

MULTIPLE PARAMETER RADIATION INJURY ASSESSMENT USING A NON-HUMAN PRIMATE RADIATION MODEL – BIODOSIMETRY APPLICATIONS

Blakely, William F;¹ Ossetrova, Natalia I.;¹ Whitnall, Mark H.;¹ Sandgren, David J.;¹ Krivokrysenko, Vadim I.;² Shakhov, Alexander;² and Feinstein, Elena², ¹Armed Forces Radiobiology Research Institute (AFRRI), 8901 Wisconsin Ave., Bethesda, MD, 20889-5603, USA, ²Cleveland Biolabs, Inc. (CBL), Buffalo, NY 14203, USA, Corresponding author email: blakely@afri.usuhs.mil

The need to rapidly assess radiation injury in mass casualty and population monitoring scenarios has prompted an evaluation of suitable biomarkers that can provide early diagnostic information after radiation exposure (1). These biomarkers need to be validated in suitable radiation model systems. We recently reported results from two nonhuman primate (*Macaca mulatta*) total-body irradiation models characterizing the radioresponse for early changes in blood cell counts (1), serum amylase activity (1), and several secreted and blood cell derived proteins (salivary amylase, p21 WAF1/CIP1, IL-6, and C-reactive protein) (1,2) measured in blood plasma of 10 animals irradiated with 6 Gy 250-kVp x-rays (0.13 Gy/min) (2) and 8 animals irradiated with 6.5 Gy ⁶⁰Co γ -rays (0.4 Gy/min) (1). In one of these cohorts we analyzed the proteomic response with use of multivariate discriminant analysis and established very successful separation of samples from exposed animals (24 hr after irradiation) vs. samples from the same animals before irradiation. An enhanced separation was observed as the number of biomarkers increased (2).

Here we present results from another nonhuman primate (*Macaca mulatta*) total-body irradiation model (6.5 Gy ⁶⁰Co- γ at 0.6 Gy/min) study demonstrating: a) time-dependent changes in blood cell counts (-2d, 1- 4 days after irradiation), b) time dependency for serum amylase activity (-2 day to 27 days after irradiation), c) time course for changes in C-reactive protein (-2 days to 15 days after irradiation), and d) separation of samples from exposed animals (24 hr after irradiation) vs. samples from the same animals taken before irradiation using a discriminant analysis based on blood plasma protein biomarker (i.e., serum amylase activity) and blood cell counts (i.e., neutrophils, lymphocytes, ratio of neutrophils to lymphocytes). These results demonstrate the practical utility for use of multiple parameter biomarkers to enhance the discrimination of exposed vs. non-exposed individuals and justify a follow-on dose response study. [AFRRI supported this research under project# BD-10; Cleveland Biolabs partially supported the *in vivo* studies under grant 1R01AI066497-01 from NIAID BioShield program].

References

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