Cancer Res. 2014 Jul 15;74(14):3890-901. doi: 10.1158/0008-5472.CAN-13-3694. Epub 2014 May 28.

Selenium suppresses leukemia through the action of endogenous eicosanoids.

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Abstract

Eradicating cancer stem-like cells (CSC) may be essential to fully eradicate cancer. Metabolic changes in CSC could hold a key to their targeting. Here, we report that the dietary micronutrient selenium can trigger apoptosis of CSC derived from chronic or acute myelogenous leukemias when administered at supraphysiologic but nontoxic doses. In leukemia CSC, selenium treatment activated ATM-p53-dependent apoptosis accompanied by increased intracellular levels of reactive oxygen species. Importantly, the same treatment did not trigger apoptosis in hematopoietic stem cells. Serial transplantation studies with BCR-ABL-expressing CSC revealed that the selenium status in mice was a key determinant of CSC survival. Selenium action relied upon the endogenous production of the cyclooxygenase-derived prostaglandins Δ(12)-PGJ2 and 15d-PGJ2. Accordingly, nonsteroidal anti-inflammatory drugs and NADPH oxidase inhibitors abrogated the ability of selenium to trigger apoptosis in leukemia CSC. Our results reveal how selenium-dependent modulation of arachidonic acid metabolism can be directed to trigger apoptosis of primary human and murine CSC in leukemia.