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HHV8 Regulates Vascular and Lymphatic Endothelial Cell Specific Genes Producing Distinct/Mixed Profile in Kaposi's Sarcoma

Parkash S Gill* ‡

Address: USC- Keck School of Medicine, Norris Cancer Center, Los Angeles, CA

Email: Parkash S Gill* - parkashg@hsc.usc.edu

* Corresponding author ‡Presenting author

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Kaposi's sarcoma represents a vascular proliferative process. Characterization of genes expressed in vascular endothelial cells in particular arterial and venous endothelial cells when examined in KS indicate that KS displays profile that resembles arterial endothelial cells. These include certain Notch receptors and their ligands including Delta like 4 (dll4), neuropilin-1, ephrinB2, connexin 37, but not venous specific marker (ephB4). Furthermore HHV8 infection, and viral proteins vGPCR, leads to the induction of several proteins that preferentially induce genes expressed in artery endothelial cells (ephrinB2) but not venous specific (EphB4). KS gene expression profile also shows expression of lymphatic endothelial cell specific markers as well. Thus the phenotype of KS is distinct from the profile in resting or angiogenic response in physiological responses as in wound healing or tumor vasculature. Distinct phenotypic characteristics provide opportunities for novel targeting and therapeutics. For example inhibition of EphrinB2 expression with siRNA leads to detachment of the cells from matrix, and loss of cell viability represents a prototype. Growing understanding of KS biology is thus likely to offer novel targets for therapy.