

in about 45 minutes, but with 100% increase in resistance. With a 2-fold increase in resistance, PEG is one of the most potent barrier-enhancing agents tested among all the barrier-enhancing agents, such as S1P, FTY720, phospho-FTY720, and HGF. Immunofluorescence data revealed that PEG altered the EC actin cytoskeleton to form a defined cortical actin ring that may help strengthen cell-cell junctional adhesion. PEG rapidly induced dephosphorylation of ERK and MLC as early as 1 minute and completely inhibited thrombin-induced ERK and MLC phosphorylation. More importantly, pretreatment with PEG for 1 hour attenuated thrombin-induced endothelial barrier dysfunction. In summary, PEG activates a rapid, actin-associated, barrier-enhancing signal transduction pathway in EC, which may have therapeutic potential to prevent and reverse pulmonary edema.

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PARAMETERS OF CARDIOPULMONARY RESUSCITATION QUALITY ARE IMPROVED DURING IN-HOSPITAL CARDIAC ARREST USING A NOVEL ELECTRONIC FEEDBACK SYSTEM.

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EARLY EXPOSURE TO BUTYRATE INCREASES FETAL HEMOGLOBIN DURING ADULT ERYTHROID DEVELOPMENT IN VITRO.

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Introduction: Histone deacetylase inhibitors (HDIs) like butyrates increase fetal hemoglobin (Hb F) in β -thalassemia major and sickle cell disease patients through a mechanism that is not well understood. Since HDIs act globally and may activate silenced oncogenes, it is necessary to determine how these compounds increase Hb F in order to design targeted therapeutics to increase Hb F and at the same time minimize potentially harmful side effects. **Purpose:** To examine the developmental window during which sodium butyrate (NaBut) maximally increases Hb F in adult-derived hematopoietic progenitor cells (HPCs), and to determine the effect of NaBut on histone acetylation patterns across the β -like globin gene cluster. **Hypotheses:** There is a particular window of opportunity during which NaBut optimally up-regulates Hb F and increases γ -globin expression. In addition, the NaBut-mediated increase in Hb F involves a change in occupancy of acetylated histones (acH) at specific sites of the β -like globin cluster. **Methods:** HPCs isolated from adult peripheral blood are treated with 0.5 mM NaBut on day 1, 2, or 7 of in vitro culture and harvested for protein and total RNA on day 10. Control cells are cultured without NaBut. Cell morphology is determined by Giemsa staining, and ELISA and spectrophotometric measurements are performed to determine percent Hb F. Transcription of γ -globin is assessed by RT-PCR. Occupancy of acH across the β -like globin cluster is examined by chromatin immunoprecipitation (ChIP) with anti-acH4 antibody, followed by hybridization of ChIP products to custom-made arrays (chip) containing tiled PCR products spanning the 70 kb β -like globin gene cluster. **Results:** NaBut treatment of HPCs on day 1, 2, or 7 of culture resulted in Hb F levels of 14% (7-fold increase compared to control cells), 11% (5.5-fold), and 5% (2.5-fold), respectively. Results of γ -globin mRNA analyses showed a similar trend, with fold induction decreasing with later exposures to NaBut. Preliminary results of ChIP-chip in control cells showed areas of enrichment and depletion of acH4 across the β -like globin cluster during differentiation. **Conclusion:** The earlier stages of adult erythroid maturation are more amenable to NaBut-mediated increase in Hb F protein and γ -mRNA compared to later stages. Further studies will compare and contrast the histone acetylation pattern seen in adult-derived HPCs with that of NaBut-treated adult cells in order to determine and further examine candidate regions and signal pathways involved in drug-mediated increase in Hb F.

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BIOTERRORISM KNOWLEDGE AMONG HEALTH CARE PROFESSIONALS: A

COMPARISON STUDY ACROSS DISCIPLINES AND EDUCATION STATUS. **K.M. Boehm,**¹ R.B. McFee,¹ J.B. Leikin,² ¹Long Island Regional Poison Information Center, Mineola, NY; ²ENH Omega, Glenbrook, IL.

Background: National preparedness against emerging infections and biological weapons hinges upon clinician recognition of and knowledge about biothreats. **Objective:** We set out to assess the bioterrorism knowledge base of second-year medical students and compare it to dental students, pharmacy students, physician assistant students, family medicine residents, emergency medicine residents, attending physicians, and a control of elementary school teachers. **Methods:** A 20-question, 25–data point survey was ran-

domly distributed to the aforementioned cohorts. IRB approval and informed consent were obtained.

Results:

| | MZ | PA | DS | PS | PGY | DO | ER | CTRL | AVG |
|--------------|--------|---------|---------|---------|---------|--------|---------|---------|-----|
| Avg | 57% | 48% | 45% | 46% | 56% | 63% | 58% | 45% | 52% |
| SD | 0.2634 | 0.31946 | 0.27239 | 0.29125 | 0.36918 | 0.2794 | 0.30046 | 0.26662 | |
| ρ Value | 12% | 16% | 13% | 12% | 42% | 18% | 17% | 12% | 10% |
| Sample size | 20 | 16 | 18 | 22 | 3 | 9 | 12 | 17 | 117 |

Discussion: Practicing physicians scored higher than other cohorts; as expected those with prior WMD training outperformed those without. One notable exception was the question of whether it was safe to administer smallpox vaccine in the presence of sunburn; lay people correctly felt comfortable receiving a vaccine; physicians felt uncomfortable administering vaccine. The control group outperformed other cohorts on 16% of questions; of these most of the underlying topics had been in the media at the time of the survey, implying that those outside the health care arena gain their knowledge from the popular press, suggesting the importance of accurate reporting. **Conclusion:** The threat of bioterrorism and emerging infectious diseases persists; additional education needs to be made available to those in health professions. This education should be started not only as continuing medical education for current physicians but as dedicated curricula for those still in school. As education efforts rise, more research needs to be conducted to check the effectiveness of said education.

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NOVEL ANALOGS OF FTY720 PROMOTE PULMONARY VASCULAR BARRIER FUNCTION.

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Rationale: Modulation of pulmonary vascular barrier function is an important clinical goal given the devastating effects of vascular leak in ARDS. We and others have demonstrated that FTY720, an analog of the potent barrier-enhancing phospholipid sphingosine 1-phosphate (S1P), is also barrier protective through incompletely characterized mechanisms. We utilized various FTY analogs to better define FTY effects on endothelial cell (EC) barrier function. **Methods/Results:** FTY (1 μ M) significantly increased cultured human pulmonary artery EC barrier function in a sustained manner as measured by transendothelial electrical resistance (TER) but with a delayed onset and slower rate of TER rise relative to S1P (1 μ M). Previous siRNA experiments have suggested that FTY does not exert its barrier-enhancing effects through the same S1P₁R receptor required for S1P. We now report that FTY also increases TER in EC derived from embryonic S1P₁R^{-/-} mice, providing further support for a novel FTY barrier-enhancing pathway. In addition, S1P₁R is not the responsible receptor as S1P₁R siRNA did not alter FTY-induced TER increases. Increasing concentrations of phosphorylated FTY (0.1–50 μ M) produced a faster TER elevation rate of onset than FTY itself but never reached the rate of rise observed with S1P. (R)-phosphonate and enephosphonate analogs of FTY (1–50 μ M) produced rapid TER elevations similar to S1P, while the (S)-analogues were less potent or even barrier-disruptive. Both (R)- and (S)-regioisomers of FTY were barrier disruptive. **Conclusion:** These results support a novel mechanism of FTY action and provide further insights into the vascular barrier enhancing effects of FTY720. HL58064, HL70013–01, FTY720 supplied by Novartis.

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CORRECTION OF THE PHASE-OFFSET ERROR IN QP/QS MEASUREMENT.

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Background: MRI can noninvasively quantify blood flow by using phase-contrast imaging. Accurate flow measurements depend on placement of a "background" region of interest (ROI) on stationary tissue that is immediately adjacent to the flowing blood. This method does not work well in the heart and great vessels because there is little stationary tissue adjacent to the flowing blood. Therefore, flow measurements suffer from baseline offset errors due to artifacts from gradient eddy currents. The purpose of this study was to quantify the magnitude of the flow error and to propose a method to correct for this error. **Methods:** Blood flow in the ascending aorta and the main pulmonary artery was quantified in 10 healthy volunteers using MRI. Pulmonary blood flow (Qp) was measured in the main pulmonary artery just distal to the pulmonary valve. Aortic blood flow (Qs) was measured in the ascending aorta just distal to the coronary artery origins. (As such, aortic flow underestimates systemic blood flow by ~5% because coronary flow is excluded. Consequently, for this study normal Qp/Qs is assumed to be 1.05.) To correct for baseline flow errors, immediately following the human subject's MR flow measurements, an identical MRI scan with the same parameters was performed on a stationary bottle of water ("phantom"). An ROI was placed on the phantom in the same image location where blood flow had been measured. Since there is no flow in a stationary phantom, nonzero flow values obtained from the phantom were assumed to be due to a baseline offset error, and this amount was subtracted from the flow of the corresponding ROI in the aorta or main pulmonary artery to correct the baseline flow error. **Results:** Before baseline correction, the measured Qp/Qs was 1.3 ± 0.2 (mean \pm 1 SD, $p < .01$). After correction the measured Qp/Qs was 1.05 ± 0.07 ($p = .89$). Uncorrected difference between pulmonary and aortic flow was 26 ± 21 mL. After baseline correction with the phantom, the mean difference in flow was 7 ± 7 mL. Review of the measurements from all subjects showed a moderate correlation between the magnitude of error and the distance of the vessel from the center of the scanner ($r^2 = .55$ for the aorta and $r^2 = .61$ for the pulmonary artery for offsets in the anterior-posterior direction). **Conclusion:** Baseline offset errors significantly affect MRI flow measurements in the heart and great vessels. These errors are large and are especially problematic for larger patients whose aortas lie further away from the center of the scanner. The correction method we propose substantially reduces the baseline offset. It thereby enables more accurate detection and quantification of blood flow, shunts, and valvular disease.