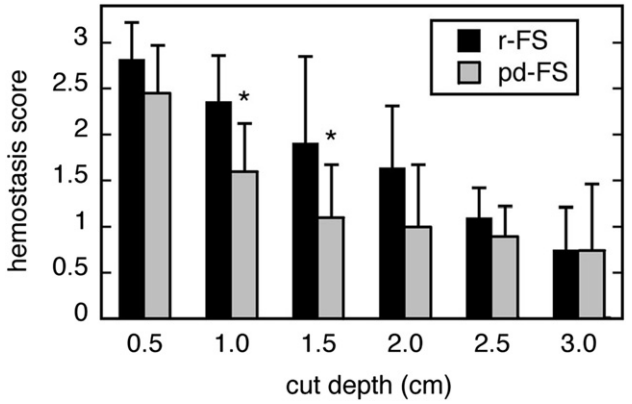
of the RBC-age groups in ADP induced aggregation. None of the TEG parameters of enzymatic clotting function (R, delta), fibrin cross-linking (angle), thrombin induced platelet aggregation (MA, G), or fibrinolysis (LY30) were significantly different between RBC-age groups. There were no significant differences in Hct and PLT counts between the different samples studied. **Conclusions:** Storage of RBCs ≥21 days may be responsible for decreased platelet function when transfused. An association has been noted between RBC age and the AA pathway during platelet aggregation. Further *in vivo* studies are needed to determine if platelet dysfunction related to transfusion of RBCs ≥21 days is contributory to poor clinical outcomes.

RBC age (days)	Enzymatic Activity (R)	Thrombin Generation (Delta)	Rate of Clot Formation (Angle)	Maximum Amplitude (MA)	Clot Strength (G)	Lysis at 30 min. (LY30)	ADP inhibition	AA inhibition
1	4.73±0.9	1.0±0.3	51.0±3.4	58.7±4.4	8.3±2.1	0.5±0.3	5.1±0.9	1.4±1.1
14	5.0±1.1	0.8±0.5	60.7±5.1	61.7±3.7	9.7±1.5	0.4±0.3	3.9±1.5	7.9±3.8
21	4.9±1.3	0.8±0.3	62.3±2.9	62.4±3.0	10.0±1.7	0.1±0.1	5.2±4.4	34.6±7.4*,**
42	5.5±1.1	0.6±0.2	59.8±3.9	61.6±4.0	9.6±2.2	0.1±0.1	4.4±2.7	43.6±18.0*,**

* $P<0.05$ vs. RBC-day 1, ** $P<0.05$ vs. RBC-day 14, .

44.4. A Totally Recombinant Factor XIII-Supplemented Fibrin Sealant. M. A. Carlson,[1] W. H. Velander,[2] I. I. Pipinos,[1] J. M. Johanning,[1] J. Calcaterra[2]; [1]University of Nebraska Medical Center, Omaha, NE; [2]University of Nebraska Lincoln, Lincoln, NE

Introduction: Plasma-derived (pd) fibrin sealants (FS) have had limited applications because of cost, supply, and utility issues. We now describe a totally recombinant Factor XIII-supplemented FS which may be able to address these issues. **Methods:** Human recombinant (r) fibrinogen (FI) and activated Factor XIII (FXIIIa) were generated in the milk of transgenic cows and in yeast, respectively; human r-thrombin (FIIa) was purchased (Recothrom®). r-FS made from these three factors was optimized with thromboelastography (TEG). pd-FS (Tisseel™) was used as directed. FS testing consisted of series of hepatic wedge excisions ("pie-slice") in domestic swine (male, 3 months, 30 kg; N = 6/group) with a constant base (1 cm) and step-wise increasing depth (0.5 to 3 cm, in 0.5 cm increments; 6 excisions/series, 2 series per swine) made on a lobar edge. Each excision was treated with up to 1 mL of FS without compression or other aid, and then hemostasis was scored: 0 = failure/minimal effect; 1 = steady bleeding; 2 = oozing; 3 = hemostatic. **Results:** Minimal factor concentrations in the r-FS which yielded optimal TEG performance (data not shown, DNS) were 9 mg/mL FI, 0.36 mg/mL FXIIIa, 106 U/mL FIIa, and 12 mM CaCl2. Removal of r-FXIIIa decreased r-FS clotting kinetics ("alpha angle") and ultimate clot strength ("maximal amplitude") by 60 and 70%, respectively (DNS). pd-FS (N = 3 lots) contained 34-53 mg/mL FI, 200-312 U/mL FIIa, and trace/undetectable FXIIIa. Ultimate clot strength at 20 min was not different between the r-FS and pd-FS (DNS), but the r-FS gained strength more quickly (time to half-maximal strength = 30 vs. 100 sec, respectively; derived value from TEG plots). Ultimate clot strength of both sealants was twice that of human whole blood (N = 22 normal donors), except that the latter had a 5-6 minute latency before detectable strength ("R value;" DNS). In the wedge resection model, the hemostatic scores of the r-FS were equivalent or better than those of the pd-FS (Figure; *$p<0.05$, Wilcoxon; each bar represents mean score±sd of 10-12 excisions). **Conclusions:** r-FS had equivalent or better hemostatic efficacy than pd-FS in this wedge resection model, despite the FI concentration in the r-FS being about one-fourth that in the pd-FS. TEG data indicated that this result was dependent on the r-FXIIIa in the r-FS. Given that r-FS production is scalable, and the fact that FXIIIa supplementation greatly reduced FI requirement without sacrificing efficacy, r-FS production cost potentially should be much less than that for pd-FS. An abundant, economic source of r-FS might lead to increased innovation in hemostasis, acute wound stabilization, and related fields.



44.5. Propranolol Attenuates The Burn Induced Endoplasmic Reticulum Stress Response. M. G. Jeschke,[1,2] D. Boehning,[2] R. Kraft,[2] C. C. Finnerty,[2] D. N. Herndon,[2] J. Song[2]; [1]Sunnybrook Health Science Centre and University of Toronto, Toronto, ON; [2]Shriners Hospital for Children and UTMB, Galveston, TX

Introduction: Severe burn is associated a wide array of stress, metabolic, and physiologic processes in an attempt to restore homeostasis. The catecholamine induced stress response following severe burns is particularly exaggerated and manifests detrimentally as inflammation, insulin resistance, hypermetabolism, and associated profound protein catabolism. Recently, endoplasmic reticulum (ER) stress and the unfolded protein response (UPR) were identified as central intracellular stress signaling pathways that modulate and enhance inflammatory responses and cell death. We hypothesize that catecholamine blockade using Propranolol, a non-selective β1/2 receptor antagonist, will attenuate ER stress and lead to restored IR signaling, and improved cell survival. **Methods:** Rats received a 60% total body surface area burn and were assigned to receive 5mg/kg/day of Propranolol p.o or saline (control). On post-burn day 3 liver was harvested before and 1 min after insulin injection (1 IU/kg) into the portal vein and expression patterns of various proteins known to be involved in insulin and ER-stress signaling cascades were determined by Western blotting. Apoptosis and caspase-3 by TUNEL assay and luminescent technique, IL-6 by ELISA. **Results:** Burn induced ER stress as shown by increased expression of phospho-PKR-like ER-Kinase (PERK) and phospho-inositol requiring enzyme (IRE)-1. Induction of ER stress was associated with a significant increase of p-Jun N-terminal Kinase (JNK) ($p<0.05$). Propranolol significantly decreased the ER stress markers phospho-PERK and phospho-IRE-1 when compared with burn which was associated with significantly decreased pJNK, attenuated cell apoptosis and decreased IL-6 levels, $p<0.05$. In terms of insulin signaling, we found that burn phosphorylated insulin receptor substrate (IRS)-1 at serine 307 and de-phosphorylated at tyrosine 612 which was associated with an impaired PI3K/Akt signaling, $p<0.05$, indicating the impairment of insulin sensitivity post-burn injury. Propranolol treatment partially restored the impaired insulin signal pathway by significantly increasing IRS-1 and pAkt, $p<0.05$. **Conclusions:** Propranolol significantly alleviated the burn induced ER stress response which was associated with alleviated inflammation, improved cell viability, and improved insulin signaling.

44.6. The Role Of The Vagus Nerve In Preventing Acute Lung Injury: Uncovering the Gut-Lung Axis. M. J. Krzyzaniak, G. Cheadle, L. Reys, Y. Ortiz-Pomales, N. Lopez, A. Hageny, J. Putnam, B. Eliceiri, A. Baird, V. Bansal, R. Coimbra; University of California San Diego, San Diego, CA

Introduction: We have previously shown that vagal nerve stimulation (VNS) has a protective effect against gut epithelial barrier