Anti-Cancer Effects of Vitamin D

Effect of vitamin D	How vitamin D acts	Details of molecular mechanisms
Stops uncontrolled reproduction of cells (proliferation)	Inhibits proteins and signals that are needed for cells to divide	Inhibits growth factors ($\downarrow$IGF-1, $\uparrow$IGF-1 binding protein, $\uparrow$TGF-β) - Arrests cell cycle ($\uparrow$p21, $\uparrow$p27, $\downarrow$CDKs, $\downarrow$cyclins, $\downarrow$MYC and $\downarrow$RB)
Induces maturation of immature cells	Increases cell-line specific signals for maturation and specialization	Increased expression of differentiation factors (lipids, casein, PSA, E-cadherin)
Kills cells by initiating programmed cell death	Activates process of breaking cell down into small packets that are disposed of by immune cells	Activates internal apoptosis pathway ($\uparrow$BAX, $\downarrow$BCL-2)
Prevents inflammation	Inhibits pro-inflammatory factors and increases anti-inflammatory signals	Inhibits inflammation ($\downarrow$COX-2, $\downarrow$PG receptors, $\downarrow$stress kinase, $\downarrow$NF-κB, $\uparrow$15-PGDH, $\uparrow$MAPKP5)
Prevents blood vessels from feeding cancerous cells	Prevents the signals needed for new blood vessels to form	Inhibits angiogenesis ($\downarrow$VEGF, $\downarrow$HIF1-α)
Prevents cancerous cells from spreading	Decreases signals that allow cells to move through tissue and bind other cells	Inhibits invasion and metastasis ($\downarrow$MMP-9, $\downarrow\alpha$6- and β4-integrins, $\downarrow$plasminogen activator, $\uparrow$TIMP-1, $\uparrow$E-cadherin)

BAX, pro-apoptotic protein; BCL-2, apoptosis regulating protein; COX-2, cyclooxygenase 2; IGF-1, insulin-like growth factor-1; CDK, cyclin-dependent kinase; HIF1-α, hypoxia inducible factor 1-α; MAPKP5, mitogen-activated protein kinase phosphatase 5; MMP-9, matrix metalloproteinase 9; MYC, proto-oncogene; p21 and p27, cell cycle checkpoints; PSA, prostate-specific antigen; PG, prostaglandin; 15-PGDH, 15-hydroxyprostaglandin dehydrogenase; RB, tumor-suppressor protein; NF-κB, nuclear factor-κB; TIMP-1, tissue inhibitor of metalloproteinases 1; TGF-β, tumor necrosis factor β; VEGF, vascular endothelial growth factor.

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