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Lymphoma: Potential Viral Antagonism between HTLV-1 and JCV Associated with Increased Survival Time

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Abstract

This short note points to a potential interplay between Human T-lymphotropic virus 1 (HTLV-1) and John Cunningham virus (JCV). It delves into the potential antagonism between HTLV-1 and JCV, examining how this interaction might influence lymphoma survival rates and the risk of developing this disease.

Introduction

Leukemia and lymphomas are cancers of white blood cells, distinction being in the type of tissue they originate from. Leukemia typically originates in bone marrow, while lymphoma usually originates in lymph nodes or the spleen.

Despite this, T-lymphocytes or B-lymphocytes are commonly affected in both types. Adult T-cell leukemia (ATLL) is associated with Human T-cell Leukemia (Lymphoma) Virus (HTLV1), a retrovirus sharing similarities with HIV. While both retroviruses infect the T lymphocytes, HTLV1 can also infect other cell types [1]. The polyproteins of HIV and HTLV1 show significant similarities. Notably, HIV inhibitors have been found to inhibit HTLV1 enzymes [2].

HIV and HTLV1, though sharing similarities, differ in their pathogenic mechanisms. HIV induces CD4 lymphocyte apoptosis, leading to AIDS, while HTLV1 transforms lymphocytes via its Tax protein [3]. Tax deregulates multiple signaling pathways, promoting cell proliferation and inhibiting apoptosis [4]. HTLV1 has also been found to transform B-lymphocytes, suggesting its potential role in B-cell lymphomas [5].

Main content

A study assessing HTLV1 prevalence in non-Hodgkin's lymphoma (NHL) patients found HTLV1 in 18.8% of samples[6]. Another study explored polyomaviruses (JCV and BKV) in lymphoma patients, revealing a higher survival rate in those patients with detected polyomaviral DNA in serum [7]. JCV antibodies were also less prevalent in NHL patients compared to the healthy control group, 59% of control group had antibodies to JCV detected, in comparison 49% of NHL patients had antibodies to JCV detected [8].

Comparative analysis of JCV and HTLV1 proteins with BLAST showed short peptide alignments, indicating potential similarities. Best alignment was between JCV capsid protein and HTLV1 polyprotein.

Discussion

Even though HTLV1 is a known cancer causing virus in humans, testing for this virus is rarely done and there are few population studies [9].

The detection of polyomavirus DNA in lymphoma patients is associated with longer survival times. Additionally, the healthy control group exhibits a higher seropositivity for JCV polyomavirus. This intriguing correlation hints at a yet unexplained protective mechanism conferred by JCV polyomavirus, warranting further investigation. One possibility is virus antagonism between HTLV1 and JCV.

Because JCV polyomavirus capsid protein and HTLV1 polyprotein show a region of similarity, it is possible the two proteins have similar enough epitopes that an antibody raised against one protein could also recognize and bind to the other protein. This phenomenon is known as cross-reactivity.

Another possibility is interference between two similar proteins during virus assembly, or perhaps JCV proteins competing for HTLV1 protease (competitive inhibition).

Perhaps more importantly, more research should be done regarding HTLV1 and its effect on cancer considering if the inhibition of HTLV1 by JCV is proven true and does effect increased survival then inhibition of HTLV1 by antiretroviral drugs would also have a positive effect.

Conclusion

Understanding the connection between viruses and tumors is crucial for cancer treatment. HTLV1, a known lymphoma-causing virus, presents an avenue for potential therapies. Polyomaviruses, contrary to expectations, showed a protective effect against lymphoma in two different experiments. The similarity between HTLV1 and JCV proteins raises questions about potential antagonistic effects between the viruses or potential enhancement of immune response to HTLV1 due to presence of JCV. These hypotheses require further investigation in controlled conditions for validation.

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