DR52 and -DR7) and HLA-DQ (-DQ2) for one donor. Finally we demonstrated that purified peptide-induced CD4+ from one donor could inhibit the growth of EBV-infected autologous B-cells in the early phase of transformation.
Conclusion: This EBNA2 synthetic peptide is very promising to design an EBV vaccine for nonimmune individuals awaiting solid organ transplantation.

The pathogenesis of hepatitis c virus (HCV) is strongly influenced by cytomegalovirus (CMV)

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Background: Virus-virus interactions may influence the pathogenesis of defined human viral infections. Using the clinical setting of liver transplantation (LT), we investigated the potential role that β-herpesviruses may play in the course of HCV infection.
Methods: In 93 consecutive HCV-infected patients followed for a mean of 32 months post-LT, the incidence of CMV, human herpesvirus (HHV) -6 and -7 replication (assessed by PCR on 6 weekly serum samples) and CMV disease were evaluated for their impact on HCV-induced cirrhosis, retransplantation or mortality (primary end point). HCV replication and recurrence of HCV-induced hepatitis and fibrosis (assessed at 16 and 52 weeks post-LT) were evaluated as secondary end points. Statistical analysis was performed using frequency tables, Kaplan Meier estimation, and proportional hazards regression.
Results: The primary end point developed in 28% of patients. Independent of other significant predictors, we observed that CMV (40/91 [35.2%]) but not HHV-6 and -7 reactivation, and CMV disease (23/93 [24.7%]) were associated with the primary end point (Risk Ratio [RR], 1.003; 95% CI, 1.001–1.004; P=0.002; and RR, 4.189; 95% CI, 1.838–9.546; P=0.001, respectively). Early CMV reactivation was strongly associated with mortality (8/32 [25%] vs 0/59 [0%]; P<0.001). CMV disease was also associated with higher fibrosis stage (mean (SD, 1.0±1.19 vs 0.49 (0.83; P=0.04), modified hepatitis activity index (mean±SD, 4.17±3.07 vs 2.96±2.42; P=0.09), and plasma HCV RNA level (mean±SD, 55.71±50.47 vEq/ml vs 36.17±46.95 vEq/ml; P=0.07) at 16 weeks post-LT.
Conclusion: Using the human model of LT, our study demonstrates that the pathogenesis of HCV is strongly and independently influenced by its interaction with CMV but not HHV-6 and -7. The lack of association between HCV and the other β-herpesviruses implies that the impact of CMV on HCV may be mediated by a direct HCV-CMV interaction that is beyond immunomodulation. Importantly, it is observed that even low level CMV replication that does not evolve into clinical disease influences HCV outcome. Thus, aggressive CMV prevention may positively influence the clinical outcome of HCV-infected LT patients.

An X-linked lymphoproliferative disease (XLP) patient with uneventful primary infection and fatal reactivation with Epstein-Barr virus (EBV)

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Background: XLP is an inherited immunodeficiency caused by *SAP* mutations. XLP often manifests itself as fulminant or fatal infectious mononucleosis after primary EBV infection; however, EBV is apparently unrelated to development of lymphoma or dysgammaglobulinemia, other major manifestations of XLP. Thus, how this virus involves the pathogenesis of XLP remains obscure. We experienced a patient with XLP who did not acquire any serious condition after primary EBV infection but eventually developed virus-associated hemophagocytic syndrome (VAHS) and malignant lymphoma (ML) upon reactivation of EBV.
Case Report: A 12-year-old boy presented with a 16-day history of fever and lumbago. Both the patient and his 9 year old brother have been known to have hypogammaglobulinemia of unknown etiology, and were seropositive to EBV with uneventful past medical histories, except for several episodes of otitis media and an episode of pneumonia in the patient. Abdominal CT revealed paraaortic and pelvic lymphadenopathy. Open biopsy of the lymph nodes was performed, which showed necrotic tissue with no malignant cells. He did not respond antibiotics, and subsequently VAHS was diagnosed. Despite intensive therapy including plasma exchange, immunosuppressants and VP16, he deteriorated with development of multiple novel nodular lesions in lungs and bilateral pleural effusions, and died from multiple organ failure. Cytological analysis of pleural fluid was compatible to malignant transformation.
Immunologic Studies: Intracellular staining of SAP protein showed decreased SAP expression in T cells derived from these brothers. Direct sequencing revealed missense mutation S34G in their SAP genes. Plasma EBV load in the patient, determined by real-time PCR, was undetectable on admission, but markedly increased to 2.2×10^5 copies/ml when he developed VAHS. In striking contrast, EBV-specific CTL was barely detectable by MHC-peptide tetramer method.
Conclusions: Despite impaired EBV-specific immunity, primary EBV infection in the patient, and also in his brother, appeared insignificant. Nevertheless, he ultimately developed such serious EBV-associated diseases as VAHS and ML. Thus, role of EBV infection in the pathogenesis of XLP may be complex.