

## FISH for BK Viral Nephropathy

### Background Information

BK viral nephropathy is a not infrequent complication of the immunosuppression required for successful renal transplantation. Graft loss will occur if the process is not managed appropriately. Recognition of BK viral nephropathy is essential to the successful management of immunosuppression in patients undergoing renal transplantation, since the appropriate treatment for BK viral nephropathy is usually a reduction in immunosuppression. Conversely, if the underlying cause of increasing renal insufficiency is acute allograft rejection, the appropriate response is usually increased immunosuppression. While viral inclusions can be recognized in many, if not most, cases by conventional histopathologic examination, *in situ* hybridization is a valuable ancillary tool to confirm the presence or absence of BK viral nephropathy in a renal transplant biopsy.

The BK virus is one of three polyoma viruses (BK, JC and Merkel) in the family Polyomaviridae. The human BK virus is a relatively small, common, non-enveloped, double-stranded DNA virus. The lytic destruction of infected tubular renal epithelium induces an influx of activated T lymphocytes not dissimilar to the interstitial infiltrate of T cells associated with acute allograft rejection.

The Cleveland Clinic Department of Molecular Pathology has developed a fluorescence *in situ* hybridization (FISH) assay for detection of BK viral DNA sequences in infected tissue.

### Clinical Indications

The assay is performed using tissue biopsy specimens with suspected BK virus infection. Although the assay is most commonly utilized for the diagnosis of BK viral nephropathy in renal allograft biopsies, other tissue specimens such as urinary bladder biopsies may also be evaluated.

### Interpretation

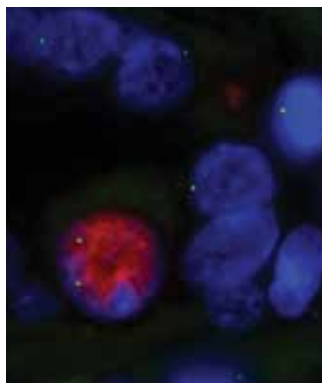
Results are reported qualitatively as positive or negative for the BK virus by FISH.

### Limitations of the Assay

The tissue submitted for analysis must not be necrotic. An on-slide internal positive hybridization control for chromosome 8 centromeric sequences must be positive.

### Methodology

The assay format utilizes an external positive control (renal allograft tissue with previously established BK viral nephropathy) that is probed 1) using BK-specific sequences, and 2) using the pBR322 negative control probe (plasmid DNA without the specific BK complementary DNA sequences). The tissue biopsy specimen is probed with BK-specific DNA that has been labeled with SpectrumRed and also contains a SpectrumGreen-labeled CEP8 centromeric probe as an internal control for successful hybridization. A separate negative control slide is probed with the pBR322 plasmid control that does not have BK complementary sequences; this negative control probe has been labeled with SpectrumRed and also contains CEP8-SpectrumGreen as a control for successful hybridization.



**Figure 1:** Renal allograft biopsy specimen positive for BK virus in tubular epithelial cell nuclei (red). Note the presence of CEP8 green signals in both BK-positive and BK-negative nuclei, confirming successful probe hybridization.

**References**

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3. Hirsch, H.H. *et al.* Polyomavirus-associated nephropathy in renal transplantation: interdisciplinary analyses and recommendations. *Transplantation.* 2005;79(10):1277-86.
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6. Wadei, H.M. *et al.* Kidney transplant function and histological clearance of virus following diagnosis of polyomavirus-associated nephropathy (PVAN). *Am J Transplant.* 2006;6(5 Pt 1):1025-322.

**Test Overview**

<b>Test Name</b>	FISH for BK Virus
<b>Reference Range</b>	FISH Negative for BK Virus
<b>Specimen Requirements</b>	Unstained paraffin sections (4) of formalin-fixed tissue
<b>Ordering Mnemonic</b>	BKVFSH
<b>Billing Code</b>	87808
<b>CPT Code</b>	88368 (x2)

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