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Correspondence

Vitamin D May Reduce Prostate Cancer Metastasis by Several Mechanisms Including Blocking Stat3

To the Editor-in-Chief:

The recent article by Abdulghani and colleagues[1] in reporting that Stat3 promotes metastatic progression of prostate cancer opens the door to new approaches to fight this cancer. This letter proposes that vitamin D might be beneficial in reducing the risk of prostate cancer mortality by inhibiting the action of Stat3.

Solar UVB and vitamin D have long been hypothesized to reduce the risk of prostate cancer mortality.[2] Whereas solar UVB is correlated with increased survival for those diagnosed with prostate cancer,[3] serum 25-hydroxyvitamin D (calcidiol) measured 1 to 8 years before detection of prostate cancer generally does not show a significant correlation with incidence, although higher calcidiol levels are significantly correlated with more aggressive forms of prostate cancer.[4] These findings suggest that vitamin D is more effective at reducing metastasis than progression of prostate cancer. Similar results have been found for many other cancers, based on the dependence of cancer survival on season in Norway[5] and that solar UVB is more highly correlated with cancer mortality rates than cancer incidence rates for many cancers in the United States.[6]

Laboratory studies with the hormonal metabolite of vitamin D, 1,25-dihydroxyvitamin D (calcidiol), indicate that calcidiol might be effective in combating prostate cancer. One study found that calcitriol inhibits the synthesis and actions of pro-inflammatory prostaglandins by three mechanisms.[7] Another study identified calcitriol as a negative regulator of androgen inactivation in prostate cancer LNCaP cells.[8] With respect to Stat3, it was reported that *in vitro* treatment of activated T cells with calcidiol inhibited the interleukin-12-induced tyrosine phosphorylation of Stat3.[9] Several studies have reported that inhibiting phosphorylation of Stat3 impairs the role of Stat3 in carcinogenesis. In one study, decreased phosphorylation decreased induction of Stat3 target genes and increased apoptosis[10]; in another, decreased phosphorylation decreased transforming growth factor-β-mediated invasion and metastasis in pancreatic cancer cells.[11]

To date the beneficial role of calcidiol in reducing the risk of death from prostate cancer[3] is stronger than that of calcitriol.[12] Prostate cells express vitamin D-25-hydroxylase (25-OHase) and can convert calcidiol to calcitriol.[13] Thus, making sure that those diagnosed with prostate cancer have high calcidiol levels might be appropriate.

In conclusion, the findings by Abdulghani and colleagues[1] might help to explain the benefit of vitamin D in increasing the survival rate for prostate cancer, and the findings by Muthian and colleagues[9] might help lead to a therapeutic way to reduce the role of Stat3 in leading to metastasis of prostate cancer.

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