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### Scientific Comment

## Torque teno virus: a ubiquitous virus<sup>☆</sup>



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Torque teno virus (TTV) is a non-enveloped human DNA virus isolated by Nishizawa et al. in 1997.<sup>1</sup> TTV, recently classified as the *Alphatorquevirus* genus within the *Anelloviridae* family by the International Committee on Taxonomy of Viruses (ICTV), was the first human virus with a single-stranded circular DNA genome to be identified.<sup>2</sup> Thus far, five main genetic groups (Groups 1–5) involving at least 39 genotypes have been identified based on phylogenetic analysis.<sup>3</sup>

The TTV genome can be divided into an untranslated region (UTR) of 1.2 kb and a potential coding region of 2.6 kb. The UTR is relatively conserved, suggesting that it plays an important regulatory role in viral replication. The coding region contains two large open reading frames: ORF1 and ORF2. Several other open reading frames have been described, and the peptides that they encode differ in length for different isolates.<sup>4</sup>

This virus is characterized by an extremely high prevalence, with relatively uniform distribution worldwide and a high level of genomic heterogeneity.<sup>4</sup> Although this virus has a very high prevalence in the general population across the globe, neither its interaction with its hosts nor its direct involvement in the etiology of specific diseases is fully understood.

After the discovery of TTV, its detection has been by polymerase chain reaction (PCR) with primers targeting the ORF1 (N22 region, the first described sequence), nevertheless primers derived from the N22 region can detect only a portion of TTV variants mainly representing genetic group 1 TTV (Genotypes 1–6).<sup>5,6</sup> As the UTRs of the viral genome are more conserved when compared to the ORF regions, UTR-targeting primers (used later for the detection of TTV DNA) can detect

essentially all known TTV strains reported, thereby detecting a larger number of genotypes giving a higher detection rate.<sup>5,7,8</sup>

In this issue of the *Revista Brasileira de Hematologia e Hemoterapia*, there is an important study entitled “Prevalence of Torque teno virus in healthy donors of Paraná State, southern Brazil”. In this article, the authors demonstrated the prevalence of the TTV in healthy donors in the northern and northwestern regions of the state of Paraná, southern Brazil, by nested PCR using a set of primers for the N22 region.<sup>9</sup>

The authors demonstrated a high prevalence of TTV (69%) among healthy blood donors by using primers targeting the N22 region. It is therefore possible that if the authors had used primers for the UTRs the prevalence would have been even higher.

This high prevalence of the virus makes it almost ubiquitous in the human population and able to evade clearance by the host immune response thereby establishing long-term persistent infections.<sup>10</sup> In this context we can highlight the MicroRNAs (miRNAs), small 22 nt noncoding RNAs that direct posttranscriptional gene regulation, that have been recognized as important regulators of gene expression in many eukaryotes and even in viruses.<sup>11</sup> Emerging themes of viral miRNA function include immune evasion, prolonging longevity of host cells, and regulation of persistent infection.<sup>12–14</sup>

The TTV makes use of viral miRNAs to modulate the innate immune response and promote its persistence. Kincaid et al.<sup>15</sup> showed that the TTV encodes a miRNA *in vivo* that targets N-myc (and STAT) interactor (NMI), thus mediating a decreased response to interferons and increased cellular proliferation in the presence of interferon. These facts support the

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<sup>☆</sup> See paper by Mazzola et al. in *Rev Bras Hematol Hemoter.* 2015;37(5):336–40.

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theory that miRNA-mediated immune evasion contributes to the immense ubiquity of these viruses by antagonizing the host antiviral response.

It has been suggested that TTV infection is associated with many diseases, however there is no direct evidence of links between infection and specific clinical diseases, and many questions remain to be clarified for example, how can TTV interfere in many pathological processes and in the dysregulation of the immune system? These questions undoubtedly represent rich fields for research on TTV.

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### Conflicts of interest

The author declares no conflicts of interest.

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