

MEETING ABSTRACTS

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Distinct profiles of antibodies to Kaposi sarcoma-associated herpesvirus antigens in patients with Kaposi sarcoma, multicentric Castleman's disease, and primary effusion lymphoma

Peter D Burbelo^{1*}, Alexandra T Issa¹, Kathryn H Ching¹, Kathleen M Wyvill³, Richard F Little³, Michael J Iadarola¹, Joseph A Kovacs², Robert Yarchoan³

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Clinical background

Kaposi sarcoma-associated herpesvirus (KSHV), also called human herpesvirus-8 (HHV-8), is the causative agent of all forms of Kaposi sarcoma (KS), as well as two rare B-cell HIV lymphoproliferative disorders, primary effusion lymphoma (PEL) and multicentric Castleman's disease (MCD). Like other herpesviruses, KSHV has two phases of gene expression, latent and lytic. In KS, many of the KSHV-infected spindle cells express only latent genes, while a small percentage express lytic genes. By contrast, a substantial percentage of MCD cells express lytic KSHV genes. The majority of PEL cells express KSHV latent genes, but in addition can show limited expression of certain lytic genes. Given the differential expression of KSHV lytic and latent proteins in KS, PEL, and MCD, we hypothesized that different antibody profiles to KSHV antigens might distinguish these diseases.

Materials and methods

Antibodies were evaluated in sera from patients or volunteers under IRB-approved protocols at the NIH Clinical Center, NIAID, and the NCI including from 35 patients with KS, 14 with both MCD and KS (MCD +/KS+), 6 with MCD but no KS (MCD+/KS), 5 with PEL, and 34 KSHV-uninfected controls. Luciferase

Immunoprecipitation Systems (LIPS) was used for profiling antibodies to latent and lytic KSHV antigens.

Results

Using LIPS, antibodies against the lytic antigen K8.1 were 5-fold higher in MCD than in KS patients. In contrast, markedly higher antibodies to v-cyclin, a latent KSHV gene, were found in the KS and PEL patients compared to the MCD. Antibodies to another latent antigen, LANA, were also markedly higher in the KS compared to the MCD patients. Antibodies to the sum of latent antigens v-cyclin and LANA were 27-fold higher in KS compared to MCD patients ($p < 0.0001$). The sum of anti-v-cyclin and anti-LANA antibody titers discriminated patients with KS without MCD from those with MCD and KS with 93% sensitivity and 83% specificity.

Conclusion

These results suggest that antibody responses to lytic and latent KSHV antigens differ between KS, MCD, and PEL.

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*Correspondence: burbelop@nidcr.nih.gov

¹Neurobiology and Pain Therapeutics Section, Laboratory of Sensory Biology, NIDCR, NIH, Bethesda, MD, USA

Full list of author information is available at the end of the article

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Author details

¹Neurobiology and Pain Therapeutics Section, Laboratory of Sensory Biology, NIDCR, NIH, Bethesda, MD, USA. ²Critical Care Medicine Department, Clinical Center, NIH, Bethesda, MD, USA. ³HIV and AIDS Malignancy Branch, Center for Cancer Research, NCI, NIH, Bethesda, MD, USA.

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