Inhibiting the Growth of CAL-1 Cells with Retinol and Retinoic Acid to Prevent Blastic Natural Killer Cell Lymphoma

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Until the discovery of the CAL-1 cell line, blastic natural killer cell lymphoma (BNKCL), a highly fatal form of leukemia, was an insurmountable obstacle for oncologists. Even with CAL-1, current viable treatments are scarce. However, retinol and retinoic acid (RA) serve as gateways to new treatment research. RA, the active metabolite of retinol, utilizes retinoic acid receptors (RARs) in the nucleus to affect transcription of genes, proving effective in the treatment of acute promyelocytic leukemia (APL) in the form of all trans retinoic acid (ATRA). BNKCL's similarity to APL suggest that ATRA might become a successful treatment. In a controlled laboratory setting, retinol and ATRA were tested, in various molarities, for CAL-1 growth inhibition. BMS 493, an inverse agonist of RARs, was added in certain trials to test that retinoic acid was truly causing growth inhibition. MTT testing determined that retinoic acid is concentration-dependent in inhibiting CAL-1 cells, while retinol is most likely dependent on initial cell count, as retinol inhibits CAL-1 cells through its metabolization into RA. BMS 493 prevented this inhibition with both retinol and retinoic acid, showing that CAL-1 cells are indeed inhibited by RA. Concerns about toxicity to healthy cells were addressed by a paper written in 2007 that used 13-cis RA on emphysema patients. Low levels of 13-cis RA eventually isomerized into ATRA, and the reported ATRA molarities were higher than the molarities used in this experiment, allowing the conclusion that using retinol and ATRA treatments for BNKCL could be safe and effective in humans.

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