Circulating cytokine signatures for radiation biodosimetry in a mouse PBI/BM5 model

Wanchang Cui [1,2*], Lisa Hull [1, 3], Asher Rothstein [1,3], Li Wang [1,3,4], Bin Lin [1,3], Min Zhai [1,3], Mang Xiao [1]

[1] *Armed Forces Radiobiology Research Institute, Uniformed Services University of the Health Sciences, Bethesda, MD 20814, USA*
[2] *Department of Pharmacology and Molecular Therapeutics, Uniformed Services University of the Health Sciences, Bethesda, MD 20814, USA*
[3] *Henry M Jackson Foundation for the Advancement of Military Medicine, Inc., Bethesda, MD 20817, USA*
[4] *Department of Pathology, Uniformed Services University of the Health Sciences, Bethesda, MD 20814, USA*

Accurate radiation biodosimetry is urgently needed for medical management after large scale radiation exposure. Partial-body irradiation with 5% bone marrow sparing (PBI/BM5) provides a realistic radiation model. We defined the survival profile of male C57BL/6 mice after PBI/BM5 and found that doses of 13.5–14.0 Gy were nonlethal within 12 days, while 15.0–15.5 Gy doses caused 100% mortality within 12 days. A separate cohort of 14.0 Gy showed 100% survival up to 90 days post radiation. To develop serum cytokine-based biodosimetry, mice were exposed to 12.0–16.0 Gy PBI/BM5 and serum was collected on days 1, 3, and 7. A multiplex cytokine assay was used to quantify 70 total cytokines/chemokines. After exclusion of 4 targets outside detection limits, 66 markers were utilized for downstream analysis. PCA, clustering and heatmaps, and LASSO classification revealed that cytokine signatures can classify radiation groups/status/dose. A 4-cytokine panel (IL-7, GDF-15, IL-16 and FLT3L) could distinguish naïve vs irradiated mice on all study days. A 24-cytokine signature distinguished radiation survivors vs. non-survivors, and another 34-cytokine panel separated radiation doses (12–16 Gy); the prediction was better on day 7 compared to earlier time points. These findings show that serum cytokines have strong potential for biodosimetry and outcome prediction in a clinically relevant PBI model.