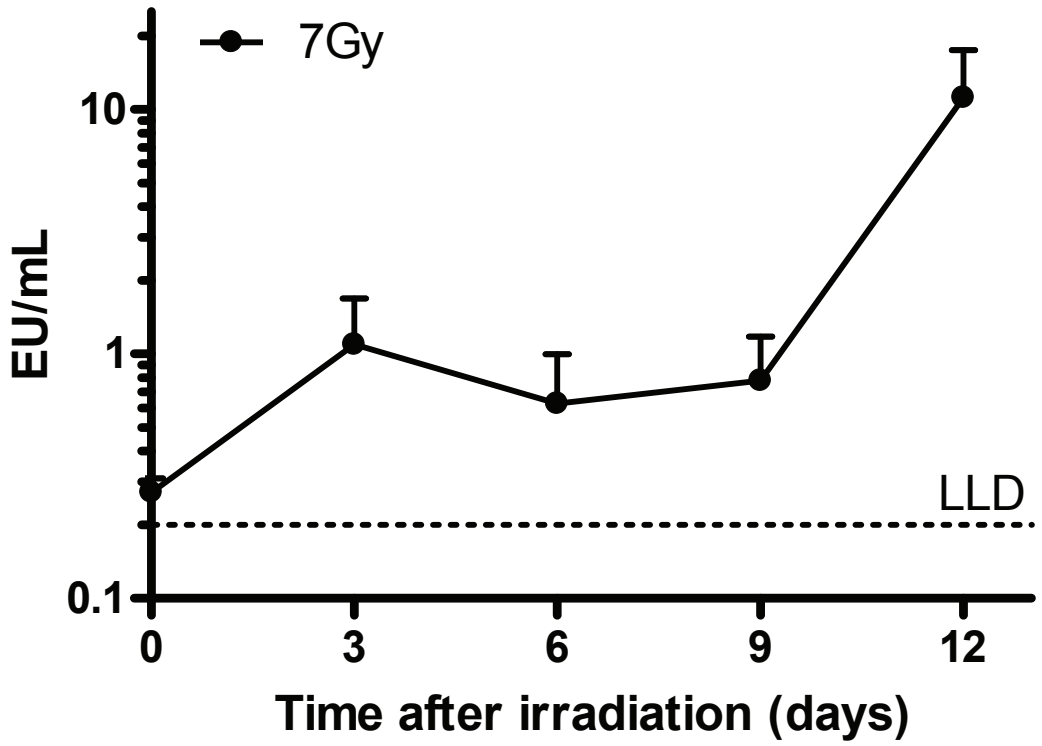
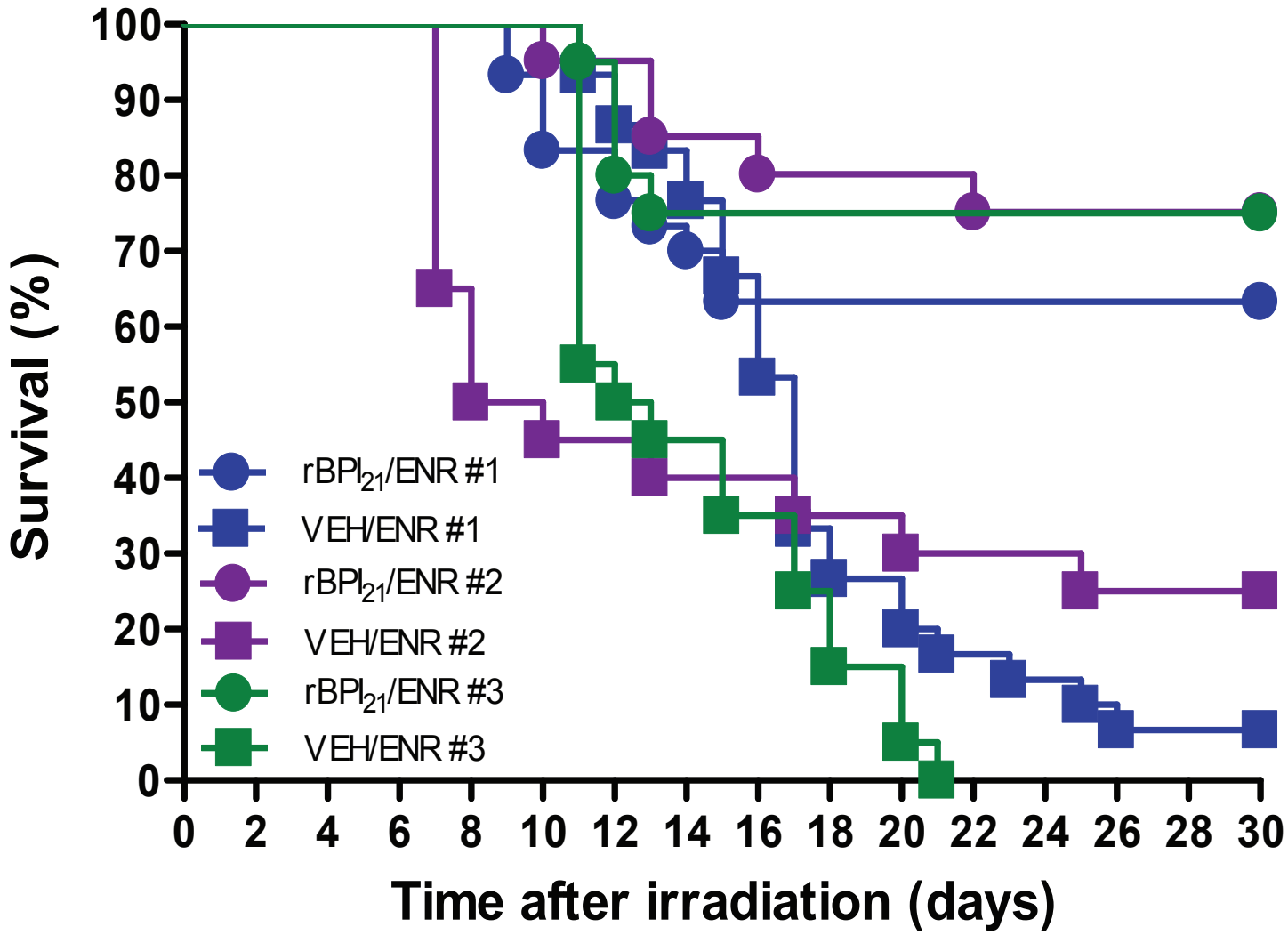
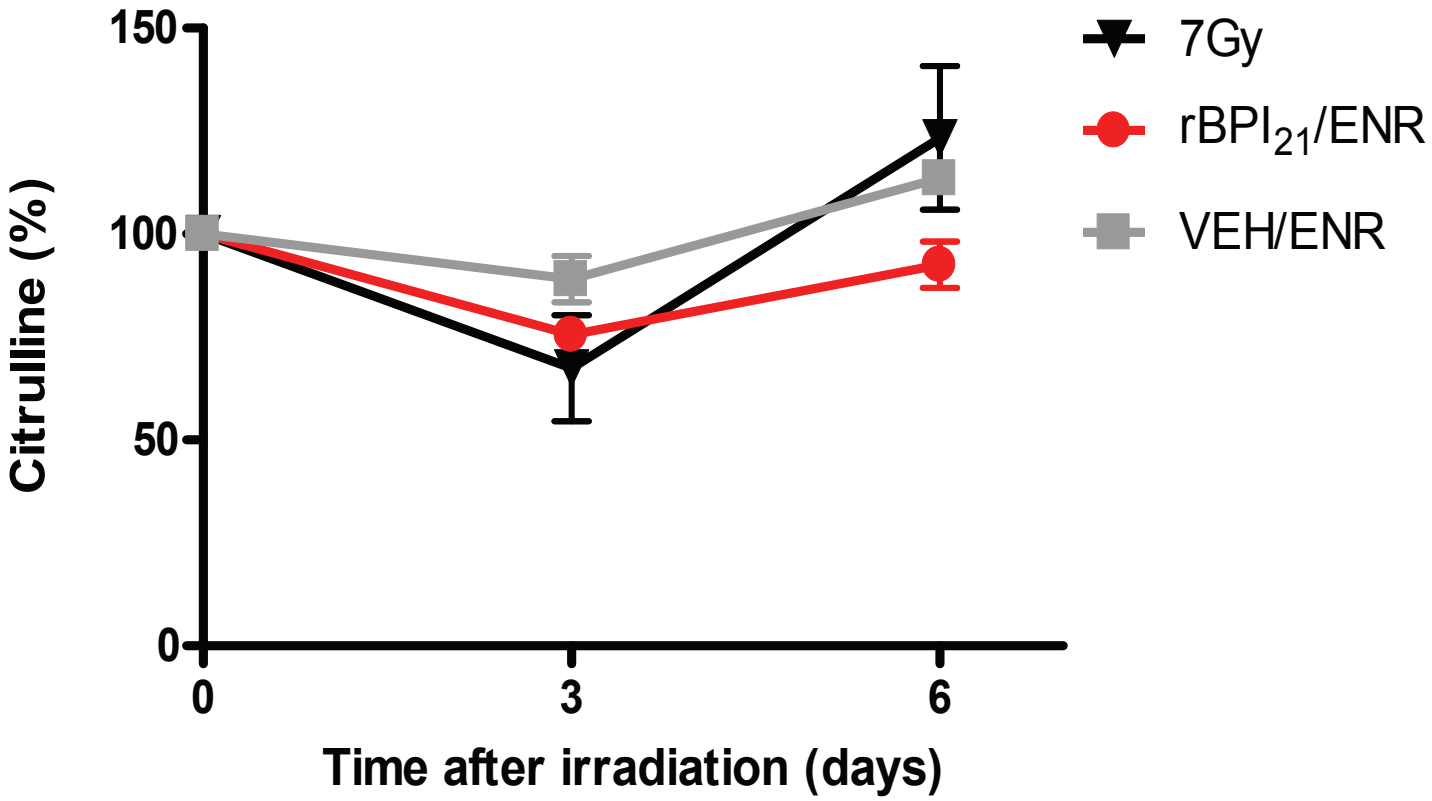


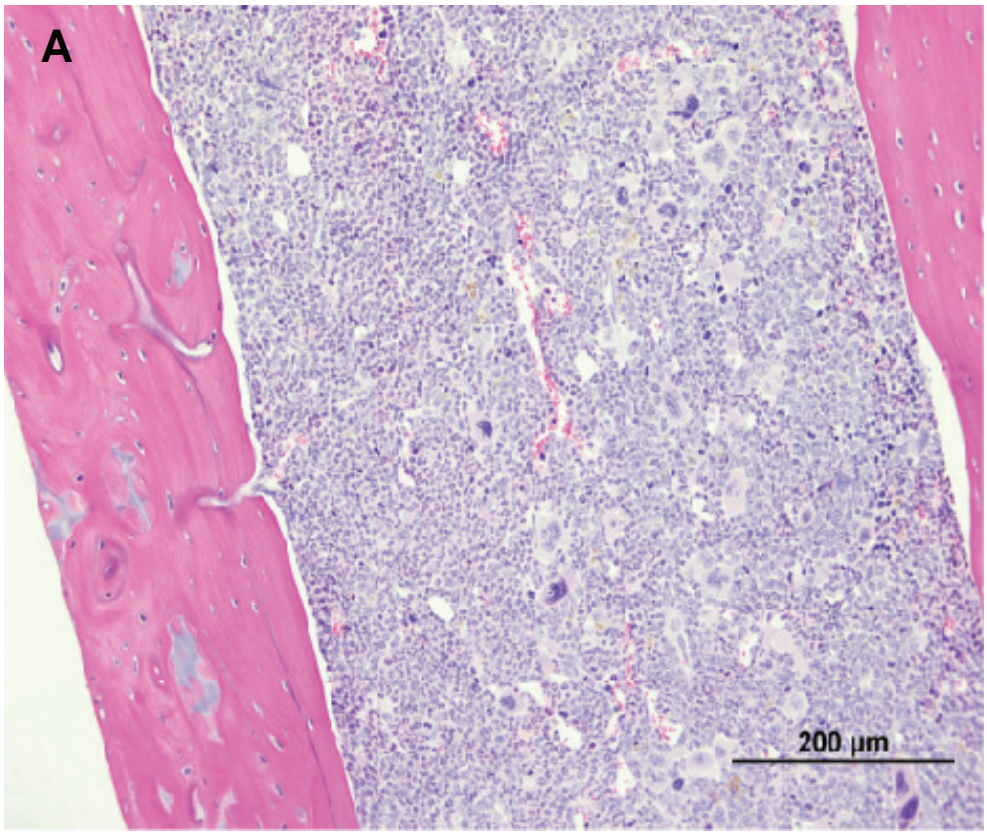

**S1. 7 Gy irradiation of BALB/c mice is associated with subsequent endotoxemia.** Results of LAL endotoxin assay on PB obtained on indicated days are shown as mean ±SEM. Endotoxin was present from D3 onwards. N=9 mice/timepoint on days 0, 3, 12, n=6 on D6, and n=8 on D9. Mortality of 7 Gy irradiation precluded evaluation of sufficient mice for analysis beyond D12

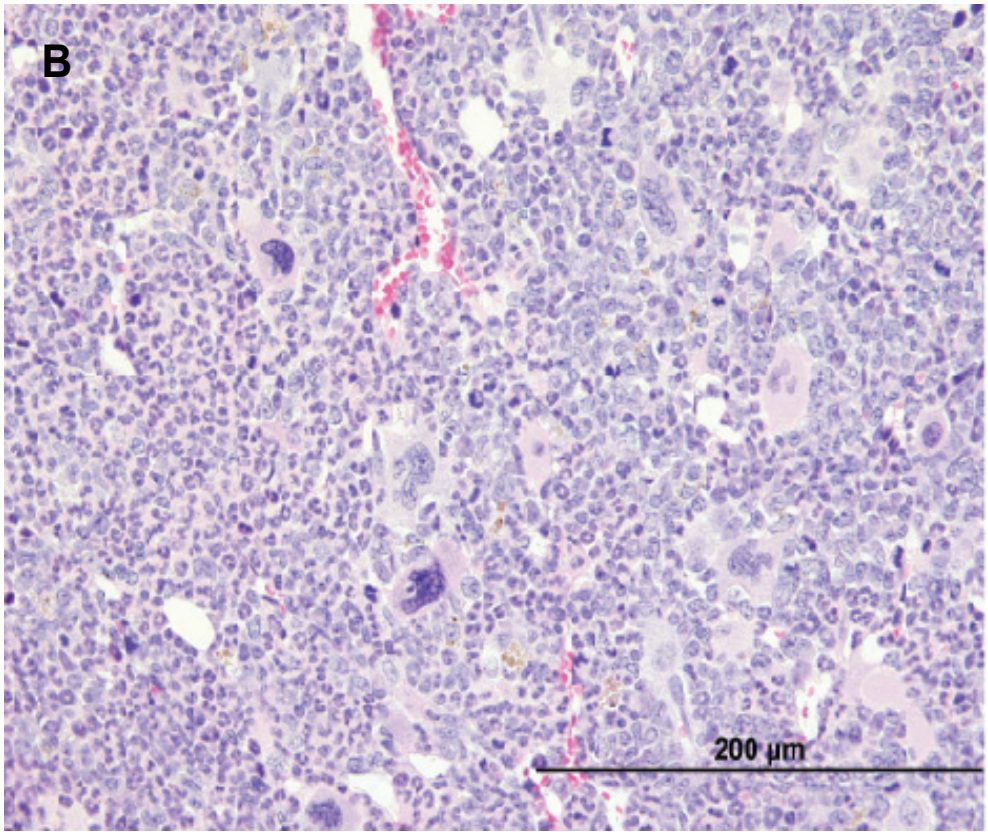



**S2. The effect of rBPI$_{21}$/ENR and VEH/ENR on survival of BALB/c mice after 7 Gy TBI is reproducible.** Three replicate experiments depict survival of different cohorts of BALB/c mice initiated on rBPI$_{21}$ (or its formulation buffer (VEH)) plus ENR 24 hours after irradiation and continuing 30 days. Significant improvement in survival of rBPI$_{21}$/ENR relative to VEH/ENR treated mice was observed in all 3 experiments ($p<0.0001$ by pairwise Mantel-Cox log-rank, n=30, 20 and 20 mice/arm, respectively).

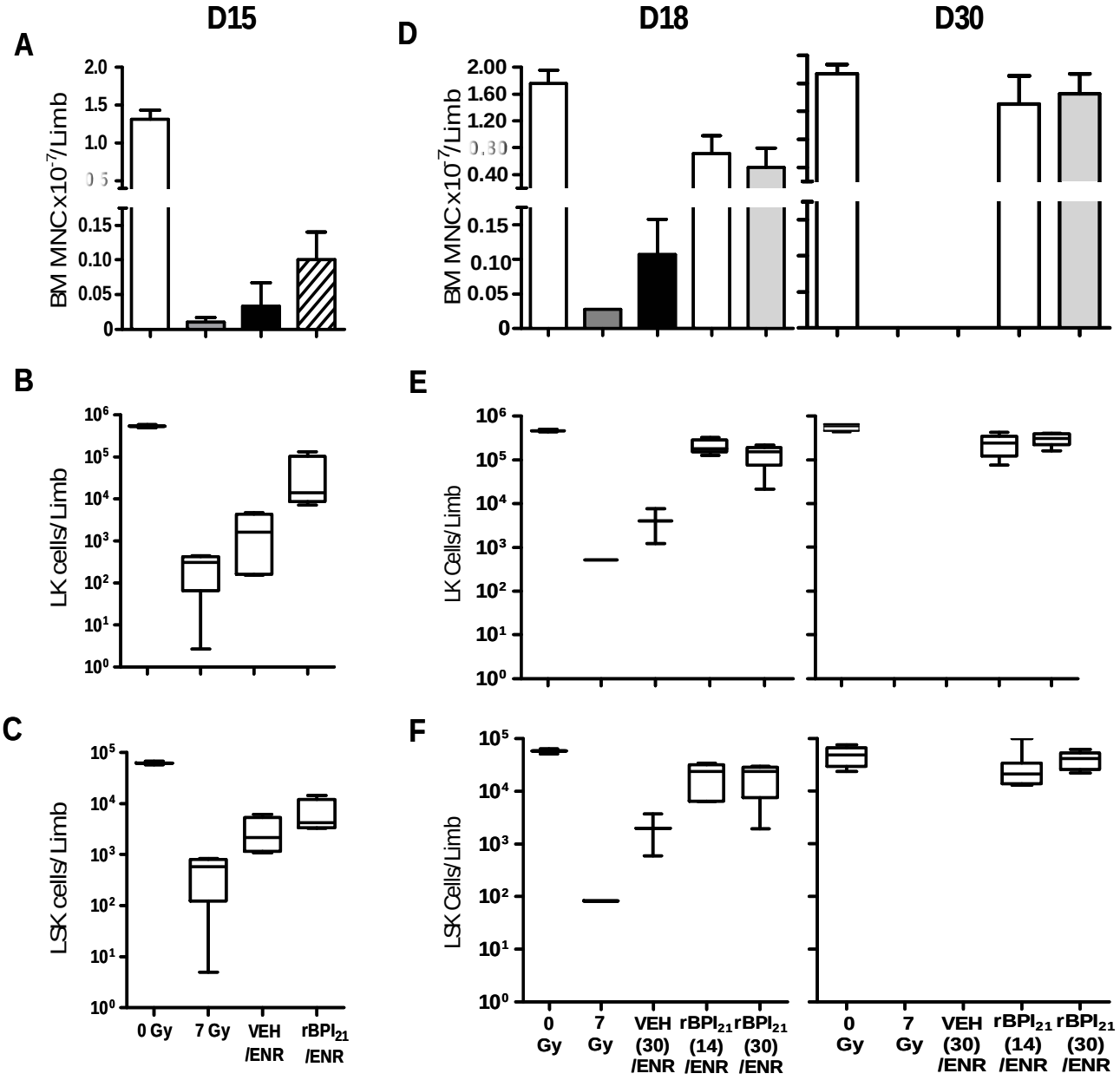



**S3. rPBI$_{21}$/ENR does not mitigate early mucosal damage after 7 Gy irradiation.** Rapid onset of mucosal cell loss documented by nadir in plasma citrulline levels (n=4; D3), depicted normalized to the mean level in unirradiated mice (n=4; D0=100%). Statistical analyses by Mann Whitney tests revealed within-group significant changes from D0 for 7Gy (D3 $p<0.05$; D6 $p<0.05$), VEH/ENR (D3 $p<0.05$; D6 $p<0.05$) and rBPI$_{21}$/ENR (D3 $p<0.05$). No statistically significant changes were found between treatment groups.

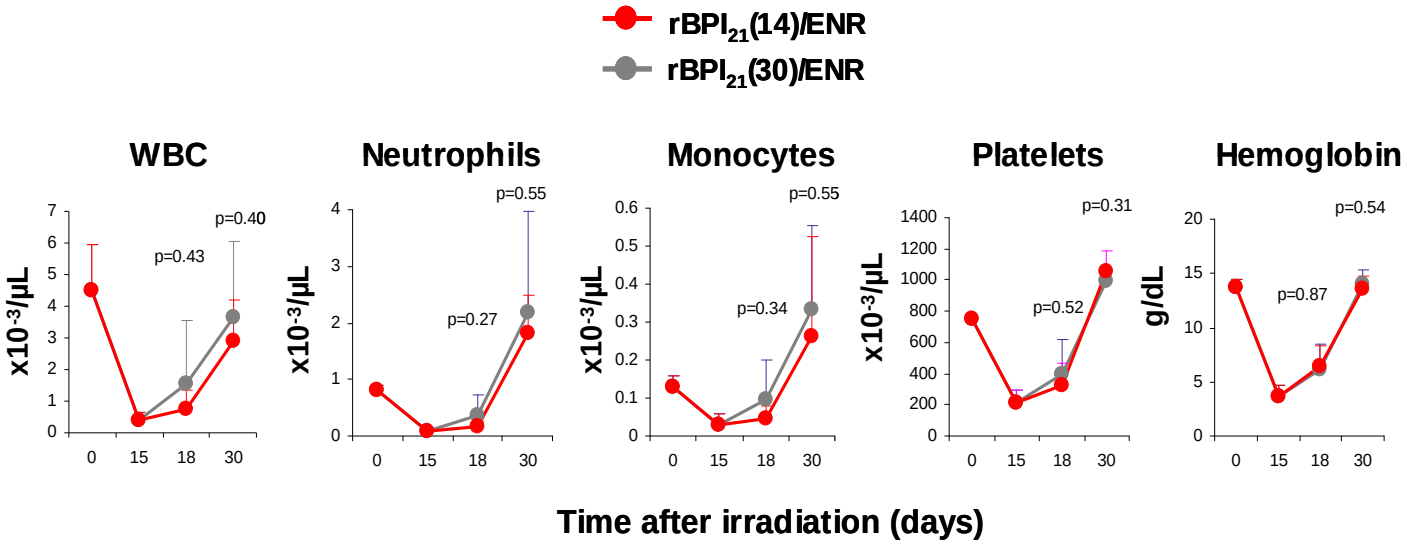


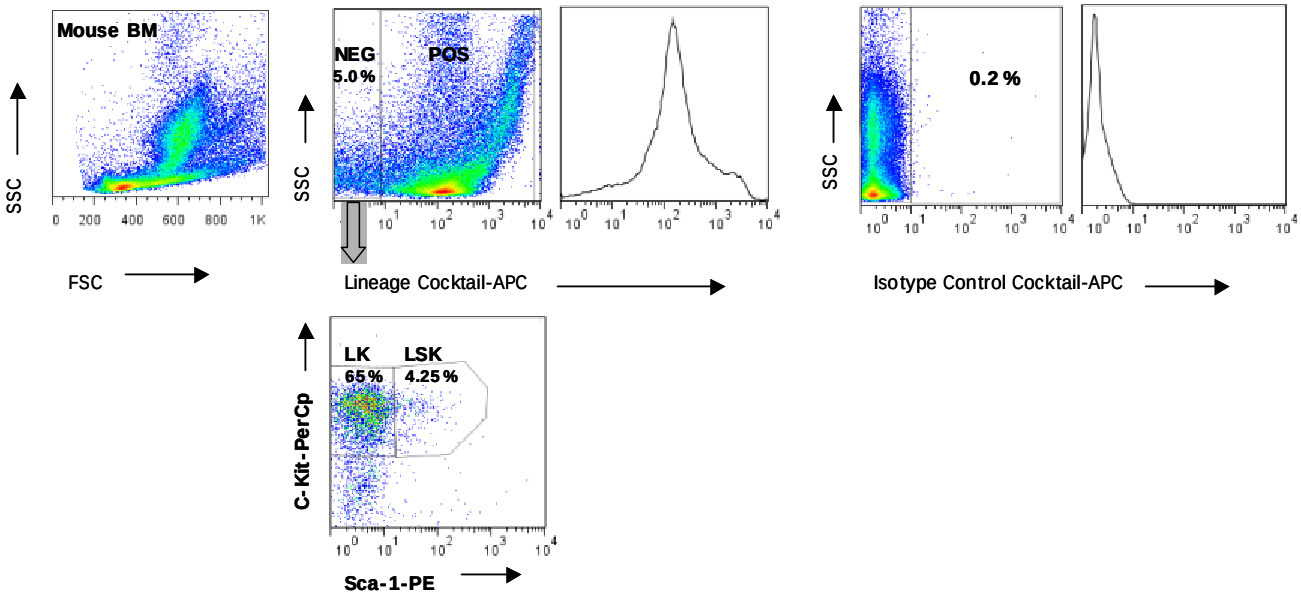

**S4. Trilineage hematopoiesisis evident in BM of rBPI$_{21}$/ENR treated mice.** BALB/c mice irradiated to 7 GY were initiated on rBPI$_{21}$/ENR treatment 24 hours thereafter. Mice were euthanized 19 days after irradiation. Low power images of H&E stained coronal sections of femur in rBPI$_{21}$/ENR treated mouse are shown in Fig. 3. These images show higher power images at (A) 20X and (B) at 40X. BM demonstrates trilineage hematopoiesis, relative myeloid hyperplasia, robust recovery of megakaryocytes and no dysplasia.




**S5. Effects of 14 and 30 days of $rBPI_{21}$ plus ENR on bone marrow mononuclear cells, LK and LSK cells are equivalent.** BALB/c mice were irradiated to 7 Gy and treatments were initiated 24 hours thereafter. Some mice received twice daily $rBPI_{21}$ SC in combination with ENR until D15 at which time the remainder were divided equally into one group called $rBPI_{21}$(14)/ENR in which $rBPI_{21}$ was discontinued but ENR was continued until D30, and another group, $rBPI_{21}$(30)/ENR, in which both $rBPI_{21}$ and ENR were continued until D30. The VEH/ENR group was treated as previously described. $rBPI_{21}$(14)/ENR and $rBPI_{21}$ (30)/ENR had comparable levels of bone marrow mononuclear cells (panels A, D), LK (panels B, E) and LSK (panels C, F) at all timepoints. Quantification was performed as per Methods. Bar graphs + SD depict bone marrow mononuclear cells, and box and whisker graphs depict the range, 25$^{th}$ and 75$^{th}$ percentiles and median number of LK or LSK phenotype cells within BM from one hind limb of each animal in each treatment group. For the $rBPI_{21}$(14)/ENR and $rBPI_{21}$ (30)/ENR groups, D15: n=4/group, D18: n=5-6/group, and D30: 8-10/group. Due to early mortality, there was n=1 (7 Gy) and n=2 (VEH/ENR) at D18 and no survivors in those groups at D30. Values obtained from 2 normal animals are depicted as the 0 Gy values. Data obtained from a single study are shown.




**S6. Peripheral blood counts are equivalent after 14 or 30 days of $rBPI_{21}$ plus ENR treatment.** Comparable levels of white blood cells (WBC), neutrophils, monocytes, platelets, and hemoglobin were measured in the peripheral blood of BALB/c mice treated with $rBPI_{21}$ for 14 days, $rBPI_{21}$ (14)/ENR-red circles, as compared to treatment with $rBPI_{21}$ for 30 days, $rBPI_{21}$ (30)/ENR-gray circles. Treatments began 24 hours after 7 Gy irradiation. Peripheral blood counts were obtained as described in Methods. All mice received twice daily $rBPI_{21}$ SC in combination with ENR until D15 at which time 4 mice were bled for peripheral blood cell analysis. The remainder were divided equally into one group called $rBPI_{21}$(14)/ENR in which $rBPI_{21}$ was discontinued but ENR was continued until D30, and another group, $rBPI_{21}$ (30)/ENR, in which both $rBPI_{21}$ and ENR were continued until D30. Results show the mean + standard deviation of the peripheral blood count values measured on D18: n=5-6/group, and D30: 8-10/group. Values obtained from 2 normal animals are depicted as the D0 values. Data obtained from a single study are shown.




**S7. Gating strategy for determining LK and LSK cells in bone marrow from BALB/c mice by FACS.** A gate is drawn on the FSC vs. SSC dot plot of bone marrow cells in order to exclude small debris. Committed lineage cells were determined in the FL-4 channel (APC positive) vs. SSC, and gates drawn to bifurcate these from cells negative for lineage marker expression (neg-low APC fluorescence). Gating was confirmed through the use of a matched isotype control cocktail also conjugated to APC. Lineage negative cells are visualized on Sca-1PE x c-kit-PerCP5.5 dual fluorescence dot plots to assess the content of $Lin^{-}Sca\text{-}1^{-}c\text{-}kit^{+}$ (LK- progenitor cells) and $Lin^{-}Sca\text{-}1^{+}c\text{-}kit^{+}$ (LSK- stem cells) in mouse bone marrow. Histograms shown are from the analysis of a normal mouse.

Abbreviations: MRD = matched related donor, URD = unrelated donor, BU = busulfan, CY = cyclophosphamide, ATG = anti-thymocyte globulin, BM = bone marrow, PBSC = peripheral blood stem cells, GVHD = graft-versus-host disease, CSA = cyclosporine A, MTX = methotrexate, ANC = absolute neutrophil count

**Table S1. Characteristics and treatment of patients undergoing myeloablative transplantation on the observational cohort study.**

| Characteristic | Data |
|---|---|
| **Subjects:** pediatric / adult (total) | 13/35 (48) |
| **M/F** | 29/19 |
| **Age in years**: median (range) | 39 (1-60) |
| **Diagnosis** | |
| Acute leukemia | 25 |
| Chronic leukemia | 8 |
| Myelodysplasia | 7 |
| Lymphoma | 6 |
| Aplastic anemia | 2 |
| **MRD donor / URD donor** | 37/11 |
| **Conditioning** | |
| Radiation & chemotherapy | |
| TBI 1400 cGy/CY 1800 mg/$M^2$ x 2 doses | 38 |
| TBI 1375 cGy/CY 60 mg/kg x 2 doses/ ATG 2.5 mg/kg x 1 dose/ Thiotepa 5 mg/kg x 2 doses | 1 |
| Chemotherapy alone | |
| BU 0.5-1.1 mg/kg x 16 doses/CY 1500 mg/ $M^2$ x 4 doses | 2 |
| BU 0.8 mg/kg x 16 doses/CY 1800 mg/ $M^2$ x 2 doses | 5 |
| CY 1500 mg/$M^2$ x 4 doses/ATG 30 mg/kg x 3 doses | 1 |
| CY 1500 mg/$M^2$ x 4 doses/ATG 1.5 mg/kg x 4 doses | 1 |
| **Stem cell type:** BM/PBSC | 16/32 |
| **Total nucleated cells x $10^8$/kg**: median (range) | 6.48 (0.07-21.35) |
| **GVHD prophylaxis** | |
| CSA/MTX | 13 |
| MTX/Tacrolimus | 30 |
| Sirolimus/Tacrolimus | 4 |
| T cell depletion | 1 |
| **Days to ANC engraftment:** median (range) | 16 (9-50) |
| **Days to platelet engraftment:** median (range) * | 22 (13-143) |
| **Culture positive bacteremia** | |
| Gram negative organism | 1 |
| Gram positive organism | 15 |

* 2 patients died prior to platelet engraftment

**Table S2. Median fold-difference in peripheral blood levels of chemokines and cytokines after radiation alone, radiation with indicated treatment, or no irradiation**

| Chemokine/cytokine | Day* | 7 Gy | ENR | VEH/ENR | $rBPI_{21}$/ENR |
|---|---|---|---|---|---|
| CXCL10 (IP10) | 3 | 8.9 ♦ | 4.1 ■ | 5.4 | 8.0 |
| | 6 | 3.7 ♦ | 3.3 ● | 4.0 | 4.5 |
| CCL2 (MCP-1) | 3 | 68.8 ♦ | 17.3 ● | 31.5 | 152.4 |
| | 6 | 10.2 ♦ | 10.2 ● | 9.2 ● | 120.1 ■ |
| CCL3 (MIP-1α) | 3 | 1.1 | 6.0 | 1.5 | 3.1 |
| | 6 | 31.2 ♦ | 8.1 | 16.7 | 32.3 |
| CCL4 (MIP-1β) | 3 | 6.4 | 8.3 | 6.2 | 2.5 ■ |
| | 6 | 13.8 ♦ | 6.9 | 8.8 | 11.6 |
| CCL5 (RANTES) | 3 | 0.6 | 0.5 | 0.6 | 0.5 |
| | 6 | 0.5 | 1.5 | 1.8 | 1.6 |
| IL-1α | 3 | 1.9 | 2.4 | 2.5 | 1.1 |
| | 6 | 18.3 | 2.7 | 1.9 | 3.6 |
| IL-1β | 3 | 0.4 | 1.3 | 0.4 | 0.4 |
| | 6 | 3.2 | 8.5 | 2.4 | 3.9 |
| IL-6 | 3 | 1.6 ♦● | 10.1 | 6.0 | 12.2 ■ |
| | 6 | 4.7 ♦● | 4.2 ● | 4.6 ● | 26.1 ■ |
| IL-10 | 3 | 0.4 | 0.8 | 0.5 | 0.4 |
| | 6 | 1.5 | 0.7 | 1.0 | 2.2 |
| IL-12p40 | 3 | 0.9 | 1.1 | 0.8 | 1.8 |
| | 6 | 3.0 | 0.1 | 0.2 | 0.2 |
| IL-12p70 | 3 | 2.1 | 2.9 | 0.9 | 0.9 |
| | 6 | 16.0 ♦ | 8.2 | 3.7 | 4.6 |
| TNFα | 3 | 7.9 | 0.8 | 0.6 | 0.6 |
| | 6 | 0.6 | 0.8 | 0.6 | 0.8 |
| IFNγ | 3 | 1.1 | 1.5 | 1.0 | 1.0 |
| | 6 | 1.2 | 1.8 | 1.0 | 1.0 |
| GM-CSF | 3 | 12.4 ♦ | 4.2 | 21.0 | 10.6 |
| | 6 | 32.0 ♦ | 21.0 | 18.3 | 26.9 |

Levels determined by multi-analyte bead array (see Methods). A value of 0.5 pg/ml, one half of the lower limit of detection, was assigned to assay values below detection in the assay. N=4 mice/value. * Day after TBI.

♦ indicates median fold value differs from that seen in control (0 Gy) mice ($p < .05$)

■ indicates median fold value differs from that seen in 7 Gy alone group ($p < .05$)

● indicates median fold-value differs from that seen in $rBPI_{21}$/ENR group ($p < .05$)