Weill Cornell Medicine

Noninvasive Biomarker for Distinguishing BK Polyomavirus-Associated Nephropathy in Kidney Transplant Patients

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Background & Unmet Need

- Despite advances in immunosuppression and transplant management, kidney graft failure remains a major clinical challenge, with approximately 30% of kidney allografts failing within 5 years
- BK polyomavirus is a nearly ubiquitous dsDNA virus which establishes lifelong, quiescent persistence in the genitourinary tract
- In kidney allograft recipients, immunosuppressive therapy can precipitate viral reactivation, leading to BK polyomavirus-associated nephropathy (BKVN)
- BKVN often mimics T-cell mediated rejection (TCMR), impeding proper diagnosis of kidney rejection diagnosis and clinical management
- Current diagnostic methods rely on invasive kidney biopsy or assess viral load, which does not provide sufficient mechanistic insights to guide therapy
- **Unmet Need:** Methods for diagnosing BKVN and differentiating it from other kidney graft failure modes, such as TCMR

Technology Overview

- **The Technology:** A ratiometric biomarker measuring CXCL10 mRNA/CD3E mRNA ratio in urinary cells to differentiate BKVN from acute TCMR in human kidney allografts
- **The Discovery:** Unbiased RNAseq of urinary cells matched to biopsies classified as BKVN with intragraft inflammation (BKVN-P), BKVN without inflammation (BKVN-N), or TCMR revealed profound reprogramming of host and immune pathways in BKVN patients, including disproportionate amplification of chemokine CXCL10
- **PoC Data:** In an external validation cohort (n=230), CXCL10 mRNA to CD3E mRNA ratio was significantly higher in BKVN-N urine (3.49) and BKVN-P urine (1.79) vs. TCMR urine (0.23) ($p<.0001$)
- In the external validation cohort, AUROC values were 0.92 for BKVN-N vs. TCMR, 0.82 for BKVN-P vs. TCMR, and 0.84 for all BKVN cases vs. TCMR

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Patents:
Provisional Filed

Publications:
Mueller et al. *JCI Insight.* 2026.

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Technology Applications

- Diagnostic biomarker for differentiating BKVN from acute TCMR during kidney transplant dysfunction
- Diagnostic biomarker for identifying BKVN in other organ transplant procedures
- Biomarker for identifying efficacy of novel antiviral therapeutics for BK polyomavirus infection

Technology Advantages

- Non-invasive collection method via urine sample
- Can be measured using RT-qPCR, a readily available diagnostic modality
- Analysis of both chemokine and T-cell lineage signal mitigates confounding from global inflammation and inter-sample variability
- Reads on BKVN etiology rather than histologic gradation, an attribute desirable for guiding therapy

Supporting Data / Figures

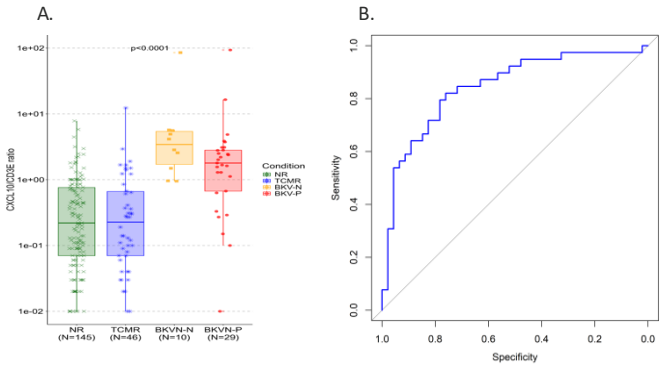

Figure 1A: Box-and-whisker plot of CXCL10 mRNA to CD3E mRNA ratios in 230 urines matched to 230 biopsies (External validation cohort). The ratios were significantly higher in BKVN samples compared to NR and TCMR samples.
Figure 1B: ROC AUC for distinguishing BKVN from TCMR. Urinary cell ratios of CXCL10 mRNA to CD3E mRNA accurately discriminated kidney allograft recipients with BKVN biopsies from those with TCMR biopsies, ROC AUC: 0.85 (95% CI, 0.78-0.92, P=1.52E -10).

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