

associated with ischemic reperfusion injury, abdominal adhesion or infection. Immunomodulation via disruption of lymphocyte trafficking with FTY720 or depletion of lymphocytes is a viable therapeutic strategy for such treatment option.

DESCRIPTION OF THE FIGURES

[0021] FIG. 1. A) Schematic illustrating experimental design for control group. B) Schematic illustrating experimental design for PATG group.

[0022] FIG. 2. Hemodynamic profiles during hemorrhage period for experimental and control groups. A) Heart rate. B) Mean arterial pressure. C) Cardiac output.

[0023] FIG. 3. Kaplan-Meier survival curve for experimental groups versus control with log-rank test for statistical comparison. A) Overall survival. B) Reperfusion period survival.

[0024] FIG. 4. Peripheral lymphocyte counts during hemorrhage and reperfusion periods (using PATG). One-way ANOVA with repeated measures design was used for statistical comparison. Error bars represent \pm SEM.

[0025] FIG. 5. Representative FACS plots for CD3+CD4+ and CD3+CD8+ peripheral lymphocytes. A) Sample lymphocyte gating and IgG plots for control and PATG groups. B) CD3+CD4+ and CD3+CD8+ peripheral lymphocytes at time of liver injury (t=0). C) CD3+CD4+ and CD3+CD8+ peripheral lymphocytes at peak reperfusion period (t=24 hours). D) Quantification of CD3+CD4+ and E) CD3+CD8+ lymphocytes throughout the experiment. One-way ANOVA with repeated measures design was used for statistical comparison. Error bars represent \pm SEM.

[0026] FIG. 6. Central lymphocyte counts at time of necropsy. Quantification of CD3+ reactivity by ACIS. * indicates $p < 0.05$ compared to normal, unmanipulated tissue. Data is depicted as mean \pm SEM.

[0027] FIG. 7. Peripheral neutrophil counts during hemorrhage and reperfusion periods. One-way ANOVA with repeated measures design was used for statistical comparison. Error bars represent \pm SEM.

[0028] FIG. 8. Lung tissue neutrophil counts at time of necropsy. B) Quantification of MPO+ reactivity. * indicates $p < 0.05$ compared to normal, unmanipulated tissue. † indicates $p < 0.05$ compared to control group. Data is depicted as mean \pm SEM.

[0029] FIG. 9. Gene transcript expression in liver tissue of PATG relative to the control group. Median value of relative fold expression is depicted on a logarithmic scale. >2 fold difference from control was considered statistically significant and is indicated by *.

[0030] FIG. 10. Experimental design. Liver injury was initiated at t=0. Uncontrolled hemorrhage occurred until 1 hour, at which time the abdomen was packed and temporarily closed (pre-hospital phase). The animal was observed until 2 hours when hospital care was initiated. The liver was repaired and the abdomen definitively closed. The animal was then observed for a total of 72 hours. Blood transfusion was administered as indicated. Necropsy was performed when the animal expired or at 72 hours following euthanasia. The uncontrolled hemorrhage and pre-hospital phases were considered the hemorrhage period, while the hospital care phase was considered the reperfusion period. In the experimental group, FTY720 (0.3 mg/kg) was administered 15 minutes following liver injury.

[0031] FIG. 11. Hemodynamic profiles during hemorrhage period for experimental and control groups. a) Heart rate. b) Mean arterial pressure. c) Cardiac output.

[0032] FIG. 12. Kaplan-Meier survival curve for experimental groups versus control with log-rank test for statistical comparison. a) Overall survival. b) Reperfusion period survival. Central lymphocyte counts at time of necropsy. Dashed red line indicates end of hemorrhage and beginning of reperfusion period. C) Quantification of CD3+ reactivity by ALIS. * indicates $p < 0.05$ compared to normal, unmanipulated tissue; † indicates $p < 0.05$ compared to control. Data is depicted as mean \pm SEM.

[0033] FIG. 13. Peripheral neutrophil counts during hemorrhage and reperfusion periods. b) Quantification of MPO+ reactivity. * indicates $p < 0.05$ compared to normal, unmanipulated tissue. † indicates $p < 0.05$ compared to control group. Data is depicted as mean \pm SEM. c) Inflammatory gene transcript expression in liver tissue of PATG relative to the control group. Mean value of relative fold expression is depicted on a logarithmic scale.

[0034] FIG. 14. Dosing Schema for Thymoglobulin

DETAILED DESCRIPTION OF THE INVENTION

[0035] It is shown in this application, lymphocyte (especially T or B lymphocytes) sequestration or depletion significantly prevents or treats inflammation caused by an infection or injury, such as ischemic reperfusion injury caused by a trauma or abdominal adhesion after an surgery. Lymphocyte immunomodulation appears to attenuate innate cellular and molecular activation. Specifically, disruption of the innate lymphocyte response resulted in significantly decreased circulating and lung tissue infiltrating neutrophils and decreased expression of inflammatory genes.

[0036] To prevent a harmful inflammation, before the onset of an inflammation, the immune lymphocytes of a subject can be modulated (depleted or sequestered) by administering to the subject one or more doses of a lymphocyte depletion or a sequester agent or both. For example, one or more doses of a lymphocyte depleting or sequestering agent may be administered to a subject during or after an inflammation causing event, such as an injury or an infection.

[0037] The lymphocyte modulated may include B lymphocytes, T lymphocytes, NK cells, and platelets. An example of a lymphocyte sequestering agent is FTY720. The lymphocyte depletion agent may include PATG, Thymoglobulin (Genzyme, Cambridge, Mass.) or Alemtuzumab (Genzyme, Cambridge, Mass.). The lymphocyte depletion/sequestering agent may be administered within 7 days of an inflammation via a variety of routes, including oral, transdermal, transmucosal, intradermal, subcutaneous, intravenous and intramuscular routes. The agent may be administered with a pharmaceutical carrier. Alternatively, one or more doses of a lymphocyte depleting or sequestering agent may be administered to a subject during or after an inflammation causing event, such as an injury or an infection. In particular, administering one or more doses of a lymphocyte depletion or a sequestering agent before, during or after hemorrhagic shock can treat ischemic injuries associated with hemorrhagic shock and improves survival.

[0038] To treat a harmful inflammation, upon the onset of an inflammation, the immune lymphocytes of a subject is depleted or sequestered by administering to the subject one or more doses of a lymphocyte depletion or a sequester agent or both. An example of a lymphocyte sequestering agent is