Ultrastructural damage of CHO AA8 cells in the presence of uranyl acetate (UA): The cytotoxicity of hexavalent uranium (U(VI)).

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The Four Corner region of the southwest is known for its abundance of uranium (U) mines and tailings. The carcinogenic effects related to uranium radioactive decay and the production of radon gas are well documented and linked to lung cancer among Native American miners. However, some reports have shown an incidence of pancreatic, stomach, colon, and prostate cancers as well as birth defects among residents of the Four Corner region suggesting a possible non-radioactive toxic effect of U exposure.[1,2] We are therefore interested in the chemical genotoxicity of U.

We hypothesize that the biochemistry of U(VI) maybe similar to that of the human lung carcinogen Cr(VI). Cr(VI) has been shown to target DNA resulting in chromosome damage and apoptosis in Chinese Hamster Ovary (CHO) cells.[3,4] Cr(VI) treated CHO cells have been observed via TEM and marked abnormalities with respect to cell morphology have been observed.[4] Consistent with this hypothesis, CHO cells exposed to UA show similar ultrastructural abnormalities(Figures 1-4).

The uranyl cation, UO$_2^{2+}$ is the most naturally abundant form of uranium. CHO-AA8 cells were exposed to 300µM uranyl acetate (UA) for 24 and 48hour incubation periods at which time cells were washed and processed for TEM. UA crystals were visible within CHO cell ultra-thin sections providing evidence for U(VI) uptake (Figure 2&3). U(VI) exposed CHO cells showed marked abnormalities among the mitochondrial, nuclear and outer plasma membranes. Disruption of chromatin and mitochondrial cristae were apparent (Figure 2&4). Localization of the U(VI) appears random although crystals have not been observed in organelles, with the exception of the nucleus (the electron dense nature of the nucleus precludes clear distinction of UA crystals) (Figure 4). The sum of these observations in treated cells suggests cytotoxicity with apoptosis being the mode of cell death.

References
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Figure 1. TEM micrographs of untreated CHO cell. (a) Whole untreated cell. (b) Representative mitochondrion.

Figure 2. TEM micrographs of CHO cell exposed to 300µM UA for 24hrs. (a) Whole cell. (b) UA crystal (left) and disrupted mitochondria (right) within cell.

Figure 3. Unstained TEM micrographs of a CHO cell exposed to 300µM UA for 24hrs. (a) Whole cell. (b) UA crystals within cell.

Figure 4. TEM micrographs of CHO cell exposed to 300µM UA for 48hrs. (a) Whole cell. (b) Disrupted nuclear membrane.