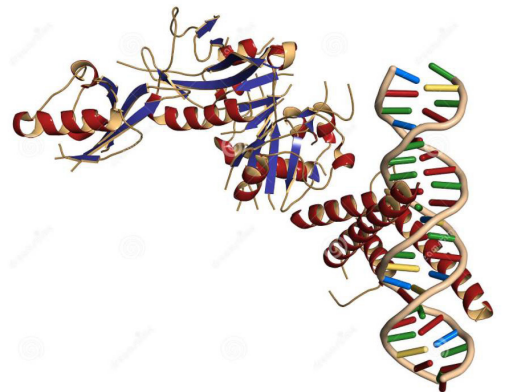
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## Abstract

My primary research interests surround the pathophysiological implications of Vitamin B1 (thiamine) deficiency and supplementation. These research efforts have centered on how HIF1 $\alpha$  impacts thiamine homeostasis and how changes in thiamine status can in turn regulate HIF1 $\alpha$ . HIF1 $\alpha$  is an essential adaptive stress response transcriptional factor that can contextually mediate either pro-survival or pro-death cellular responses. In hypoxic tumor microenvironments, HIF1 $\alpha$  was found to be a direct transcriptional activator for the thiamine transporter SLC19A3. Furthermore, HIF1 $\alpha$  upregulates thiamine pyrophosphokinase-1 (TPK1). Thus, HIF1 $\alpha$  activation during hypoxic conditions attempts to upregulate thiamine homeostasis in a pro-survival capacity. In contrast, thiamine deficiency (TD) can activate HIF1 $\alpha$  independent of low oxygen conditions. Reduced activity of thiamine dependent enzyme PDH during TD resulted in a buildup of pyruvate capable of activating HIF1 $\alpha$ . Activation of HIF1 $\alpha$  during TD mediated pro-apoptotic and amyloidogenic processes. Therefore, HIF1 $\alpha$  may be a possible transcriptional mediator promoting neurological injury in TD associated neuropathologies.



1. Jonus HC, Hanberry BS, Khatu S, Kim J, Luesch H, Dang LH, Bartlett MG, Zastre JA. **The adaptive regulation of thiamine pyrophosphokinase-1 facilitates malignant growth during supplemental thiamine conditions.** *Oncotarget*, 9 (83):35422-35438 (2018).
2. Zera, K. and J. Zastre (2018). **Stabilization of the hypoxia-inducible factor-1 alpha in thiamine deficiency is mediated by pyruvate accumulation.** *Toxicol Appl Pharmacol.*355:180-188.
3. Zera, K. and J. Zastre (2017). **Thiamine deficiency activates hypoxia inducible factor-1alpha to facilitate pro-apoptotic responses in mouse primary astrocytes.** *PLoS One* 12(10): e0186707.