RESULTS: Exposure of BAECs to CLF for 4 hours significantly decreased the levels of IkBα compared to static control (56.4% ± 24.7%; p<0.05) but caused no significant change in the level of p-IκBα (204.2% ± 83.1%; p=NS). Addition of MG132 significantly increased the level of p-IκBα (1758.0% ± 442.7%; p=0.02), but failed to inhibit the decrease in the level of IkBα caused by CLF (58.4% ± 29.0%; p=NS) (Fig).

CONCLUSIONS: Degradation of IkBα under CLF occurs via an alternative, UPS-independent pathway. Further studies are to be done to elucidate this novel mechanism of degradation.

Deletion of Newly Described Molecule, Pellino1, Aggravates Blood Perfusion and Neovascularization and Exerts Increased Tissue Fibrosis in a Murine Model of Hind-Limb Ischemia

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INTRODUCTION: Peripheral vascular disease (PVD) is a cause of significant morbidity and mortality, which continues to remain a challenging ailment for clinicians. We have recently shown Pellino1 (Peli1) to be a powerful pro-angiogenic molecule downstream of VEGF/Flk-1 signaling. This study attempts to evaluate the role of Peli1 in a murine model of hind limb ischemia (HLI).

METHODS: Adult 8-12 week old wild-type Peli1fl/fl (WT) and Peli1 knockout (Peli1-/-) mice underwent right femoral artery ligation followed by laser Doppler imaging (LDI), motor function assessment, and muscle immunohistochemistry 28 days after ligation. We further validated our results in a gene therapy model (gain of function) by injecting either Ad.LacZ (control) or Ad.Peli1 (1×109 PFU) in the hind limb after femoral artery ligation followed by LDI.

RESULTS: Peli1-/- mice showed reduced blood perfusion when compared with WT mice at postoperative day 28 (0.34 ± 0.03 vs 0.67 ± 0.06 [n=15-16]; p<0.05), decreased motor function score (2.0 ± 0.44 vs 3.98±0.02 [n=5]; p<0.05), increased fibrosis (13.17 ± 1.51 vs 2.15 ± 0.47 [n=4-7]; p<0.05), reduced capillary/vessel density (750.0 ± 69.96 vs 1,690 ± 126 counts/mm² [n=4-6]; p<0.05) and reduced capillary/myocyte ratio (1.44 ± 0.11 vs 2.093 ± 0.23 [n=4]; p<0.05). With Ad.Peli1 gene treatment, we observed a significant recovery of blood perfusion when compared to Ad.LacZ mice at postoperative day 28 (0.58 ± 0.04 vs 0.20 ± 0.02 [n=10-11]; p<0.05).

CONCLUSIONS: Our results show that Peli1 is a critical molecule in neovascularization in mice with hind limb ischemia. This could translate to a potent therapeutic agent assisting vascular surgeons in treating patients at risk for tissue and limb loss.

Effects of Pharmacotherapeutic Agents on Microembolization Rates During Carotid Revascularization

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INTRODUCTION: The management of carotid stenosis must balance the benefits of surgical and endovascular intervention against the risks of peri/postoperative cerebrovascular events. Higher rates of intraoperative microembolization during elective carotid revascularization are associated with increased risks of clinically detectable cerebrovascular accidents, and the identification of pharmacotherapeutic agents that prevent vulnerable plaque formation can be useful in decreasing embolic potential during revascularization.

METHODS: One hundred fifty patients (symptomatic, stenosis>50%; asymptomatic, stenosis>70%) undergoing either carotid artery stenting or carotid endarterectomy will be enrolled. A preoperative Mini-mental Status Exam (MMSE), carotid MRI, and cerebral diffusion-weighted MRI (DW-MRI) are obtained 1 week before intervention. Intraoperatively, transcranial Doppler is performed to monitor for microembolic signals (MES), detected as high-intensity unidirectional transient signals. A postoperative DW-MRI and MMSE are performed within 72 hours to examine for microinfarcts and changes in neurocognitive function. Analysis of pharmacotherapeutic use is performed retrospectively.

RESULTS: Preliminary analysis demonstrated an average of 44 MES generated during carotid revascularization in 22 patients on statins compared with 60 MES in patients not taking statins (p=0.59). A comparison of aspirin use in a carotid angioplasty/stenting cohort paradoxically demonstrated an average of 66 MES for patients on aspirin compared with 44.7 MES for patients not on aspirin (p=0.21). A carotid endarterectomy cohort demonstrated an average of 11 MES for patients on ACE inhibitors compared with 23.8 MES for patients not taking ACE inhibitors (p=0.22).