VDR and Cancer Risk

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The vitamin D receptor (*VDR*) gene is involved in multiple pathways that may be important in the etiology of cancer. Most epidemiological studies have included six polymorphisms of the *VDR* gene, five of which are in linkage disequilibrium. The Fok1 polymorphisms is at the 5' region of the gene while the Bsm1, Tru91, Taq1, Apa1, and poly A microsatellite repeat are in linkage disequilibrium at the 3'UTR region. Different regions of the gene have different functions so that associations with specific polymorphisms may indicate unique mechanisms. The first epidemiological study of *VDR* and cancer was reported in 1997 and showed that more repeats of the polyA polymorphisms was associated with over a 4-fold increased risk of prostate cancer. Since then several studies have reported associations with colorectal adenomas and cancer. Associations for colorectal adenomas show reduced risk with the BB, ff, and uu genotypes of the Bsm1, Fok1, and Tru91 polymorphisms. Similar reduced risk is observed for colorectal cancer, prostate cancer, breast cancer, bladder cancer, and melanoma. Some studies suggest associations for colon and rectal cancer vary by polymorphisms as well as by tumor site. The importance of dietary calcium, vitamin D, energy, and fat in modifying the association between *VDR* genotype and cancer risk has been shown repeatedly. In addition to these dietary factors that modify cancer risk, use of aspirin, level of BMI, and age also appear to be effect modifiers of the association between *VDR* and cancer. Significant interaction between *VDR* and androgen receptor (*AR*) and leptin (*LEP*) genes further suggest the importance of *VDR* in multiple pathways that include insulin, estrogen, inflammation and energy balance.