

Uranium Mimics ER-Dependant Responses Mediating Rapid Cell Surface Morphological Changes in Mcf-7 Human Breast Cancer Cells

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Decades of uranium (U) mining and milling activities in the Four Corners region of the U.S. has left hundreds of contaminated drinking water sources on the Navajo Nation [1]. Our laboratory's recent results suggest that U mimics E2 *in vivo* and *in vitro* to elicit estrogen receptor-dependant responses over several days. However there have not been studies conducted indicating that U can mediate rapid, non-genomic dependent responses. The reproductive steroid, 17 β -estradiol (E2), induces responses that occur over hours to days or within minutes in estrogen receptor-dependent responses of Mcf-7 breast cancer cells [2].

In the present study we examined the morphological changes in Mcf-7 breast cancer cells within minutes of exposure to U. Mcf-7 cells were cultured in long term estrogen deprived (LTED) media, E2 had been absorbed to activated charcoal in repeated steps, resulting in a significantly increased sensitivity E2 treatment which was determined by measuring Mcf-7 cell proliferation with lowered E2 doses. The LTED cells were exposed to 28 μ g/L U or 60 μ g/L diethylstilbestrol (DES), a potent synthetic form of estrogen, and incubated for 15, 30, or 60 minutes at 37°C. The cells were processed for scanning electron microscopy (SEM) to visualize the effect U had on cell surface morphology.

DES and U-treated cells rapidly increased the size, length and number of surface microvilli and induced membrane ruffling when compared to control cells (Figs 1-3). These results mimic morphological changes that have been reported in Mcf-7 cells exposed to estrogens [3]. The results also show that U, in doses below the EPA safe drinking water level of 30 μ g/L, mimics E2-induced cell surface morphological responses.

Our results suggest that U can mediate both long term and rapid estrogen receptor-dependant responses *in vitro* and provides evidence that environmental U may be an endocrine disruptor potentially causing reproductive problems in the Navajo people [4].

References

- [1] <http://yosemite.epa.gov/r9/sfund/overview.nsf>
- [2] Song RX et al. Linkage of rapid estrogen action to MAPK activation by ER α -Shc association and Shc pathway activation. *Molecular Endocrinology* (2002)16(1):116-127.
- [3] Vic P et al. Effect of estradiol on the ultrastructure of the Mcf-7 human breast cancer cells in culture. *Cancer Research* (1982)42(2):667-673.
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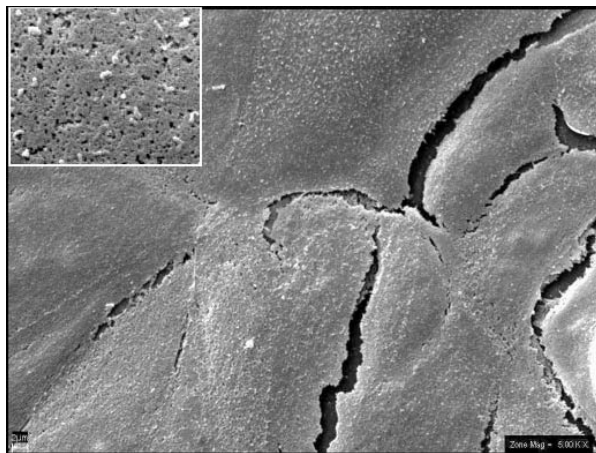


Fig. 1. Scanning Electron Micrograph of untreated MCF-7 Breast Cancer Cells. 5.00 Kx, 20 kV. Inset, high magnification of microvilli, 30 Kx. (Bar, 10 μm).

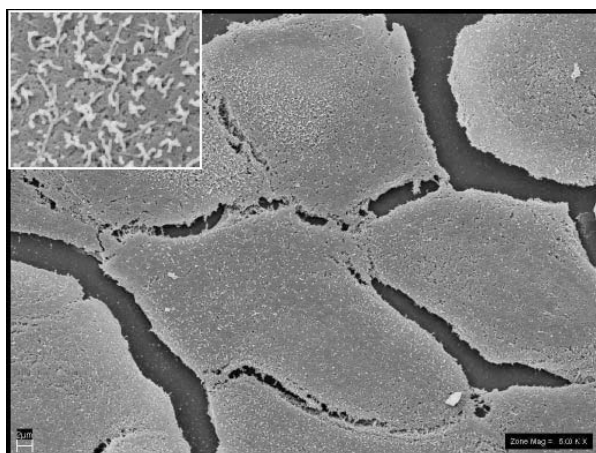


Fig. 2. Scanning Electron Micrograph of MCF-7 Breast Cancer Cells treated with 60 ug/L DES for 60 minutes. 5.00 Kx, 20 kV. Inset, high magnification of microvilli, 30 Kx. (Bar, 10 μm).

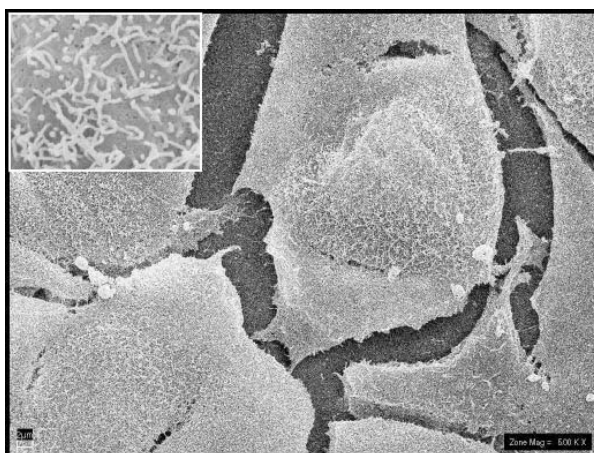


Fig. 3. Scanning Electron Micrograph of MCF-7 Breast Cancer Cells treated with 28 ug/L Uranium for 60 minutes. 5.00 Kx, 20 kV. Inset, high magnification of microvilli, 30 Kx. (Bar, 10 μm).