REPLY TO LETTER TO THE EDITOR

BJC

British Journal of Cancer (2013) 108, 2624 | doi: 10.1038/bjc.2013.196

Integrated and mutated forms of Merkel cell polyomavirus in non-small cell lung cancer

Y Hashida[1], M Imajoh[1] and M Daibata*[,1]

[1]Department of Microbiology and Infection, Kochi Medical School, Kochi University, Nankoku, Kochi 783-8505, Japan

Sir,

We appreciate the insightful comments provided by Shuda *et al* (2013) regarding our recent report 'Detection of Merkel cell polyomavirus with a tumour-specific signature in non-small cell lung cancer' (Hashida *et al*, 2013).

According to GenBank data, two amino-acid sequences of the non-tumour-derived Merkel cell polyomavirus (MCPyV) strain Appendix206 (GenBank accession numbers JN038578 and JN038579) are deposited under the same title 'Merkel cell polyomavirus isolate Appendix206 large T antigen gene, partial cds; and small T antigen gene, complete cds'. In our study (Hashida *et al*, 2013), we compared the sequences of Appendix206 (JN038578) with the sequences of viral strains isolated from our four MCPyV-positive non-small cell lung cancers (NSCLCs) (SCC15, AC35, AC39 and AC43). As Shuda *et al* (2013) noted, the two sequences deposited in GenBank with the same descriptions of 'definition', 'source of organism' and 'features' are confusing and indistinguishable.

Our MCPyV strains had the wild-type retinoblastoma tumour-suppressor protein-binding motif. The more important results in our paper are the detection of integrated and *large T* (*LT*) gene mutated forms of MCPyV in one squamous cell carcinoma (SCC15) and one adenocarcinoma (AC43). The tumour AC43 possessed both an integrated MCPyV and frameshift mutations that truncate the *LT* gene to eliminate its helicase activity. The tumour SCC15 appears to have wild-type MCPyV, as the full-length *LT* gene sequence was determined by direct sequencing of polymerase chain reaction products, as shown in Figure 4 in our previous report (Hashida *et al*, 2013). However, we demonstrated that the AC43 tumour also carried integrated virus with the virus–host junction located in the *LT* gene at nucleotide position 2738, interrupting the helicase domain (nucleotide positions 1947–3017). These findings suggest the coexistence in the tumour of an integrated/truncated form and an episomal form of MCPyV. This phenomenon was also reported in MCPyV-positive Merkel cell carcinoma (Laude *et al*, 2010; Martel-Jantin *et al*, 2012).

Thus, we found two cases of NSCLC infected with MCPyV possessing a tumour-specific feature, which to our knowledge has not been reported in any specific malignancy other than Merkel cell carcinoma and chronic lymphocytic leukaemia. As Shuda *et al* (2013) commented, a follow-up study of these MCPyV-positive NSCLC cases is well worth doing.

REFERENCES

Hashida Y, Imajoh M, Nemoto Y, Kamioka M, Taniguchi A, Taguchi T, Kume M, Orihashi K, Daibata M (2013) Detection of Merkel cell polyomavirus with a tumour-specific signature in non-small cell lung cancer. *Br J Cancer* **108**: 629–637.

Laude HC, Jonchère B, Maubec E, Carlotti A, Marinho E, Couturaud B, Peter M, Sastre-Garau X, Avril MF, Dupin N, Rozenberg F (2010) Distinct Merkel cell polyomavirus molecular features in tumour and non tumour specimens from patients with Merkel cell carcinoma. *PLoS Pathog* **6**: e1001076.

Martel-Jantin C, Filippone C, Cassar O, Peter M, Tomasic G, Vielh P, Brière J, Petrella T, Aubriot-Lorton MH, Mortier L, Jouvion G, Sastre-Garau X, Robert C, Gessain A (2012) Genetic variability and integration of Merkel cell polyomavirus in Merkel cell carcinoma. *Virology* **426**: 134–142.

Shuda M, Feng H, Moore PS, Chang Y (2013) Merkel cell polyomavirus and non-small cell lung cancer. *Br J Cancer* **108**(12): 2623.

*Correspondence: Dr M Daibata; E-mail: daibatam@kochi-u.ac.jp

Published online 4 June 2013