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The relationship between vitamin D status and the risk of cancer among older adults

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It is generally accepted and also well known that vitamin D plays an important role in bone homeostasis and contributes to an optimal bone health. Many ecological, epidemiological and clinical investigations have claimed that vitamin D may also be involved in cancer development, but overall there is still a lack of consensus for these claims. The epidemiological evidence is more consistent for an association of 25(OH)D concentrations, the best marker of vitamin D status, with colorectal and breast cancer risk. However, biological mechanisms of inhibition of cell proliferation and angiogenesis and induction of cell differentiation and apoptosis attributed to vitamin D may not only apply to the colorectal and breast cancer development. Only a few studies have assessed the association of vitamin D with total cancer risk. Their findings have been inconclusive and limited to selected study populations. An overall assessment of the association of vitamin D status with total cancer incidence in a more representative setting has been missing. Additionally, no investigation has assessed whether vitamin D status at old age may still be relevant with regards to cancer prevention. Genetic polymorphisms associated with 25(OH)D concentrations have also been suggested as a new marker of vitamin D status unaffected by environmental changes in sunlight exposure, diet and supplement intake. Studies assessing associations of these genetic polymorphisms with total cancer incidence are few and their results have been inconclusive.

This dissertation aimed to understand what role vitamin D plays on carcinogenesis from a global perspective looking at total cancer incidence, but also focusing on cancer incidence in major sites (lung, colorectal, breast and prostate), with a special focus as well on the elderly population. This was done in three stages.

In the first stage, a systematic review and meta-analysis of epidemiological studies assessing the association of circulating 25(OH)D concentrations with total cancer incidence and mortality was conducted. Higher, compared to lower, 25(OH)D concentrations were significantly associated with a reduction in total cancer incidence and mortality.

In the second stage, an analysis was performed of the association of circulating 25(OH)D concentrations with total and site-specific cancer incidence among older adults. No significant

reductions in cancer risk were observed for higher 25(OH)D concentrations. Overall, increasing 25(OH)D concentrations at older age may not reduce cancer risk. On the other hand, vitamin D status in the range of the IOM's recommendations for vitamin D sufficiency (50 nmol/L) was associated with the lowest risk of total and breast cancer incidence.

In the third stage, genetic polymorphisms within or around genes of the vitamin D pathway (DHCR7, GC, CYP2R1 and CYP24A1) were significantly associated with 25(OH)D concentrations, but not significantly associated with total and site-specific cancer incidence. Genetic polymorphisms associated with 25(OH)D concentrations provide at best little evidence that vitamin D may be involved in cancer development.

To conclude, the research performed within the scope of this doctoral dissertation suggests that vitamin D may play a role (possibly small) in cancer development, although this could not be verified in the analyses conducted among older adults in the CHANCES Consortium and ESTHER study. Improving vitamin D status beyond the IOM's recommendation for vitamin D sufficiency (50 nmol/L) at older age may not bring any additional benefits in reducing cancer risk, but it may be nonetheless very relevant for maximizing bone health.

Future research should make big efforts towards bringing epidemiological data on vitamin D and cancer together in order to form large consortia where the influence of vitamin D status (be it as expressed as 25(OH)D concentrations or as genetic polymorphisms) on the global burden of cancer can be adequately studied. Lastly, ongoing randomized controlled trials, although with methodological limitations, will probably contribute in the future to clarify whether cancer can or cannot be partially prevented by improving vitamin D status.