Molecular Mechanism Underlying Cellular Response in 3D Skin to Low Dose Radiation

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Investigation of the effect of low-dose radiation is challenged by the need to detect a probable low-level biological response. At PNNL we are applying a system biology approach to identify molecular targets in complex human tissue exposed to low-dose ionizing radiation. Our goal is to distinguish between a short term transient effect and long term adaptive change in homeostasis that could have either a positive or negative effect on human health. As a member of this systems biology team we are using protein microarray technology to detect and identify biochemical pathways induced by low-dose radiation. Using an *in vitro* 3-D human skin tissue model system we performed a 72 hour time course to identify changes in protein abundance in the keratinocyte and fibroblast layer of skin tissue. Tissue samples were irradiated with 10cGy of low-dose radiation and samples harvested at 3, 24, and 72 hour time points. The keratinocyte and fibroblast layer were analyzed separately to support understanding of the signaling pathways in this complex tissue system.

Protein microarrays used to investigate the tissue response to low-dose radiation included receptor proteins, inflammatory proteins and chemokines. Statistically significant changes in abundance were observed for 12 proteins. The majority of these changes were observed in the keratinocyte layer except for chemokine (C-C motif) ligand 8 (CCL8/MCP2), which shows a decrease in the fibroblast layer. A complimentary increase in CCL8 is also observed in associated media and correlates with CCL8's function as an activator of immune cells involved in an inflammatory response. These results indicate a low level inflammatory response may occur in reaction to low-dose radiation. Further investigation will determine if this results in an adaptive change to tissue homeostasis that has the potential to modify the time scale and/or extent to which the system responds to additional stressors.