

Gene Expression Profiles Provide Accurate, Specific and Durable Biodosimetry in Mice and Humans

Meadows, Sarah K.; Dressman, Holly K.; Muramoto, Garrett G.; Himburg, Heather A.; Salter, Alice B.; Wei, Zhengzheng; Ginsburg, Geoffrey S.; Chao, Nelson J.; Nevins, Joseph R.; Chute, John P.

Division of Cellular Therapy, Department of Medicine, Duke University Medical Center; Institute for Genome Sciences and Policy, Duke University Medical Center, Durham, North Carolina, United States of America, 27708. Email: john.chute@duke.edu

Previous work has demonstrated the potential for peripheral blood (PB) gene expression profiling for the detection of disease or environmental exposures. Our group has recently demonstrated that patterns of gene expression can be identified in the PB which predict radiation status and levels of radiation exposure in mice and humans.¹ We have subsequently aimed to determine the impact of several variables on the PB gene expression profile of ionizing radiation, and to determine the specificity of the PB signature of radiation versus other genotoxic stresses. Neither genotype differences nor the time of PB sampling caused any lessening of the accuracy of PB signatures to predict radiation exposure, but sex difference did influence the accuracy of the prediction of radiation exposure at the lowest level (50 cGy). A PB signature of sepsis was also generated and both the PB signature of radiation and the PB signature of sepsis were found to be 100% specific at distinguishing irradiated from septic animals.² We also identified human PB signatures of radiation exposure and chemotherapy treatment which distinguished irradiated patients and chemotherapy-treated individuals within a heterogeneous population with accuracies of 90% and 81%, respectively. We conclude that PB gene expression profiles can be identified in mice and humans that are accurate in predicting radiation status within a heterogeneous population, are specific to ionizing radiation exposure and remain highly accurate over time.

1. Dressman HD, Muramoto GG, Meadows S, Marshall D, Chao NJ, Ginsburg G, Nevins JR, Chute JP. Gene expression signatures that predict radiation response. *PLoS Medicine* 4:690-701, 2007.
2. Meadows S, Dressman H, Muramoto G, Himburg H, Salter A, Wei Z, Ginsburg G, Chao N, Nevins J, Chute JP. Gene expression signatures of radiation response are specific, durable and accurate in mice and humans. *PLoS ONE* 3:1-9:2008.