FINAL TECHNICAL REPORT – DE-FG02_07ER64339

Results Summary

This is a 'glue grant' that was part of a DOE Low Dose project entitled 'Identification and Characterization of Soluble Factors Involved in Delayed Effects of Low Dose Radiation'. This collaborative program has involved Drs David L. Springer from Pacific Northwest National Laboratory (PNNL), John H. Miller from Washington State University, Tri-cities (WSU) and William F. Morgan then from the University of Maryland, Baltimore (UMB). In July 2008, Dr. Morgan moved to PNNL and Dr. Janet E. Baulch became PI for this project at University of Maryland. In November of 2008, a one year extension with no new funds was requested to complete the proteomic analyses. The project stemmed from studies in the Morgan laboratory demonstrating that genomically unstable cells secret a soluble factor or factors into the culture medium, that cause cytogenetic aberrations and apoptosis in normal parental GM10115 cells. The purpose of this project was to identify the death inducing effect (DIE) factor or factors, estimate their relative abundance, identify the cell signaling pathways involved and finally recapitulate DIE in normal cells by exogenous manipulation of putative DIE factors in culture medium.

As reported in detail in the previous progress report, analysis of culture medium from the parental cell line, and stable and unstable clones demonstrated inconsistent proteomic profiles as relate to candidate DIE factors. While the proposed proteomic analyses did not provide information that would allow DIE factors to be identified, the analyses provided another important set of observations. Proteomic analysis suggested that proteins associated with the cellular response to oxidative stress and mitochondrial function were elevated in the medium from unstable clones in a manner consistent with mitochondrial dysfunction. These findings correlate with previous studies of these clones that demonstrated functional differences between the mitochondria of stable and unstable clones. These mitochondrial abnormalities in the unstable clones contributes to oxidative stress

Papers and Products

J.H. Miller, S. Jin, W.F. Morgan, A. Yang, Y. Wan, J.S. Peters, and D.L. Springer, Profiling mitochondrial proteins in radiation-induced genome-unstable cell lines with persistent oxidative stress by mass spectrometry. *Radiat. Res*. **169**, 700-706 (2008).

E.C. Laiakis, J.E. Baulch, W.F. Morgan. Interleukin 8 exhibits a pro-mitogenic and pro-survival role in radiation induced genomically unstable cells. *Mutat. Res*. **640**, 74-81 (2008).

S.N. Thomas, K.M. Waters, W.F. Morgan, A.J. Yang, and J.E. Baulch. Quantitiative proteomic analysis of mitochondrial proteins reveals prosurvival mechanisms in the perpetuation of radiation-induced genomic instability. *Free Radical Biol. Med*. **53**, 618-628 (2012).