

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Transplantation

**Manuscript NO:** 32642

**Title:** Polyoma virus nephropathy in kidney transplantation

**Reviewer's code:** 00503339

**Reviewer's country:** United States

**Science editor:** Xiu-Xia Song

**Date sent for review:** 2017-01-19

**Date reviewed:** 2017-01-20

**Review time:** 1 Day

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

## COMMENTS TO AUTHORS

A much needed Review that has the potential to stimulate derivative studies of a widespread challenge to kidney transplant stability. It would have been helpful to have included advice as to when and how frequently to test kidney transplant recipients for BKV infection (if found to be negative) along with a step by step regimen for therapy.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Transplantation

**Manuscript NO:** 32642

**Title:** Polyoma virus nephropathy in kidney transplantation

**Reviewer's code:** 00227610

**Reviewer's country:** Norway

**Science editor:** Xiu-Xia Song

**Date sent for review:** 2017-01-19

**Date reviewed:** 2017-01-23

**Review time:** 3 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

ESPS Manuscript NO: 32642 The review by Scadden et al. provides a nice and comprehensive overview on the mechanism that affect the pathogenesis of BKVAN. However, there are a few aspects the authors should elaborate. In Figure 1, the authors summarise the mechanisms that may be involved in the pathogenesis. However, in the text the mechanism virulence of BKPyV and renal tubular cells and ischemic injury are not discussed. The authors should review the role of these mechanism in BKVAN in their main text. The use of everolimus in BKVAN is not mentioned in this review. Minor comments The authors are advised to use the abbreviation BKPyV as suggested by the ICTV (Calvignac-Spencer et al., 2016) BKVAN (BK virus-associated nephritis) or PVAN (polyomavirus-associated nephritis) is a more appropriate abbreviation than BKNV. Section Background: -line 2: BKNV is part of should be replaced by BKPyV is a member of -line 3: Polyomavirus subcategory should be replaced by genus



**Baishideng  
Publishing  
Group**

7901 Stoneridge Drive, Suite 501,  
Pleasanton, CA 94588, USA  
**Telephone:** +1-925-223-8242  
**Fax:** +1-925-223-8243  
**E-mail:** bpgoffice@wjgnet.com  
**https://** www.wjgnet.com

Betapolyomavirus Section Virology of BKV: -First line: BKV is a member of the Polyomaviridae family -The genome of Dunlop is 5,153 while the archetypal strain (WW) is 5,141 bp. -The early stage encodes.... As well as late structural capsid proteins. This is wrong. Expression of the late genes occurs after the onset of DNA replication and not in the early stage of infection. -The NCCR encodes transcriptional control elements. The word encodes is wrong because the NCCR is a non-coding region. Encodes should be replaced by e.g. "encompasses". Section Pathogenesis of BKV. -This title should be replaced by Pathogenesis of BKVAN. -3rd last line: and means that cases of BKPyV Section Effect of HLA Matching -a reference should be included after ....do not develop. Section Donor and Recipient Blood group: -A reference should be included in the very beginning of this section Section Screening for BKV Infection -paragraph 2: BKV nephropathy should be replaced by its abbreviation. Figures: -Figure 2C and Figure 3: SV40 staining. Is this with anti-large tumour antigen antibodies? -Size bars are lacking in all figures.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Transplantation  
**Manuscript NO:** 32642  
**Title:** Polyoma virus nephropathy in kidney transplantation  
**Reviewer's code:** 01200577  
**Reviewer's country:** Italy  
**Science editor:** Xiu-Xia Song  
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**Review time:** 15 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
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<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

## COMMENTS TO AUTHORS

The topic and the paper are interesting and generally well-written, considering that Scannen et al apparently wants to propose a greater focus on virology and pathogenesis of BK nephropathy, compared to what was done in the past. However, in-depth analysis on the paper highlights, in my opinion, the following weaknesses: -the relationship between virology and clinical use of SV40 should be better elucidated (considering that the 70% percent homology between the BK and SV40 explains the use of SV40 as a marker for immunohistochemistry, essential for the diagnosis of BK nephropathy on the biopsy sample) -I suggest using more recent epidemiological data than those cited in the paper (for example, Stolt A, Sasnauskas K, P Koskela et al. Seroepidemiology of the human polyomaviruses. January J Virol 2003; 84: 1499-1504; -Unlike the recent review of Kuppachi et al (Clinical Kidney Journal, 2016) there is no mention of the discovery of two other genotypes (V and VI) Focusing on the



**Baishideng  
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Group**

7901 Stoneridge Drive, Suite 501,  
Pleasanton, CA 94588, USA  
**Telephone:** +1-925-223-8242  
**Fax:** +1-925-223-8243  
**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
**https://** [www.wjgnet.com](http://www.wjgnet.com)

pathogenesis: -I think that the authors should further underline the role of immunosuppressive therapy (MMF, CNI, thymoglobuline) as a risk factor, definitely proven, in the onset of BK nephropathy; moreover, the possible protective effect of mTOR inhibitors has not been reported; -Scannen et al allude to the possible risk of BK nephropathy with the use of alemtuzumab in induction therapy: actually, there are also studies with large cohort of patients, such as Dharnidharka (Transplantation 2009), who in 48000 kidney transplants showed that alemtuzumab does not predispose to viral nephritis, in line with what was demonstrated by previous work; -the authors cite the paper by Hirsch et al to demonstrate the role of FK as a risk factor for BK nephropathy. However, that work is based on a second analysis performed on the DIRECT trial data, actually drawn to evaluate the combination "FK / basiliximab" in inducing diabetes mellitus with high doses of steroids. So, it is possible that their results confirm that is the immunosuppression itself to predispose to viral nephritis, rather than a single specific drug -With regard to the role of the recipient and donor, there is no mention of other important predisposing factors, such as age, gender and ethnicity (Hirsch, Am J Transplant 2013)