How is vitamin A able to treat blood cancer?

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The human body consists of an uncountable number of cells, which despite their obvious differences hold the same genetic material (DNA). This is only possible because each cell is able to respond to numerous internal and external stimuli and these stimuli ultimately guide the process of cell growth and development. Cancer cells often become insensitive to such stimuli and through their uncontrolled division become threat to the integrity of the whole human body.

The vitamin A derivative *all-trans* retinoic acid (ATRA) is one of the stimuli that can guide cells to become more mature and stop dividing. Because of these properties ATRA is used for the treatment of a type of blood cancer, the acute promyelocytic leukemia (APL). In APL a portion of the white blood cells become insensitive to the stimuli triggering their normal maturation process. These cells remain in an immature stage of their development and divide uncontrollably. When treating patients with ATRA their cancer white blood cells stop dividing, become mature and fulfill their normal functions. Despite this, a proportion of APL patients do not respond to the ATRA treatment or in the process of treatment become insensitive to it. Better understanding of the way in which ATRA is able to promote proper cell development is needed to be able to understand why these patients do not respond to the treatment and help them.

In this thesis I studied the function of a cell compound (a protein) called IKKα, known to be involved in regulation of the cell development, to determine a possible connection between it and the effect ATRA has on cells. To do this I used a specific technique to decrease the level of IKKα in the cell to observe if these cells will have different sensitivity towards ATRA. Additionally I also treated cells with a chemical compound (BMS-345541) known to inhibit the function of IKKα and again studied if they become differentially sensitive to ATRA. All my studies were performed on human cancerous white blood cells, similar to those observed in patients with APL. My results show that reducing the level of IKKα in the cell did not disturb its response to ATRA. On the contrary, when IKKα function was inhibited by BMS-345541 cells did not respond to ATRA in their usual manner. Thus, at present my results are contradictory, but they do suggest a possible involvement of IKKα in the maturation process of the white blood cells caused by ATRA.

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