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 colleagues1 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 Norway5 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 apoptosis10; 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 cancer3 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 colleagues1 might help to explain the benefit of vitamin D in increasing the survival rate for prostate cancer, and the findings by Muthian and colleagues9 might help lead to a therapeutic way to reduce the role of Stat3 in leading to metastasis of prostate cancer.

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References

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