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## *Letter to the Editor*

# JC viremia and multiple sclerosis

Daniele Focosi,[1] Richard Eric Kast,[2] and Mario Petrini[1]

[1]*Division of Hematology, Azienda Ospedaliera Santa Chiara, University of Pisa, Pisa, Italy*
[2]*Department of Psychiatry, University of Vermont, Burlington, Vermont, USA.*

Delbue *et al* (2007) report that JC virus (JCV) DNA was significantly less frequent in the peripheral blood of 59 interferon (IFN)-$\beta$–treated relapsing-remitting multiple sclerosis (RRMS) patients (13.6%) compared to the 39 untreated patients (46.1%) and the 98 healthy controls (28.6%). The authors infer that the presence of JCV in the blood of MS patients cannot be considered as a marker or a risk factor for progressive multifocal leukoencephalopathy (PML) development.

We have two major concerns on these results. First, the prevalence of JCV DNA in healthy controls is far higher than that occurring in previous studies. Koralnik *et al* (1999) did not find JCV DNA in 18 peripheral blood mononuclear cell (PBMC) and 13 plasma samples of human immunodeficiency virus (HIV)-negative control subjects. Tornatore *et al* (1992) did not find JCV DNA in lymphocytes from 30 immunocompetent patients with Parkinson's disease. Randhawa *et al* (2005) did not find JCV genome in blood from 23 healthy controls, 103 renal transplant recipient, and 44 liver transplant recipients, despite 20% to 30% of them had JCV viruria. Ferrante *et al* (1998) did not find any significant difference in JCV DNA detection in PBMCs between MS patients and control groups. Lafon *et al* (1998) found JCV DNA only in 2.3% of blood donors. Unless the healthy controls reported by Delbue *et al* were HIV-positive or receiving immunosuppressive drugs, we suspect that their polymerase chain reaction (PCR) could be flawed by methodological errors.

Otherwise, the high prevalence of JCV viremia in RRMS patients made us wonder whether most of them patients could actually be affected by PML. It has already been suggested that JCV could be the causal agent for both PML and MS (Altschuler, 2000), and indeed Du Pasquier *et al* (2006) showed that the cytotoxic lymphocyte (CTL) response against VP1, the major capsid protein of JCV, was significantly higher than the one against epitopes of MBP and PLP (the classical autoantigens in multiple sclerosis [MS]), and this JCV-specific CTL response was also significantly stronger in MS patients than healthy control subjects. Ferrante *et al* (1998) found JCV DNA in the cerebrospinal fluid (CSF) of 11 out of 121 MS patients (9%) but in no member of control groups [5]; on the contrary, Bogdanovic *et al* (1998) did not find JCV DNA in CSF from 45 patients with early MS. Stoner *et al* (1986) found no cells expressing T antigens were detected in plaque or periplaque regions of the MS brains or in control central nervous system (CNS) tissue.

Differences exist between JCV found in PML and in MS: Agostini *et al* (2000) showed that the excretion of JCV in MS patients is similar in both genotype and frequency to that of control individuals, whereas genotype 2B is more frequently found in PML brain than expected based on its prevalence in urine samples from a control population.

The authors also conclude that IFN-$\beta$ reduces the presence of the JCV genome in the peripheral blood of RRMS patients [1]. On the contrary, Alvarez-Lafuente *et al* (2007) did not find any statistical significant difference between 73 IFN-$\beta$–treated and 73 untreated RRMS patients ($28.6 \pm 7.2$ and $32.3 \pm 8.4$ copies/$\mu$g of DNA, respectively).

Address correspondence to Dr. Daniele Focosi Division of Hematology, Azienda Ospedaliera Santa Chiara, University of Pisa, via Roma 56, 56100 Pisa, Italy. E-mail: focosi@icgeb.org
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