

PREDICTING RESPONSE TO ANGIOTENSIN RECEPTOR (ARB) AND MINERALOCORTICOID RECEPTOR (MRA) BLOCKADE ADD-ON THERAPY IN ANGIOTENSIN CONVERTING ENZYME INHIBITOR (ACEI) TREATED PATIENTS WITH DIABETIC NEPHROPATHY (DN).

Uzma Mehdi; Kevin Rosenblatt*; Harold Garner, Guanghua Xiao, Jessica Lucas, Wayne Fisher and Robert Toto. The Univ of Texas Southwestern Medical Center, Dallas and Medical Branch at Galveston*. Clinical trials demonstrate that addition of either an ARB or a MRA to an ACEi-based regimen lowers blood pressure and proteinuria in DN. However, there are no reliable markers that predict the antiproteinuric effect of these drugs. We hypothesize that a unique set of urine proteins can predict response to long-term treatment with either a MRA or an ARB. To test this we are utilizing banked urine samples obtained from patients with DN who participated in a randomized, double-blind, placebo-controlled trial in which either placebo, or losartan 100 mg or spironolactone 25 mg once daily was added-on to lisinopril 80 mg daily for 48 weeks. We are identifying urine proteome biomarkers that 1) predict response to treatment with an MRA or an ARB, and 2) reveal drug specific alterations in the urine. Shown below is a density array of the change in UACR from baseline to 24 and 48 weeks of treatment by study group. Each vertical bar represents an individual patient. An increase in UACR from baseline is shown by a lighter shade of gray, no change by shade identical to and a decrease in UACR by a darker shade of gray. Twenty-four urine samples from responders ($\geq 30\%$ decrease in UACR) and non-responders respectively will be pooled in each study group to identify bio markers using a novel two-dimensional chromatography separation method coupled with high-resolution, matrix-assisted laser desorption/ionization-time of flight mass spectro metry (MALDI-TOF).



