**Supplemental Methods**:

Serum creatinine was measured using an enzymatic colorimetric method traceable to an isotope dilution mass spectrometry (IDMS) reference standard at St. Louis Children's Hospital Clinical Laboratory. Serial serum creatinine values and height measurements at the time of the blood draw were extracted from the medical records.

The measured iothalamate GFR was calculated from the time activity decay curve at multiple points over four hours after a single intravenous bolus of I-125 Iothalamate and reported both in ml/min, or ml/min/1.73m$^2$. Percent interstitial fibrosis at the 12 month surveillance biopsy was determined by the clinical pathologist by visual estimation of the percent of allograft tissue showing fibrotic changes on routine and special stains.

Biobank: Procurement and storage:

Whole blood was collected from patients in appropriate collecting tubes with the help of vacutainer collection system, by a phlebotomist to avoid compromising the quality of the sample. We used Lithium Heparin tubes for collecting plasma and Silica Clot Activator tubes for serum. All samples are processed immediately after the collection.

We centrifuged the samples at 2500 g for 10 minutes and using disposable pipettes, transferred aliquots of plasma into labeled cryovials. We stored around 1-1.5ml per patient in the biobank. Cryovials, organized in specimen racks, are stored in a freezer (−80 °C) with monitoring system. All samples were properly labeled, and their location recorded in a database.

At the time of analysis samples were sent to CareDx Clinical Laboratory Improvement Amendments (CLIA) certified laboratory for analyzing donor derived cfDNA. cfDNA was extracted from thawed plasma using the Circulating Nucleic Acid kit (Qiagen) and concentrated by centrifugal vacuum concentration at

CareDx facility. Even though freeze/thaw may affect the yield it's neglectable compared to what we need to determine donor derived cfDNA. Because the threshold is pretty low, the slightly lower yield has little if no impact on the diagnostic performance of the test.Immunosupression Protocol: As a part of induction therapy all subjects received 4.5 mg/kg of Thymoglobulin®(anti-thymocyte globulin) and rapidly weaned (within 7 days) steroid minimization protocol. All subjects included in the study received tacrolimus and mycophenolate mofetil (MMF) or enteric-coated mycophenolate sodium as a part of maintainance immunosuppression.

**Statistical analyses:**

Continuous data are presented as median and $25^{th}$-$75^{th}$ interquartile range (IQR) or mean and standard deviation, with 95% confidence intervals (CI) where feasible, whereas frequencies are reported as proportions. Body surface area (BSA) was validated as a proxy for nephron mass [33]. The BSA was calculated using the Mostellar formula: BSA (m2) =√ [weight (kg) × height (cm)/3600]. BSA ratios were calculated by dividing the donor's BSA by the recipient's BSA.

We used the non-parametric Mann-Whitney U test of proportions, Area under the Receiver Operating Curve , sensitivity, and specificity to evaluate the performance of donor derived cfDNA in discriminating biopsy proven acute rejection from no rejection. We quantified the accuracy of donor derived cfDNA by using area under the receiver-operating characteristic curve curve by plotting of the true positive fraction (sensitivity) versus the false positive fraction (1 – specificity). We utilized traditional pooled ROC curve combining biopsy positive samples and all biopsy negative samples together without adjusting for any covariants. We included all donor derived cfDNA results that were collected at the same time that a clinically indicated biopsy or surveillance biopsy was performed. The donor derived cfDNA level was categorized as high versus low at 2 different cutoff points, 1% and 0.5%, based on results of prior studies [13]. Biopsies were graded clinically by our local pathologists according to the Banff 2017 classification

scheme[34]. For this study, any grade of T cell or antibody-mediated rejection (T cell mediated rejection or antibody-mediated rejection), including subclinical rejection, was classified as biopsy proven acute rejection. For comparison, we performed similar analyses to assess the performance of serum creatinine in discriminating biopsy proven acute rejection.

For associations to BK virus, we compared donor derived cfDNA median (IQR) and correlation coefficients between urine or plasma samples taken when BK viral load was negative, versus when positive. Each urine or plasma sample was treated for most analyses as an independent sample, consistent with prior transplant biomarker studies[13,22,23,24]. However, given our prior work with longitudinal transplant biomarker studies that accounted for within-patient variability[35], we also performed additional such analyses in this study. Linear mixed models were performed to assess the difference of % donor derived cfDNA between BK viremia/viruria positive samples and negative samples, accounting for within-subject correlation. Spearman's correlation analysis was performed to assess the correlation between % donor derived cfDNA and BK viral load in plasma or urine (copies/mL).

For estimated glomerular filtration rate changes, we extracted from the medical records the standard of care serum creatinine values, measured at the time of the donor derived cfDNA test and again 30 days later. Comparisons between the groups were evaluated by non-parametric Kolmogorov-Smirnov two sample tests. The prognostic relationship between donor derived cfDNA and estimated GFR or serum creatinine was calculated at both the 0.5% and 1% cutoff for donor derived cfDNA.

Data were analyzed by SAS® 9.4 (SAS Institute Inc., Cary, NC, USA) and GraphPad Prism 7 (GraphPad Software, La Jolla, CA) . A P-value $< 0.05$ was considered to be statistically significant.