

"Pathogen Discovery in AIDS-related Lymphoma by Next-generation Sequencing"

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Abstract: The goal of this project is to discover novel viruses associated with HIV-related lymphomas of unknown origin, using next-generation sequencing approaches. A variety of oncogenic viruses have been found in human cancers, including Epstein-Barr virus (EBV), Kaposi's sarcoma herpesvirus (KSHV) and human papillomavirus (HPV). The incidence of malignancies caused by these viruses is greatly increased in AIDS patients, where the most common cancer is Kaposi's sarcoma (caused by KSHV), followed by malignant lymphoma and cervical carcinoma (caused by HPV). Among the AIDS-related lymphomas (ARLs), approximately 30% contain EBV, and 4% contain KSHV. This leaves a large fraction of ARLs that are potentially associated with an unknown infectious agent. Therefore, we will apply the approach of sequence-based computational subtraction to evaluate the presence of novel sequences in ARL. We will generate cDNA libraries from mRNA from frozen AIDS-Related lymphoma tissue and perform next-generation sequencing using the Illumina platform. We will subtract sequences that match the human genome and transcriptome, and test non-human sequences for their presence in larger AIDS-Related lymphoma and control sample sets. We will then use any recurrent sequences to attempt to isolate whole genomes of candidate infectious agents. Even if no novel organisms are identified, the findings would be significant as this approach would suggest that a large proportion of ARLs are not caused by conventional viruses. In contrast, identification of a novel infectious agent associated with cancer would have immediate preventive, diagnostic and therapeutic significance.