



## Editorial

## Open the black box; is urine valuable for screening BK virus-associated nephropathy?



BK virus-associated nephropathy (BKVAN) is one of the main causes of graft failure after kidney transplantation [1] and is implicated in more than 20% of graft failure. Intra-graft inflammation and insufficient immune response are regarded as the main factors of BKVAN. Although the BK polyoma virus infection is highly prevalent in general population, BKVAN does not develop in healthy individuals [2]. Primary infection occurs during childhood and is usually asymptomatic. Then, BK virus persists in the urinary tract in a latent form. Immunosuppressed status makes the latent infection to be an active illness. In fact, the immunosuppression results in viruria in 30–50% and viremia in 13–22% of kidney transplant recipients [3]. The advanced stages of BKVAN, decreased renal function, and accompanying acute rejection are the risk factors for the progression of BKVAN [4]. Therefore, early detection and balancing the adequate level of immunosuppression are key for the prevention of BKVAN, which leads to the prolongation of graft survival. The current screening guidelines are not validated in prospective studies, but Kidney Disease: Improving Global Outcomes clinical practice guidelines include screening all kidney transplant recipients for BK virus at the following time points: monthly for the first 3–6 months and then every 3 months until the end of the first posttransplantation year. Patients should undergo polymerase chain reaction-based screening for BK virus every time an unexplained rise in serum creatinine occurs and after treatment for acute rejection [5]. But the appropriate time point, frequency, and sample type (blood or urine) remain various according to centers.

In this issue of *Kidney Research and Clinical Practice*, Chon et al [6] contributed a manuscript regarding a screening tool for BKVAN in kidney transplant recipients. They retrospectively reviewed medical records of 368 recipients and analyzed the significance of BK viruria for predicting BK viremia and nephropathy. They claimed that the high-grade BK viruria was present in one-third of recipients, and the high-grade viruria imposed the development of viremia and nephropathy with a 50 times likelihood. The sensitivity and specificity of high-level viruria (> 25 million copies/mL) for diagnosing BK viremia/nephropathy were 88.6% and 88.0%, respectively. In addition, they showed that viruria preceded viremia by 7 weeks.

Although kidney transplantation represents the optimal treatment for patients with end-stage renal disease, the acute and chronic injuries may induce the eventual decrease of graft dysfunction. Acute kidney injury, acute rejection, and calcineurin

inhibitor toxicity are the main differential diagnoses during the early period after operation. Soon after the period, BKVAN, antibody-mediated rejection, and chronic allograft nephropathy should be listed for differential diagnosis of later allograft dysfunction. Unfortunately, invasive procedures are necessary because allograft biopsy is the golden criterion for definite confirmation. Therefore, unlocking the code using a noninvasive approach may be the way where every clinician wants to stand on. Among the various human biospecimens, urine is the easiest and oldest noninvasively accessed source of human biomarkers. Despite the ambiguity of the original abnormality, renal specificity of urine may be potentiated by adopting other markers such as proteinuria and glomerular filtration rate [7]. Unlocking the code using urine may broaden the concept and the way of approach for kidney disease. Considering the development of valuable techniques and understandings, the contribution by Chon et al [6] is very informative and timely. But there are several limitations to be resolved. As they stated, a large percentage of patients with viruria may not develop viremia or nephropathy, and the lag in viral load reduction on lowering immunosuppression is not established yet. Furthermore, the cutoff criteria for BK viruria are still arbitrary depending on centers. However, early diagnosis using urine polymerase chain reaction may become more useful when an effective antiviral therapy becomes available and an adequate measurement may preclude the viremia before irreversible tissue damage is established.

Finding a needle in a haystack used to be the traditional process that clinicians rely on, but understanding the value of biospecimens such as urine may expand clinicians' scope. It will bring us the way of assessing the whole haystack instead of searching through it.

### Conflicts of interest

The author has no conflicts of interest to declare.

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