Southwest Health Equity Research Collaborative
PILOT PROJECT PROGRAM

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Project Title: “Synergistic toxicity of depleted uranium and UV radiation in a humanized zebrafish model of melanoma”

Proposal Abstract:

A consequence of modern combat for many veterans and civilians is exposure to depleted uranium (DU) from armor piercing munitions that create uranium oxide particles and metal fragments upon striking hard targets. Exposure can come in many forms including wound contamination and shrapnel injuries, which may present a persistent chemical body burden. Research on U chemical toxicity provides mixed interpretations, raising uncertainty as to the risks associated with exposure and potential mechanisms of action. It is known that ultraviolet B-ray (UVB) radiation activates DU, and studies in cells show UVB potentiates DU genotoxicity. We postulate that exposure to UVB can activate DU in the epidermis or dermis. We will test if DU imbedded in skin or underlying tissue is carcinogenic and if the effect is enhanced by activation with UVB. We will leverage genetically engineered zebrafish predisposed to melanoma with incidence rates up to 90% depending on additional modifiers. We reason these fish represent a "worst-case scenario" to investigate DU +/- UVB toxicity, possibly akin to humans with a familial history of cancer. To our knowledge, our research represents the first intentional study of melanoma as a consequence of U chemical toxicity and the first to test the possibility for DU activation by UVB exposure in vivo. Outcomes derived from these studies will provide evidence for or against a carcinogenic effect from DU. Additionally, these studies will demonstrate feasibility for using disease-vulnerable zebrafish as models in toxicology experiments.