**FSL-1: Toll–Like Receptor 2/6 Agonist – a promising radiation prophylactic agent**

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**Background:** In the current geopolitical climate there is an unmet need to identify and develop prophylactic radiation countermeasures. This is particularly true to ensure the wellbeing of warfighters and first responders that may be required to perform on radiation contaminated fields for operational or rescue missions. Currently no countermeasures have been approved by the US FDA for prophylactic administration. Effective countermeasures should function to increase survival in the short term as well as to increase the overall prognosis of an exposed individual long term. Here we report FSL-1 (Toll-Like Receptor 2/6 Agonist) the protection from Acute radiation syndrome (ARS) in a murine total body irradiation model (TBI).

**Method:** A single dose of FSL-1 was administered subcutaneously in mice. The safety of the compound was assessed in non-irradiated animals, the efficacy of the compound was assessed in animals exposed to TBI in the AFRRI Co-60 facility, the dose of FSL-1 was optimized, and common hematological parameters (CBC, cytokines, and bone marrow progenitor cells) were assessed. Animals were monitored up to 60 days following exposure and radiation-induced damage was evaluated.

**Results:** FSL-1 was shown to be non-toxic when administered to non-irradiated mice at doses up to 3mg/kg. The window of efficacy was determined to be 24h prior to 24h after TBI. FSL-1 administration resulted in significantly increased survival when administered either 24h prior to or 24h after exposure to supralethal doses of TBI. The optimal dose of FSL-1 administration was determined to be 1.5mg/kg when administered prior to irradiation. Finally, FSL-1 protected the hematopoietic system (recovery of CBC, bone marrow CFU, markers of bone marrow aplasia EPO, TPO, FLt3L).

**Conclusion:** Taken together, the effects of increased survival and accelerated recovery of hematological parameters suggests that FSL-1 should be developed as a novel radiation countermeasure for soldiers and civilians, which can be used either before or after radiation in the aftermath of a radiation event.

*The opinions and assertions expressed herein are those of the author(s) and do not necessarily reflect the official policy or position of the Uniformed Services University or the Department of Defense. None of the authors or their family members have a financial interest in any commercial product, service, or organization providing financial support for this research. The work was supported by NIAID IAA and AFRRI Intramural Research.*