PROTEOMIC APPROACH FOR EARLY-RESPONSE RADIATION EXPOSURE DOSE ASSESSMENT IN TRIAGE BIODOSIMETRY APPLICATIONS

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Accidental irradiation situations management requires development and validation of biomarkers of exposure dose received by victims that provide almost immediate dosimetric information, as well as to distinguish exposed vs. non-exposed individuals (1). Early treatment of populations exposed to ionizing radiation (2-3) requires accurate and rapid biodosimetry with a precision as high as possible to determine an individual's exposure level and risk for morbidity and mortality. Proteomics is an area offering hope for potential new biological indicators of radiation exposure. Proteomic analyses may be applicable for triage purposes, providing rapid estimation of individual exposure doses (4).

We recently reported results from a study in a nonhuman primate (*Macaca mulatta*) total-body irradiation model and showed that a protein expression profile (i.e. p53, p21 WAF1, IL-6, salivary α-amylase, and CRP) measured in blood of 10 animals irradiated to 6 Gy 250-kVp x-rays (0.13 Gy/min) and 8 animals to 6.5 Gy ^{60}Co γ-rays (0.4 Gy/min) analyzed with use of multivariate discriminant analysis established very successful separation of samples from exposed animals vs samples from the same animals before irradiation. An enhanced separation was observed as the number of biomarkers increased (5-6).

Here we present results from on-going murine (BALB/c) *in vivo* studies demonstrating time- and dose-dependent increases in multiple blood protein biomarkers (i.e., GADD45a, IL-6, serum amyloid A). We demonstrate for the first time that a protein expression profile can be developed not only to predict radiation exposure in mice but also to distinguish the level of radiation exposure, ranging from 1 to 7 Gy (0.1 Gy/min). These results demonstrate proof-in-concept that proteomics shows promise as a complimentary approach to conventional biodosimetry for early assessment of radiation exposures. This approach, with additional refinement, could provide a method for practical application of a rapid screening test for the diagnosis of radiation exposure. [AFRRI supported this research under project BD-10].

References

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