genes (Lcn2, lactoferrin, ferritin, SLC11A1, SLC4A1), downstream of heme metabolism were co-activated by UTI. The metabolism of heme contributed to the detachment and shedding of urothelial cells between 8-12hrs, since deletion of SLC4A1, the heme intake transporter (I.Hamza) and Hmox1, mitigated the denudation of bladder mucosa from 70% to 40% of surface area (Pad=0.02).

Conclusions: We have identified an endogenous heme metabolic pathway in urothelia that is superactivated by excess heme or UTI likely mitigating bacterial growth. However the capture of excess heme in the setting of hematuria or UTI likely contributes to urothelial death and shedding.

Funding: NIDDK Support, Other NIH Support - Columbia Obrien Center for Benign Urology.

SA-PO995
A New Role of Acute Phase Proteins: Local Production Is an Ancient, Universal Mechanism. Papers Presented: 10.3390/ijms23062972, 10.3390/ijms21155316, and electromagnetic heat). Thus, this local acute-phase response (APR) seems to be a universal mechanism. Papers presented: 10.3390/ijms23062972, 10.3390/ijms21155316, 10.3390/ijms21113825, 10.3390/ijms21012020

Funding: Government Support - Non-U.S.

SA-PO996
Impact of Uremia on Regulatory T Lymphocytes Proliferation and Phenotype
Nicolas Valenti,1,2 Maxime Raymond,1 Caroline Lamarche,1,3 Hospital Maisonneuve-Rosemont Centre de Recherche, Montreal, QC, Canada; 2Universite de Montreal Departement de Pharmacologie et Physiologie, Montreal, QC, Canada; 3Universite de Montreal Faculte de Medecine, Montreal, QC, Canada.

Background: Chronic kidney disease (CKD) patients have a dysfunctional immune system that is chronically and non-specifically activated, leading to low grade inflammation. Inflammation is now considered both a risk factor and a consequence of reduced kidney function and is highly associated with cardiovascular disease, which is the leading cause of mortality on dialysis. Regulatory T cells (Tregs) are important inhibitors of pro-inflammatory responses. While Treg numbers are decreased in patients with CKD, their state and effectiveness remain poorly understood. We aim to investigate the impact of uremia on those cells.

Methods: Treg and conventional CD4+ cells from hemodialysis (HD) patients and healthy controls were fluorescence-activated cell sorting (FACS) sorted and cultured. We examined the transcriptional profile of uremic serum after 7 days compared to healthy donors (fold expansion 11.35 vs 19.27; p<0.001) and no significant impact on conventional CD4+ T cells (fold expansion 17.88 vs 19.52; p=0.34). They were no significant differences in Treg expansion or function, as assessed by a suppression assay, after 12 days (p=0.99). Staining for apoptosis with Annexin V/PI indicated no difference in viability or apoptosis between serums after 7 and 12 days. Markers associated with Tregs functions and activation such as CTLA4, GARP, LAP, CD69 and CD71 were expressed similarly in HD and healthy donors’ serum after 7 days (p=0.82, 0.77, 0.73, 0.23 and 0.44 respectively).

Conclusions: Serum from HD patients selectively decreases Treg proliferation in vitro and not conventional CD4+ T cells, with no impact on cell death, activation and Tregs markers expression. HD patients also have different Treg cluster composition. Further studies are needed to identify the causes and impacts of those changes.

SA-PO997
Angiotensin II Type 1 Receptor-Associated Protein Interacts With Transferrin Receptor 1 and Promotes Its Internalization
Eriko Abe,1 Hiromichi Waku,1 Keigo Hirota,1 Yamanashi Takahiro,2 Shingo Urata,1 Tomohiro Shigaki,3 Shohel Tanaka,2 Shinya Taguchi,3 Tsukamoto,1 Kengo Azashima,1 Kouichi Tamura.1 Department of Medical Science and Cardiorenal Medicine 1Yokohama City University Graduate School of Medicine, Yokohama, Japan; 2Duke-NUS Medical School, Singapore, Singapore.

Background: Angiotensin II type 1 receptor (AT1R)-associated protein (ATRAP) was originally identified as a binding protein of AT1R. ATRAP promotes constitutive internalization of AT1R so as to inhibit the pathological activation of its downstream signaling. Also, we reported that genetic knockdown of ATRAP exacerbates kidney fibrosis in mice along with functional mitochondrial abnormalities and subsequent increases in ROS production. These effects of ATRAP were suggested to be AT1R-independent actions. Thus, this study aimed to explore a novel interacting protein involved in the mechanism that ATRAP protects against kidney fibrosis independent of its interaction with AT1R.

Methods: We established Human Embryonic Kidney 293 cells which were able to induce the expression of Flag-ATRAP. In this cell line, after immunoprecipitation with anti-Flag antibodies, the Flag-ATRAP complex was analyzed with a mass spectrometer. Among identified proteins, we focused on transferrin receptor(TFR1). To confirm the molecular interaction, co-immunoprecipitation was performed. Additionally, to validate functional interactions, we analyzed intracellular iron concentrations using fluorescent probe of iron. Further more, to verify TIRI expression and localization, immunofluorescence staining of TIR1 in the whole cell or on the cell surface only.

Results: Mass spectrometry analysis revealed various proteins associated with vesicular trafficking including TIR1. We confirmed the molecular interaction between ATRAP and TIR1 by co-immunoprecipitation. Enhanced ATRAP expression decreased the intracellular iron levels and downregulated TIR1 expression on the cell surface despite no significant difference in whole cell.

Conclusions: We propose a molecular and functional link between ATRAP and TIR1. ATRAP would regulate TIR1 availability via downregulation of cell surface TIR1 via promotion of its internalization. TIR1 promotes intracellular localization of the iron-bound transferrin. Iron is a key factor in the process of kidney fibrosis via production of ROS in relation to deterioration of mitochondrial function. Taken together, this novel ATRAP-TIR1 axis might be the mechanism relevant to the ROS/mitochondrial dysfunction-mediated process of kidney fibrosis.

SA-PO998
Deficiency of Angiotensin II Type 1 Receptor Prevents Muscle Atrophy due to Denervation
Sakuragi Takayama,1 Takeshi Sugaya,1 Yugo Shibagaki,1 Atsuko Ikemori.1,2 Division of Nephrology and Hypertension, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan; 1Department of Anatomy, St. Marianna University School of Medicine, Kawasaki, Japan.

Background: Because chronic kidney disease (CKD) is a high risk of muscle wasting, managing CKD is clinically important for promoting the health and well-being of patients with CKD in aging society. Although angiotensin II (Ang II) type 1 receptor blocker was reported to attenuate muscle atrophy after muscle injury model, its model does not mimic the human pathophysiological conditions. The aim of this study is to reveal whether suppressed activation of angiotensin II type 1 receptor (AT1) prevents severe muscle atrophy after denervation which mimics disuse atrophy.

Key: TH - Thursday; FR - Friday; SA - Saturday; OR - Oral; PO - Poster; PUB - Publication Only