microspheres (μsph) of 10, 30 or 100 μm Ø into the LAD of anesthetized pigs. Fast-CT was used to estimate in vivo myocardial Blood Flow (F), intramyocardial Blood Volume (BV, as an index of microvascular endothelial surface area), and the capillary extraction factor (E) of contrast medium (Iopamidol 370, i.v. bolus of 0.33 mL/Kg). From these data we calculated the permeability-surface area product as PS = –F x ln(1–E). Values were obtained at baseline (BL1), 2-3 (ME) and 15 - 20 min after ME (BL2). Postmortem transmural biopsies from the EPT were micro-CT scanned (20μm voxel) to compute the volume and SA of individual EPTs. Micro-CT derived EPT volume and SA were 144, 238 and 290 mm^3/cm^3, 333, 283 and 279 $mm^2/cm^3$for the 10, 30 and 100 μm μsph, resp. ME increased PS/(1-EPT) by 88, 58 and 30 %, and at BL2 by 70, 60 and 24 %. ME increased MP, which was greatest during ME of small exchange vessels, inversely proportional to the size of the embolized microvessels and directly to the total SA of the EPT, but independent of the EPT volume.

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101.31

The Release of Reactive Oxidant Species (ROS) by FMLP-stimulated Leukocytes Increases Microvessel Permeability

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Our previous study demonstrated that systemic application of TNF-α induced a significant leukocyte adhesion without increasing microvessel permeability. Our present study is to investigate the effect of fMLP-stimulated leukocytes on microvessel permeability. The ROS production upon neutrophil activation was quantified by measuring the changes in chemiluminescence (CL) using a luminometer. The peak CL signal increased 3.1 fold after exposure of isolated rat neutrophils (2 x 10^6/ml) to fMLP (10 μM). Measurements of hydraulic conductivity (Lp) in single perfused rat mesenteric venular microvessels showed that perfusing the vessel with a fMLP-stimulated neutrophil suspension (2 x 10^7/ml) increased Lp to 3.7 ± 0.6 times the control (n=4). After adding fMLP (10 μM) to the perfusate (n=4) or superfusate (n=8) and perfusing the vessel under balance pressure for 5 min in the presence of TNF-α-induced adherent leukocytes (14 ± 1/100 μm), the mean peak Lp increased to 5.2 ± 0.9 and 4.6 ± 0.5 times control, respectively. The application of DFO, an iron chelator, attenuated the Lp increase to 1.5 ± 0.2 times control (n=4). In contrast, neither TNF-α-induced leukocyte adhesion nor perfusing fMLP alone changed basal Lp. These results suggest that the fMLP-stimulated leukocytes increase microvessel permeability by increased ROS production, which is independent of leukocyte adhesion and migration processes. Supported by NIH HL56237.

101.32

Microvascular permeability is modulated by normal tissue protease activity

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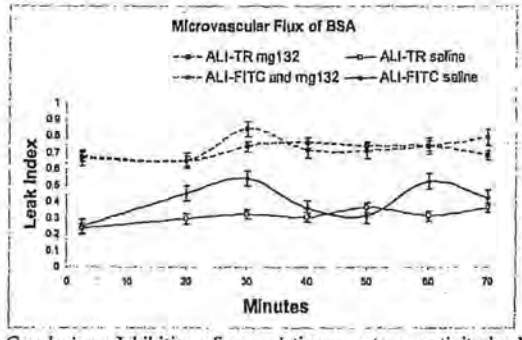
Introduction: Although numerous modulators of microvascular permeability have been described, the mechanisms responsible for this modulation are largely unknown. As tissue proteases are important in minute to minute protein metabolism within tissues, we hypothesized proteases may regulate effectors of microvascular permeability changes. We measured the effects of 26S proteasome inhibition on microvascular albumin flux.

Methods: Two groups of male Sprague-Dawley rats were anesthetized and small intestine was exteriorized and superfused with bicarbonate-buffered saline bubbled with CO_2 with or without the 26S proteasome inhibitor MG-132 (10μM), at 2ml/min. Each group received a combined dose of Texas Red-bovine serum albumin (BSA), (12.5 mg/kg), and FITC-BSA (25 mg/kg) in 1 ml saline intravenously. Mesenteric post-capillary venules were examined via intravital fluorescence microscopy.

Results:



Conclusions: Inhibition of normal tissue protease activity by MG-132 results in differential microvascular flux of fluorescent dye labeled-albumin. Microvascular permeability was higher in the groups treated with MG-132 versus control (Texas Red-BSA; 0.72 vs. 0.31, respectively: FITC-BSA; 0.73 vs. 0.40, respectively. $p < 0.0001$).

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101.33

Chronic exposure to hypertonic solutions alters the subperitoneal interstitial matrix and transperitoneal solute and water transport

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We hypothesized that chronic peritoneal exposure to hypertonic solutions alters underlying interstitial matrix and transperitoneal transport. We daily injected rats ip with 30-40 ml of (n=10 ea, in Krebs, 500 mosm/kg): 4% n-acetyl-glucosamine (NAG), 4% mannitol (M), 4% dextrose (D), and controls (C, isotonic Krebs, sham). After 2 mos, each animal underwent studies using plastic chambers affixed to the peritoneum to determine: hydrostatic pressure-driven convection(HPF); small solute mass transfer (SSMT), osmotic filtration (OsF) and albumin flux (AlbF). After euthanasia, tissue was analyzed for hyaluronan [HA], collagen [COL] or sulfated-glycosaminoglycan [GAG] content(μg/g dry tissue, mean±SE). [HA]: C, 962±42; NAG, 1428±69; M, 1029±69; D, 1169±69 ($p<.002$). [COL]: C, 57±12; NAG, 98±11; M, 44±11; D, 107±12 ($p<.02$). [GAG]: C, 79±8; NAG, 78±7; M, 103±7; D, 80±7 ($p=.02$). Transport studies demonstrated no sig changes in SSMT or HPF. AlbF decreased (μl/min/cm^2, mean±SE, $p<.05$) from controls C, 0.36±0.03; NAG, .25±.03; M, .26±.03; G, .29±.03. OsF decreased (μl/min/cm^2, mean±SE,$p<.06$) from C, 73±9; NAG, 52±7; M, 61±9; D, 39±17. We conclude that chronic glucose and NAG exposure increases COL and HA in the subperitoneum and decreases protein and osmotic water transport.

MICROVASCULAR PHARMACOLOGY/VASCULAR CONTROL (102.1-102.30)

102.1

Cholinergic responsiveness within the retinal microvasculature

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The retinal vascular network lacks autonomic innervation; signals communicating metabolic demands of neurons to the blood supply must originate from within the very tissue through which the microvessels pass. One candidate for neuron to vascular communication is the neurotransmitter acetylcholine, which is released during visual processing. We used patch-clamp recordings to monitor ionic currents in pericyte-containing microvessels freshly isolated from rat retinas. To assess electrotonic communication, dual patch-clamp recordings were obtained at sites hundreds of microns apart within a microvascular network. Oxotremorime-M, a muscarinic agonist, opened calcium-activated chloride channels, resulting in transient depolarizing currents. Time-lapse images showed that oxotremorime also induced pericytes to

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