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Vitamin D and its Role in Cell Cycle Dynamics: A Review of the Molecular and Clinical Studies

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Abstract

Vitamin D is an essential nutrient that not only plays a role in calcium homeostasis and bone health, but also has broad functions in the regulation of various biological processes, including cell cycle dynamics. This study aims to examine in depth the role of vitamin D in cell cycle dynamics based on evidence from molecular and clinical studies. The method used was qualitative research with a literature study approach, where data was collected from relevant articles such as PubMed, EuropePMC, and Google Scholar. Analysis was carried out through the process of filtering, presenting data, and drawing conclusions. The results showed that vitamin D in its active form, 1,25-dihydroxyvitamin D3, interacts with the vitamin D receptor (VDR) in cells and modulates the expression of genes involved in cell proliferation. This mechanism involves an increase in the expression of cell cycle inhibitory genes, such as p21 and p27, and a decrease in the expression of cell cycle promoting genes, such as cyclin D1, which contributes to the arrest effect on the cell cycle. Thus, in addition to being important for bone health, vitamin D has a significant role in cell cycle regulation, and its deficiency can increase the risk of various diseases, including cancer. Therefore, maintaining optimal vitamin D levels through sun exposure, consumption of foods rich in vitamin D, or supplementation is essential. Further research is needed to understand the role of vitamin D in genetic regulation, particularly in relation to cancer.

Introduction

Vitamin D, a hormone similar in structure to steroids, is essential for numerous bodily functions. It exists primarily as D3, created by sun exposure, and D2, acquired through food. The synthesis of vitamin D3 starts from pro-vitamin D3, namely 7-dehydrocholesterol, which is the result of cholesterol metabolism. When the skin is exposed to ultraviolet B (UVB) radiation, pro-vitamin D3 is converted to pre-vitamin D3. This metabolic process then continues in the skin and liver with the help of enzymes CYP27A1 and CYP2R1, which convert it into vitamin D3 (Bikle, 2014; Christakos et al., 2016; Saponaro et al., 2020).

Vitamin D3 undergoes further metabolic processes in the kidneys, where it is converted into its active form, 25-hydroxycholecalciferol. This compound plays a role in various biological

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functions of the body, including the regulation of calcium and phosphorus, which are important for bone health. The biological effects of vitamin D3 occur through interactions with the Vitamin D Receptor (VDR), which is a specific receptor found in various types of body tissues. This receptor functions as a regulator of gene expression that plays a role in various physiological processes, such as the immune system, cell growth, and mineral balance in the body.

Classically, vitamin D plays a major role in the regulation of mineral balance, especially calcium and phosphate. This function is carried out through its influence on intestinal epithelial cells in calcium absorption, paracellular calcium transport mechanisms, and the process of calcium and phosphate absorption in the kidneys. In addition, vitamin D also contributes to the process of osteogenesis or bone formation, which makes it an important factor in maintaining bone health (Bikle, 2014; Christakos et al., 2016).

As research continues to develop, the role of vitamin D is not limited to mineral homeostasis. A number of studies have revealed that vitamin D plays a role in regulating the cell cycle and contributes to cancer prevention. Vitamin D can influence the process of cell proliferation and differentiation, which plays a role in maintaining a healthy balance of cell growth. These mechanisms relate to vitamin D's function in regulating cell proliferation and differentiation, and in preventing cancer cell development through complex molecular pathways (Saponaro et al., 2020; Jeon & Shin, 2018; Bhoora & Punchoo, 2020).

As a secosteroid hormone, the active form of vitamin D, "1,25-dihydroxyvitamin D ($1,25(OH)_2D$)", plays an important role in various biological processes by binding directly to the vitamin D receptor (VDR). These receptors are found on a variety of cell types, including immune system cells, epithelial cells and even cancer cells. The interaction between vitamin D and VDR affects various molecular pathways involved in cell cycle control and cell growth regulation. These mechanisms contribute to maintaining a balance between cell proliferation and differentiation, potentially preventing abnormal cell growth that can lead to the development of diseases, including cancer.

Various molecular studies have shown that vitamin D has antiproliferative, pro-differentiation, and pro-apoptotic effects, meaning that it can control cell growth and development by suppressing excessive cell proliferation, promoting cell differentiation into its functional form, and inducing apoptosis or programmed cell death. These mechanisms play an important role in controlling normal and pathological cell growth, including in efforts to prevent degenerative diseases and cancer (Umar et al., 2018). Further studies have shown that vitamin D plays a role in controlling various mechanisms related to cell division, maturation and development. Administration of vitamin D analogs or their active metabolites is known to activate apoptotic pathways, provide antiproliferative effects, and inhibit angiogenesis, the process of forming new blood vessels that often contributes to tumor growth (El-Sharkawy & Malki, 2020). Thus, vitamin D not only has a physiological role in maintaining the body's mineral balance, but also has the potential to be a promising therapeutic agent in cancer prevention and treatment.

In addition to evidence from molecular research, clinical studies have also shown an association between vitamin D levels in the body and the incidence of several types of cancer, autoimmune diseases, and metabolic disorders (Contreras-Bolívar et al., 2021). This further emphasizes the importance of vitamin D in cell cycle regulation in various physiological and pathological conditions. Investigating how vitamin D and its receptors affect inflammation, cell death, and cancer development may reveal opportunities to use vitamin D-based therapies in medicine.

This study aims to examine the role of vitamin D in cell cycle dynamics. The results of this study are expected to provide deeper insight into the mechanism of action of vitamin D in cell cycle regulation and its potential as cancer prevention. In addition, this study can also serve as

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a basis for the development of vitamin D-based therapeutic strategies, both through supplementation and the development of its analogs as potential agents in cancer therapy. Thus, a better understanding of the role of vitamin D is expected to contribute significantly to cancer prevention and treatment efforts, as well as increase awareness of the importance of optimal vitamin D levels for overall health.

Methods

This study employs a qualitative literature review approach to thoroughly investigate the role of vitamin D in cell cycle dynamics, focusing on its molecular mechanisms and clinical implications. The methodology has been carefully refined to enhance clarity, rigor, and reproducibility while preserving the exploratory nature of the original study. The research design is structured as a systematic qualitative review with thematic synthesis, aiming to synthesize evidence from diverse sources, including molecular studies, in vitro experiments, and clinical research, into a cohesive and comprehensive framework. The scope of the review is deliberately limited to peer-reviewed studies published between 2010 and 2025 to ensure the relevance and timeliness of the findings.

Data collection follows a rigorous and transparent search strategy to identify the most pertinent literature. The review draws from reputable databases such as PubMed, EuropePMC, Google Scholar, and Scopus, utilizing a combination of primary and secondary keywords. Primary keywords include "Vitamin D" paired with "cell cycle" and terms like "oncogenesis" or "cancer," while secondary keywords focus on specific molecular interactions, such as "VDR" and "p21/p27" or "CDK inhibition." The inclusion criteria prioritize studies that explore vitamin D's role in cell cycle regulation, particularly those providing mechanistic insights into gene expression, protein interactions, or clinical outcomes related to cancer. Studies lacking molecular or cellular evidence, non-English publications, or abstracts without full-text access are excluded to maintain the review's quality and focus.

The screening process is designed to minimize bias and ensure the selection of high-quality studies. It occurs in two phases: the first involves title and abstract screening conducted independently by two reviewers, while the second entails a full-text review of the selected articles to assess their relevance and methodological rigor. Any discrepancies between the reviewers are resolved through consensus meetings involving a third reviewer, ensuring a balanced and unbiased selection of studies. This multi-stage screening process enhances the reliability of the literature included in the review.

Data extraction is systematic and organized to facilitate a thorough analysis. Key variables extracted from each study include the molecular pathways involved, such as VDR signaling or CDK inhibition, as well as critical genes and proteins like p21, p27, and cyclin D1. The type of study—whether in vitro, in vivo, or clinical—is also noted, along with relevant population or sample characteristics where applicable. A standardized Excel template is used to log this data consistently, ensuring uniformity and ease of analysis. This structured approach allows for a detailed comparison of findings across different studies and experimental models.

Thematic synthesis forms the core of the data analysis, enabling the identification of recurring patterns and overarching themes. The process begins with coding, where key concepts such as "G1/S arrest" or "p27 stabilization" are identified and categorized. These codes are then mapped to reveal broader patterns, such as the distinction between genomic and non-genomic actions of vitamin D. A comparative analysis is conducted to contrast results across different cell types, such as normal versus cancerous cells, highlighting cell-type-specific responses to vitamin D. To ensure the validity of the interpretations, the findings are cross-checked against the conclusions of the original studies, minimizing the risk of bias or misrepresentation.

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Quality assurance measures are integrated throughout the methodology to uphold the study's academic rigor. Bias is mitigated by including studies with both positive and null findings, providing a balanced perspective on vitamin D's role in cell cycle regulation. The quality of the included studies is assessed using the SANRA (Scale for the Assessment of Narrative Review Articles) framework, which evaluates aspects such as clarity, methodology, and relevance. Transparency is maintained by documenting the search dates, listing excluded studies with reasons for their exclusion, and noting any deviations from the original protocol. These steps ensure that the review process is both rigorous and reproducible.

Results and Discussion

The cell cycle plays an important role in maintaining the balance of growth at the organism level. This process allows the body to replace old or damaged cells with new healthy cells, so that tissues and organs continue to function optimally. Through the mechanism of cell division, organisms can continuously renew and repair themselves, which is essential in sustaining life. In addition to its role in cell rejuvenation, the cell cycle is also a major factor in the growth and development of multicellular organisms. From the earliest stages of life, cell division allows embryos to develop into more complex structures. As it grows, cells continue to divide to form the necessary tissues and organs. This process also plays a role in recovery after injury, where new cells are generated to replace damaged cells (Kumar et al., 2022). Highly concerted actions of many different activators and inhibitors are necessary to maintain the integrity of the DNA in two important checkpoints: G1/S and G2/M through the action of CDK inhibitors, including "p21, p27, p57, CDK4, CDK6, p15, p16, p18, and p19" (Kumar et al., 2022). Defective check of cell cycles has been implicated in several cancers.

The cell cycle is controlled by the cooperation between Cyclin Dependent Kinase (CDK) and cyclins, which play a role in ensuring that each stage takes place in an organized and timely manner. In the G1 phase, activation of the CDK-cyclin complex is a key step that allows the cell to prepare to divide. One of the main complexes involved in this phase is CDK4/6 which binds to cyclin D. When the CDK4/6 complex is activated, it phosphorylates the Retinoblastoma protein (pRB), an important regulator in cell cycle control. This phosphorylation weakens the interaction between pRB and the transcription factor E2F/DP, which under normal conditions is responsible for inhibiting the transcription of genes required for DNA replication. As a result, E2F activity becomes more restricted, but remains sufficient to trigger transcription of several key genes, including the gene encoding cyclin E. As cyclin E levels increase, the Cyclin E-CDK2 complex is formed and continues the process of phosphorylating pRB. This continued phosphorylation causes pRB to become inactive, which eventually releases the full E2F transcription factor. With the release of E2F, transcription of various genes required for DNA synthesis can take place, allowing the cell to enter S phase where DNA replication occurs (Ruijtenberg & van, 2016).

CDK inhibitors (CKIs) associating with CDKs prevent cellular cycle progression. There are two main families of CKIs that play a role in inhibiting CDKs, namely the INK4 family and the CIP/KIP family. CKIs from the INK4 family, such as p16^INK4a, specifically bind to CDK4 and CDK6. By binding directly to these kinases, INK4 CKIs prevent their interaction with D-type cyclins, so the formation of the CDK4/6-cyclin D complex is inhibited. As a result, phosphorylation of Retinoblastoma protein (pRB) does not occur, and cells cannot pass from G1 phase to S phase, leading to cell cycle arrest. Meanwhile, CKIs from the CIP/KIP family, such as p21^CIP1 and p27^KIP1, have a broader mechanism of action. They are able to inhibit various CDK-cyclin complexes, including CDK2 that binds to cyclin E or cyclin A. By blocking the activity of these complexes, CIP/KIP CKIs effectively prevent the transition from G1 phase to S phase and inhibit the process of DNA replication, so that the cell cycle can be stopped at certain control points (Goel et al., 2018; Irazoqui et al., 2015).

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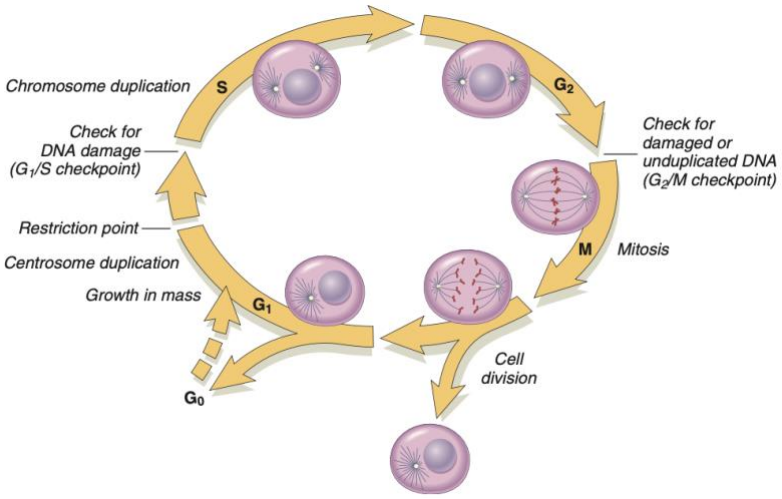

Figure 1. Cell Cycle and Its Checkpoints (Kumar et al., 2022)

Cyclin-dependent kinase (CDK) is an enzyme that plays an important role in cell cycle regulation by acting as a heterodimeric serine/threonine kinase. CDK activity depends on its interaction with cyclin proteins, which control the transition of cells from one phase to another in the cell cycle. The cyclin D-CDK4 and cyclin D-CDK6 complexes, for example, allow cells to pass the G1/S checkpoint, which is the first step before entering the DNA synthesis phase (Ruijtenberg & van, 2016). After passing this phase, the cyclin A-CDK2 complex regulates the transition from S phase to G2 phase, ensuring that DNA replication takes place properly before entering the next stage (Kumari & Jat, 2021). Ahead of cell division, the formation of the cyclin B-CDK1 complex plays a role in pushing cells through the G2/M checkpoint, so that the mitotic process can occur smoothly (Martínez-Alonso & Malumbres, 2020).

The regulation of CDK and cyclin activity is highly dependent on various factors that affect cell cycle balance and progression. One of the main factors is the presence of extracellular matrix and contact inhibition mechanisms, which help control whether cells should continue dividing or stop at certain checkpoints (Gérard & Goldbeter, 2014; Jones et al., 2019). In addition, the expression of cyclins and CDKs is also regulated by transcriptional repression mechanisms, which play a role in controlling the timing and amount of production of these proteins in the cell (Engeland, 2018).

In addition to transcriptional regulation, CDK activity is also controlled by specific inhibitors called CDK inhibitors (CKIs). These proteins act as a safeguard mechanism to prevent uncontrolled cell division by suppressing the activity of the CDK-cyclin complex (Kumar et al., 2022). Other regulatory mechanisms include phosphorylation and ubiquitination processes, which can activate or signal the degradation of cyclins and CDKs, ensuring that each phase in the cell cycle proceeds in a timely and controlled manner (Lim & Kaldis, 2013). In addition, various external stimuli, such as growth signals and environmental conditions, also affect CDK and cyclin activity, tailoring the rate of cell division to the needs of the organism (Zou & Lin, 2021).

In recent years, a growing body of evidence has shown that vitamin D has an important role in cell cycle regulation. Vitamin D is known to regulate gene transcription through its action on the vitamin D receptor (VDR), which interacts with various gene enhancers and promoters to control genetic expression (Bhoora & Punchoo, 2020; Pike et al., 2016). In vitro studies show that vitamin D3 is able to upregulate p21 and p27 proteins through several mechanisms. These two proteins are cell cycle inhibitors that play a role in inhibiting CDK activity, thus contributing to cell cycle arrest and reduced cell proliferation. In a study conducted on pluripotent mesenchymal stem cell cultures, vitamin D was shown to work through the VDR

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to inhibit cell cycle progression by suppressing the expression of cyclin E1, CDK2, and CDK4 without triggering apoptosis through the Wnt-1 pathway (Artaza et al., 2010).

In addition, the inhibitory effect of vitamin D on CDK activity was also observed in H295R cell culture. In this study, vitamin D was shown to directly inhibit CDK4 activation through its interaction with VDR, which suggests that vitamin D may act as a master regulator in controlling cell development (Pilon et al., 2014). The role of vitamin D in cell cycle arrest has also been investigated in gastric cancer cells. The addition of vitamin D in cell culture showed an increase in p21 and p27 expression, further strengthening the mechanism of cell cycle inhibition. In addition, vitamin D also enhanced the effectiveness of cisplatin in inducing apoptosis, indicating its potential in supporting cancer therapy by improving cell response to chemotherapeutic agents (Bao et al., 2014).

With these various evidences, vitamin D is increasingly recognized as a molecule that plays a role in maintaining the balance of cell proliferation. Through cell cycle regulation, vitamin D not only functions in maintaining cellular homeostasis but also has potential as a therapeutic agent in various pathological conditions, including cancer. Various studies have revealed that vitamin D and its derivatives have anti-proliferative properties against various types of cancer cells, such as malignant keratinocytes, breast cancer cells, and prostate cancer cells. One of the main mechanisms discovered is its ability to inhibit cell division by stopping the cell cycle at the G1/G0 phase. This process prevents cancer cells from continuing the division cycle, thereby reducing their growth rate and spread.

This effect mainly occurs through increased expression of p21 and p27 proteins, which function as inhibitors of cyclin-dependent kinase (CDK) enzymes. These proteins work by inhibiting the activity of the CDK complex, which plays a role in pushing the cell cycle into the next phase. As a result, the process of cell division slows down or stops, thereby preventing uncontrolled cell growth, as occurs in cancer cells. This mechanism shows how vitamin D can help control cell proliferation and has potential in anticancer therapy (Bhoora & Punchoo, 2020; Hu & Zuckerman, 2014). In addition to p21 and p27 regulation, vitamin D also contributes to cell cycle arrest through alternative pathways. One mechanism thought to play a role is the induction of the retinoblastoma protein (pRB), which acts as a major inhibitor of the transition from G1 to S phase.

pRB activation leads to suppression of E2F transcription factor activity, which is required for DNA synthesis and cell proliferation. Thus, vitamin D helps prevent uncontrolled cell replication, which is a hallmark of cancer cell growth. In addition, vitamin D can also inhibit the expression of the oncogene C-MYC, which is known to play a role in promoting cell proliferation and accelerating the cell cycle. The decrease in C-MYC expression due to vitamin D exposure may further slow cell cycle progression and enhance its anti-proliferative effects on cancer cells. Given this mechanism, vitamin D could potentially play a role in suppressing the development of various cancers through regulating the expression of genes that control the cell cycle. Furthermore, understanding the role of vitamin D in cell cycle regulation may also provide new insights into the development of therapeutic strategies for cancer. With its ability to inhibit cell proliferation and promote cellular differentiation, vitamin D could be a potential candidate in therapeutic approaches that aim to control tumor growth and improve the effectiveness of cancer treatment.

Several in vitro studies have shown that vitamin D exposure can upregulate CDK inhibitors, such as p21 and p27, which play a role in inhibiting cyclin-dependent kinase activity. CDK itself has an important role in controlling cell cycle progression, and increased expression of CKIs that target CDK2 can directly prevent cells from continuing their cell cycle. Thus, vitamin D contributes to inhibiting uncontrolled cell proliferation through this mechanism (Goel et al., 2018; Ding et al., 2020; Hydbring et al., 2016; Karimian et al., 2016). In the context of cancer,

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CDK dysregulation is often associated with uncontrolled cell growth. For example, research conducted by Ding et al. reviewed how CDK dysregulation plays a role in human breast cancer progression, where excessive CDK activity can lead to rapid cell proliferation and circumvent normal control mechanisms in the cell cycle (Hu & Zuckerman, 2014).

One of the most common forms of dysregulation is in CDK4/6, which has been known to play a role in the development of several types of cancer. Overactivation of this pathway allows cancer cells to continue growing despite signals that should halt their growth. Inhibition of CDK4/6 is therefore a potential pharmacological approach in cancer therapy, with the aim of inhibiting the cell cycle and slowing tumor growth (Goel et al., 2018). Vitamin D3 has an important role in regulating the expression of genes that play a role in the cell cycle, including the p21 gene. Studies show that vitamin D3 can increase p21 expression through a functional vitamin D response element (VDRE) located in the promoter region of the p21 gene. This mechanism allows vitamin D to directly regulate p21 transcription, ultimately increasing the likelihood of inhibiting the transition from G1 phase to S phase in the cell cycle.

This process becomes particularly important in the context of cancer, as G1/S inhibition can prevent uncontrolled cell proliferation, which is one of the main features of cancer cells (Bhoora & Punchoo, 2020). In addition, vitamin D3 also contributes to the upregulation of p27, although the underlying mechanism is different from p21. The increase in p27 levels occurs mainly at the protein level, where vitamin D inhibits the degradation of p27 resulting in increased stability of this protein. Indirectly, vitamin D may also increase p27 transcription through reduction or expression of miRNA 181a, which has a role in p27 regulation. With increased levels of p27, there is further inhibition of the G1/S transition, which slows cancer cell growth and provides potential anti-proliferative effects (Bhoora & Punchoo, 2020).

In vitro cell differentiation models have shown that p21 expression in response to calcitriol therapy can vary depending on the cell type studied. In addition to its role in cell cycle arrest, p21 also has an association with cell differentiation. Although the vitamin D response element (VDRE) is found in the promoter of the p21 gene, the effect of calcitriol in regulating p21 expression appears to be cell type specific (Pike et al., 2016). In the HL60 myeloid leukemia model, calcitriol has been shown to increase p21 expression, which in turn promotes cell cycle arrest at the G1/G0 phase. This suggests that vitamin D may act as an important regulator in inhibiting leukemia cell proliferation. In contrast, in squamous cell carcinoma (SCC), which is the malignant counterpart of keratinocytes, $1,25(OH)_2D_3$ is known to suppress cell proliferation but actually reduces p21 expression.

This phenomenon suggests an alternative mechanism in cell growth inhibition that is not entirely dependent on p21 (Bikle, 2004). Furthermore, in the myelomonocytic cell line U937, p21 mRNA expression increased significantly within just two hours after treatment with $1,25(OH)_2D_3$, leading to a transient arrest in G1 phase. However, further evaluation of the cell cycle after 24 and 48 hours showed that this initial effect did not last. After the initial period of cell cycle arrest, these cells experienced a surge in proliferation, indicating that p21 may not be the only major factor responsible for G1/G0 cell cycle arrest in leukemia (Slominski et al., 2017).

These findings suggest that although vitamin D may affect p21 expression and cause cell cycle arrest or differentiation, the specific mechanisms involved are still not fully understood. The cellular response to vitamin D seems to depend on the biological context of each cell, especially in the differences between normal and malignant cells. Therefore, the involvement of vitamin D in cell cycle regulation in healthy as well as malignant keratinocytes remains an evolving area of research and still requires further investigation. Vitamin D plays a role in regulating p27 expression mainly through a proteosome-dependent protein degradation mechanism. In

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ovarian and prostate cancer cell lines, treatment with vitamin D did not directly affect p27 mRNA levels, but instead decreased mRNA expression of p45/Skp2 and Cks1.

Both proteins are known to play a role in the ubiquitination process that marks p27 for degradation. By decreasing the expression of p45/Skp2 and Cks1, vitamin D inhibits the ubiquitination and degradation of p27, thereby increasing the stability of the protein (Slominski et al., 2017). Stabilization of p27 by vitamin D was also found in acute promyelocytic leukemia and human hepatoma cells. In this context, vitamin D plays a role in maintaining higher p27 levels, which ultimately contributes to cell cycle inhibition. Given that p27 is a key regulator of the activity of the cyclin E-CDK2 complex, increased stability of p27 by vitamin D leads to cell cycle arrest in the G1 phase. Thus, vitamin D not only functions as a regulator of gene transcription but also as a modulator of protein stability that plays a role in cell cycle control (Li et al., 2017).

This mechanism indicates that vitamin D may play a role in inhibiting cancer cell proliferation through a non-genomic pathway, namely by stabilizing proteins that control cell cycle transitions. Further research is needed to better understand how vitamin D interacts with cellular proteolytic systems and how these effects can be utilized in cancer therapeutic strategies based on cell cycle regulation (Pickholtz et al., 2014; Li et al., 2015). Proteasomes are responsible for the degradation of the tumor suppressor protein p27, which is previously phosphorylated at position Thr187 by cyclin-dependent kinase 2 (CDK2) and then binds to the ubiquitin ligase complex Skp1-Cullin-F-box/Skp2 (Skp2).

This study found that 1,25-dihydroxyvitamin D3 (1,25$(OH)_2$D3) can stabilize p27, thereby stopping the ovarian cancer cell cycle in the G1 phase. This mechanism occurs because 1,25$(OH)_2$D3 inhibits the activity of cyclin E and CDK2, which initiate a series of processes that lead to decreased phosphorylation of p27 at Thr187 and reduced interaction with Skp2. In addition, 1,25$(OH)_2$D3 suppresses Skp2 expression, which in turn increases the stability of p27. As observed in ovarian cancer cells, 1,25$(OH)_2$D3 also caused p27 accumulation in wild-type mouse embryo fibroblasts and stopped the cell cycle at G1 phase. However, this effect did not occur in cells lacking p27, indicating that p27 stability is critical in this mechanism.

In addition, when Skp2 is stably expressed in OVCAR3 cancer cells, the effect of 1,25$(OH)_2$D3 in arresting the cell cycle at G1 phase is reduced, indicating that the presence of Skp2 may inhibit the response to vitamin D3 (Pilon et al., 2014; Bao et al., 2014). Based on the results of these studies, it was concluded that 1,25$(OH)_2$D3 suppresses cancer cell growth in the G1 phase by decreasing CDK2 activity and reducing the amount of Skp2, which in turn increases the stability of p27 and inhibits cancer cell proliferation.

Conclusion

Based on research results, vitamin D has a significant role in cancer prevention and suppression through various complex biological mechanisms. As an active molecule, 1,25-dihydroxyvitamin D3 interacts with the vitamin D receptor (VDR) and affects the expression of genes involved in cell cycle regulation, immunomodulation, and inhibition of cancer cell proliferation. These mechanisms include increased expression of cell cycle inhibitory genes, such as p21 and p27, and decreased expression of cell cycle promoting genes, such as cyclin D1, which contributes to the inhibition of cancer cell growth. In addition, vitamin D also plays a role in controlling the tumor microenvironment, strengthening the immune system, and reducing chronic inflammation associated with cancer progression.

Suggestion

However, while the current study shows promising results, further exploration is still needed to understand vitamin D's mechanism of action in greater depth, confirm its effectiveness in

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different types of cancer, and identify specific molecular pathways that can be modulated to improve cancer prevention and optimal treatment.

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