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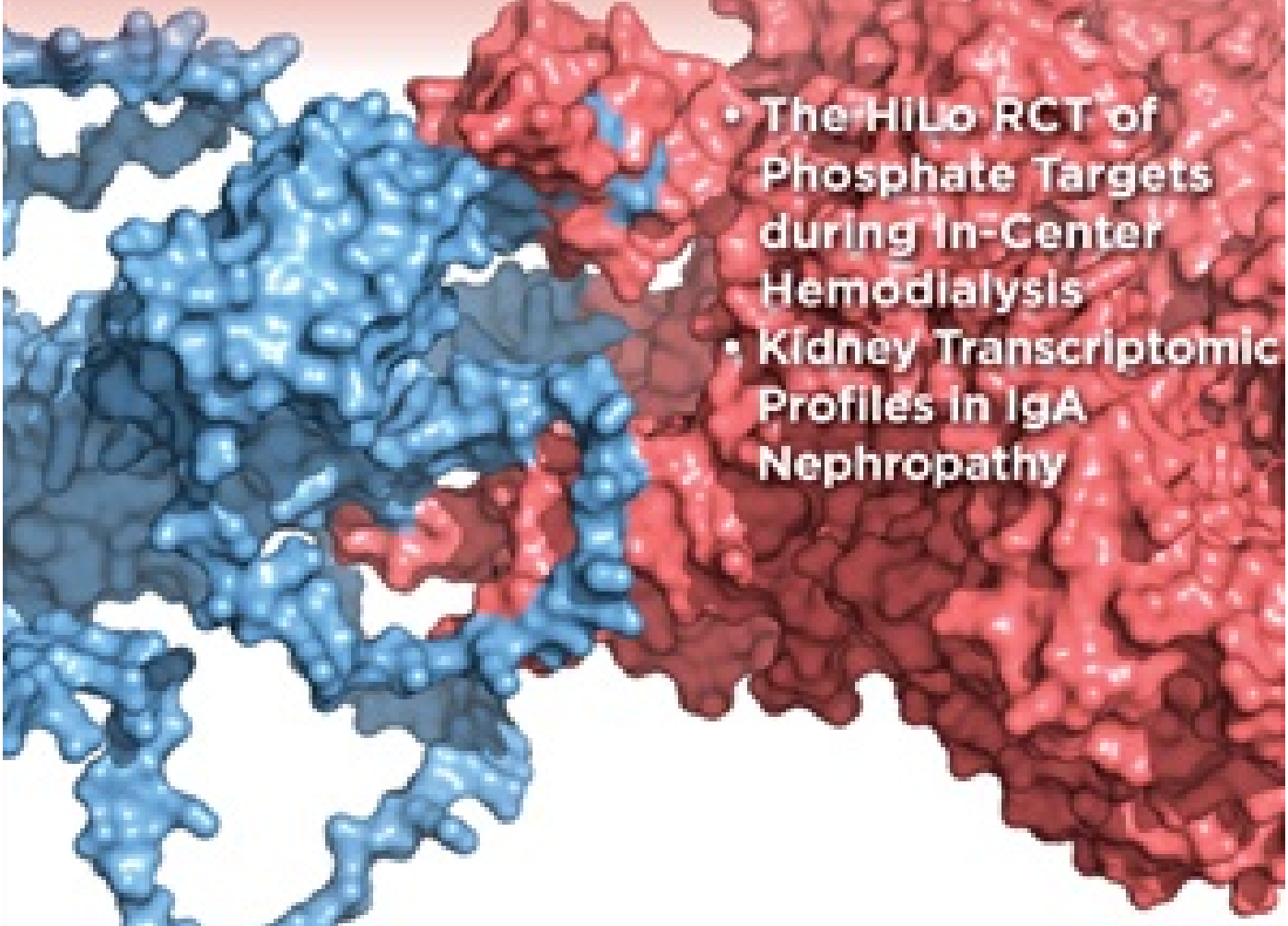

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# Subcutaneous Administration of the Anti-Tumor Necrosis Factor α, Etanercept, Immediately After Brain Death Significantly Attenuates Kidney Injury in Rats: TH-PO0892

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**Background:**

Brain death (BD) induces a systemic “cytokine storm”. Tumor necrosis factor-alpha (TNFα) has been associated with BD-induced kidney injury. The present study aims at testing whether immediate post-BD administration of the anti-TNFα agent, Etanercept, attenuates the renal damage in rats.

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**Methods:**

BD was induced under general anesthesia in 9 male 10-week-old Lewis rats by slow inflation of a 3Fr Fogarty balloon catheter in the extradural space. After confirmation of BD, animals were randomly assigned to receive either a subcutaneous injection of Etanercept (ETNCP group; 2.4 mg/kg, n = 6) or 0.9% NaCl (CTL group, n = 3). Six hours after treatment, circulating TNFα levels were quantified using ELISA. Kidneys

were harvested for histological evaluation of acute tubular necrosis (ATN). Immunohistochemistry was performed to assess kidney injury: KIM-1 for proximal tubular injury; CD11b for myeloid cell infiltration; Caspase 3 for apoptosis; and Ki67 for cellular proliferation. IHC quantification was automated using macros in ImageJ.

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**Results:**

Circulating TNFα levels were significantly lower in ETNCPT (14.3 [8.4; 18.5] pg/mL) compared to CTL (32.6 [19.0; 38.3] pg/mL, p=0.03). The extent of ATN was reduced in the ETNCP group compared to controls (ETNCPT 30 [18; 30] vs CTL 40 [40; 50] % of surface, p = 0.01). ETNCPT *versus* CTL expressions of KIM1 (0.010 [0.006; 0.013] vs 0.141 [0.094; 0.173] % of surface, p = 0.02), CD11b (0.11 [0.10; 0.16] vs 0.21 [0.19; 0.28] % of surface, p = 0.04), and Caspase 3 (0.78 [0.32; 1.15] vs 2.52 [2.45; 2.68] of positive tubules/glomeruli, p = 0.04) were significantly different. No difference was observed in Ki67 expression between ETNCPT (1.12 [0.87; 1.51] % of positive cells) and CTL (1.32 [1.13; 1.52] % of positive cells) groups (p = 0.54).

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**Conclusion:**

Etanercept administration immediately after BD significantly attenuates kidney injury in rats, thereby suggesting that targeted anti-TNFα therapy during donor management may improve kidney transplant health.

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