THROMBIN PEPTIDE TP508 PROMOTES RESISTANCE TO BACTEREMIA AND LUNG INJURY FOLLOWING LETHAL RADIATION EXPOSURE

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Following a lethal dosage of radiation exposure in mice, many physiological changes are observed leading to death. Our laboratory investigated the ability of our novel wound-healing peptide, thrombin peptide TP508, to mitigate the effects of whole body ionizing radiation exposure. It has been documented that high levels of radiation exposure can lead to bacterial escape from the intestine, followed by cytokine release and lung damage. We observed that as soon as five days after 12 Gy radiation exposure live bacteria could be isolated from the blood, spleen and peritoneum of placebo treated but not TP508 treated ICR mice. A significant consequence of bacterial release is acute lung injury caused by innate immune responses leading to multiple organ failure and death. H&E and Movat staining were performed on formalin fixed, paraffin embedded lungs to look at immune cell infiltration and edema in the lung as these are characteristics of acute lung injury. White blood cell counts from whole blood following irradiation showed mice suffered from neutropenia in both placebo and TP508 treated groups. However, day five post irradiation lung histology showed thickening of the interstitial space and increased tissue degradation and/or mucus secretion in placebo treated irradiated mice indicating edema and lung damage. Histology of TP508 treated mice showed protection of the lung and resembled sections from non-irradiated control. This indicates that the effects of TP508 may be through prevention of bacterial escape from the intestine into the circulation or protection of other cell types such as endothelial cells from the effects of LPS and other bacterial proteins rather than immune protection and clearance. Additional studies will use an LPS model of sepsis to investigate the ability of TP508 to mitigate LPS-induced lung injury and mortality in otherwise healthy mice.