What is the role of dietary calcium and vitamin D in vitamin D receptor knockout animals?

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Since the discovery of the vitamin D receptor (VDR) in transformed cells, the role of the vitamin D signaling pathway in normal cellular differentiation and in hormone dependent cancers has been extensively explored. *In vitro* studies have demonstrated that the VDR ligand, 1,25-dihydroxyvitamin D, modulates key proteins involved in signaling proliferation, differentiation and survival of normal epithelial cells derived from the mammary and prostate glands. These findings suggest a potential role for the vitamin D pathway in protection against breast and prostate cancer development. However, elucidation of the impact of vitamin D on cancer risk in epidemiologic studies has been confounded by the heterogeneity in vitamin D status as well as the modulatory influence of dietary calcium. This presentation will provide an overview of data derived from pre-clinical animal models of breast and prostate cancer, including: 1) the impact on dietary calcium on prostate cancer and 2) the effect of dietary vitamin D and VDR ablation on prostate and breast cancer in transgenic models. Furthermore, potential mechanisms whereby VDR mediated growth regulation can be dissociated from its calcemic actions at the cellular level will be discussed. This overview will emphasize the need for additional animal models such as mice with tissue specific deletions of VDR and 1-hydroxylase, as well as additional cellular models to clarify mechanisms of VDR action. Collectively, these studies have also reinforced the need to further define the regulation and function of the vitamin D pathway in cells in relation to prevention and treatment of breast and prostate cancer.

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