OVERCOMING LIMITATIONS OF ORGAN-ON-CHIP (OOC) TECHNOLOGIES TO ADVANCE THE CHARACTERIZATION AND MEDICAL MANAGEMENT OF CHEMICAL AND BIOLOGICAL (CB) THREATS

In-vitro 3d Skin Model With Applications In Biodosimetry & Toxicology

Mohammad Omar Ishak Los Alamos National Laboratory **Jennifer Harris** Los Alamos National Laboratory **Trevor Glaros** Los Alamos National Laboratory **Phillip Mach** Los Alamos National Laboratory **Ethan McBride** Los Alamos National Laboratory

Human relevant systems for predicting human dose responses are paramount for the future of biodosimetry. There is a growing need to uncover novel model systems for studying the impacts of ionizing radiation. As one of the very first organs to be exposed to external sources of ionizing radiation and also serving as the body's first line of defense from external environmental onslaughts, the skin (epidermis) is uniquely positioned in terms of model systems for studying radiation exposure events.

With recent advances in organ-on-a-chip technology, as well as in-vitro 3D cell culture, the field of skin mimetics has seen immense growth in the past decade. In-vitro 3D skin mimetics have opened the door for developing a more holistic understanding of how ionizing radiation affects the complex structural and physiological processes that occur in human skin. In this study, we have successfully surveyed some of the current state-of-the-art technology in terms of in-vitro 3D skin mimetics. These skin mimetics range from the use of full tissue biopsies to co-cultured multi cell layered models. While the approaches vary in terms of cell differentiation, stratification as well as basement membrane composition each model has its own set of advantages, disadvantages and culture time limits.

We have begun the development of our own skin mimetic model that employs full thickness skin, active immune component, active perfusion, modular stage design, variable flow rates and the ability to run in single or multi plex format. Preliminary findings have been positive for extending the lifespan of the tissue biopsies versus a static environment seen in other models. Metabolites such as glucose consumption, lactate production as well as measuring the levels of collagen pre and post culturing have been performed. Histological analysis has also been completed to survey the presence or absences of key epidermal structural features.

In conclusion, our results demonstrate the potential for a miniaturized skin mimetic system that preserves the complex micro architecture found in the human skin and can be used to observe and evaluate radiation exposure events as well as other skin related toxicants.

This research is based upon work supported [in part] by the Office of the Director of National Intelligence (ODNI), Intelligence Advanced Research Projects Activity (IARPA) under the Targeted Evaluation of Ionizing Radiation Exposure (TEI-REX) program contract #IARPA-20008-D2021-210803004 and from Los Alamos National Laboratory LDRD-20210204DR. This work was performed at the Los Alamos National Laboratory, which is operated by Triad National Security, LLC, for the National Nuclear Security Administration of the U.S. Department of Energy (Contract No. 89233218CNA000001).