

Concentrations of Uranium Below the US EPA Safe Drinking Water Level Stimulate MCF 7 Human Breast Cancer Cell Growth.

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Decades of uranium (U) mining/milling in the Four Corners region of the US, where the Navajo Reservation is located, has left scores of drinking water sources contaminated with U at levels equal to or greater than the US EPA safe drinking water level of 30 µg/L or 1.26×10^{-7} M. Half of the households on the Navajo Reservation haul and use water from water sources that may have elevated U concentration. We have found *in vivo* in mice that U acts like estrogen stimulating a uterotrophic response, accelerated vaginal opening and persistent presence of vaginal cornified cells. All of these U elicited responses are reversed if the mice are treated with the antiestrogen ICI 182,780. Here we determined if U added to MCF 7 cell culture could stimulate cell growth similar to the effect of added 17β -estradiol. MCF 7 cells, grown in phenol red free media and charcoal stripped serum, were treated with increasing concentrations of uranyl nitrate. The cells were refed every two days and on day 6 the number of cells in culture were determined using the Wst1 assay. Estradiol or U at 10^{-10} M treatment caused a significant increase in the number of cells compared to control cells. The maximum effect of U was 30-40% of the increase seen in cells treated with estradiol. The antiestrogen ICI 182,780 was used to determine if U's stimulation of MCF 7 cell growth was dependent on the estrogen receptor. The significant increase in number cells treated with estradiol or U at 10^{-10} M was completely blocked by the presence of ICI 182,780 at 10^{-6} M. Our results indicate that U, at concentrations well below the US EPA safe drinking water level, stimulates human breast cancer cell growth that is dependent on the estrogen receptor. We conclude that U similar to other heavy metals such as cadmium can act like estrogen and is a putative endocrine disrupting chemical. Although the incidence of breast cancer in Navajo women was the lowest of all ethnic groups, in the last 40 years this incidence has increased to that in Caucasian women. We suggest that U's estrogenic activity may contribute to risk of reproductive cancer in people exposed to U in their drinking water.