Low-dose Photons Modify CD4+ T Cell Signaling Response to Simulated Solar Particle Event Protons

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Purpose: Astronauts on missions are exposed to low-dose/low-dose (LDR) radiation and could receive high doses during solar particle events (SPE). This study investigated T cell function in response to LDR radiation and simulated SPE (sSPE) protons, alone and in combination.

Materials and methods: C57BL/6 mice received LDR γ-radiation (^{57}Co) to a total dose of 0.01 Gray (Gy) at 0.0179 cGy/h, either with or without subsequent exposure to 1.7 Gy simulated SPE (sSPE) protons delivered over 36 h. On days 4 and 21 post-exposure, three functional pathways were studied using negatively isolated/anti-CD3 activated splenic $CD4^+$ T cells: survival, T cell antigen receptor (TCR) signaling, and cytokine secretion.

Results: The most striking effects were noted on day 21. In the survival pathway, NF-κB (total & active forms) and p38MAPK (total) were significantly increased and JNK (total & active) was decreased in $CD4^+$ T cells from mice primed with LDR γ-rays before exposure to sSPE ($P < 0.001$). Evaluation of the TCR signaling pathway revealed that LDR exposure normalized the high sSPE-induced level of total and active LcK by day 21 ($P < 0.001$ for sSPE vs. LDR+sSPE), while radiation had no effect on active Zap70. There was increased production of interleukin-2 (IL-2) and IL-4 and decreased transforming growth factor-β1 in the combination group compared to sSPE alone.

Conclusion: The data demonstrate for the first time that protracted exposure to LDR photons can significantly modify the effects of sSPE protons on critical survival/signaling proteins and immunomodulatory cytokines produced by $CD4^+$ T cells.

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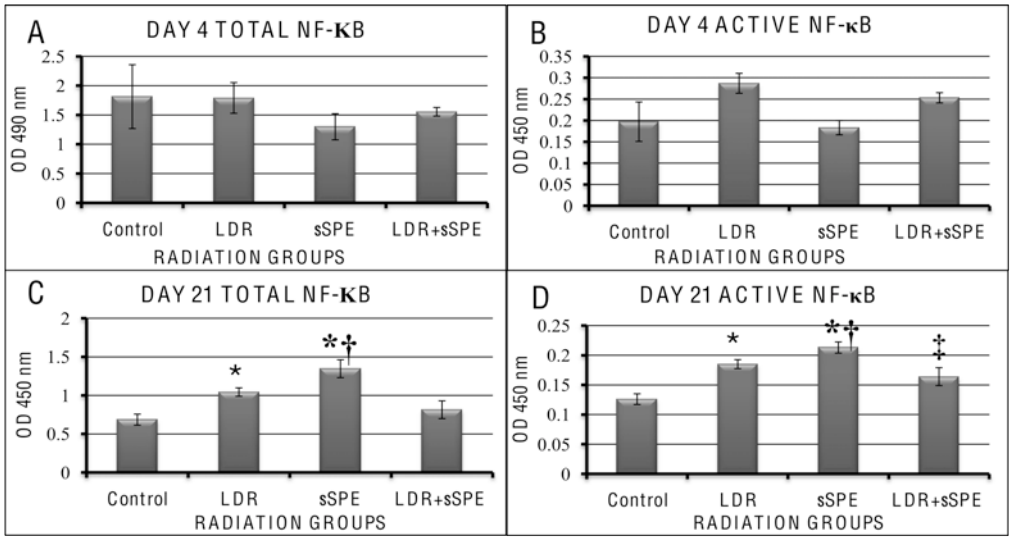
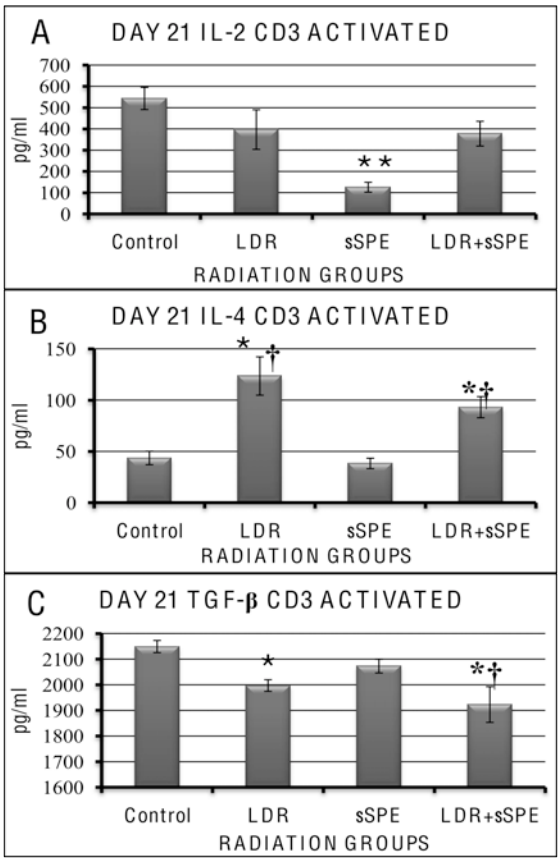
[Note: A manuscript is in review; selected data are presented on the next page.]

NF-κB Protein in CD4$^+$ T Cells Activated by Monoclonal Anti-CD3 Antibodies



Values represent mean ± SEM; day 4 had 3 samples/group, with 3-4 mice/sample; day 21 had n = 9-10 mice/group. OD: optical density. Two-way ANOVA: $P < 0.001$ for interaction between LDR and sSPE on day 21 (total and active NF-κB). *$P < 0.001$ vs. control; †$P < 0.05$ vs. LDR+sSPE; ‡$P = 0.056$ vs. control.

IL-2, IL-4 and TGF-β1 in CD4$^+$ T Cell Supernatant



Supernatants were collected after negative isolation and activation of CD4+ T cells with monoclonal anti-CD3 antibodies. Cytokine concentrations were quantified using ELISA. Values represent mean ± SEM for 9-10 mice/group. Two-way ANOVA: $P < 0.004$ for interaction between LDR and sSPE on day 21 (IL-2) **$P < 0.001$ vs. all other groups; *$P < 0.001$ vs. control; †$P < 0.05$ vs. sSPE.