

# **“Human Herpesvirus Type 8 (HHV8) infection in lymphoproliferative disorders in patients with Common Variable Immunodeficiency (CVID)”**

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## **Abstract**

### **Background:**

Patients with Common Variable Immunodeficiency (CVID) and Granulomatous or Lymphocytic Interstitial Lung Disease (GLILD) are at high risk for the development of lymphoproliferative disorders. We hypothesized the Herpes Virus Type 8 (HHV8) infection underlies lymphoproliferative disorders in CVID.

### **Methods:**

Genomic DNA from PBMC was screened by nested and quantitative real time PCR (QRT-PCR) for HHV8 infection in the followings: normal blood donors (n=10), patients receiving IVIG but without CVID (n=13), CVID patients with GLILD (CVID-GLILD: n=9), and CVID patients without GLILD (CVID-control: n=21). QRT-PCR and Immunohistochemistry (IHC) for the HHV8 protein, LANA-1, was performed on available biopsy specimens from CVID-GLILD patients. We also performed the genetic sequencing of HHV8 PCR product (ORF26).

### **Results:**

Using genomic DNA isolated from PBMC as a template, HHV8 genome was detected by nested and QRT-PCR in 1/21 (4.8%) CVID-control and 6/9 (67%) CVID-GLILD (p=0.0009). HHV8 infection was not detected in other groups. HHV8 copy numbers were high in various tissues, and highest in the malignant lymph node of a patient with CVID-GLILD and Non-Hodgkin's Lymphoma. IHC showed positive LANA-1 in 4/5 (80%) patients with CVID-GLILD. Sequence of HHV8 showed strain A pattern, which is the most prevalent form in patients with AIDS in the US.

### **Conclusion:**

HHV8 may underlie the development of lymphoproliferative disorders including Granulomatous disease and Malignant lymphoma in patients with CVID.