Vascular Endothelial Growth Factor Receptor 3 (VEGFR3/FLT4) Regulates KSHV Infection and Tumorigenesis

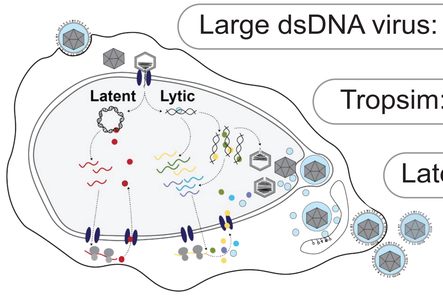
Ameera Mungale[1,2], Sarah Dremel[1], Joseph Ziegelbauer[1]

[1]HIV and AIDS Malignancy Branch, National Cancer Institute, NIH

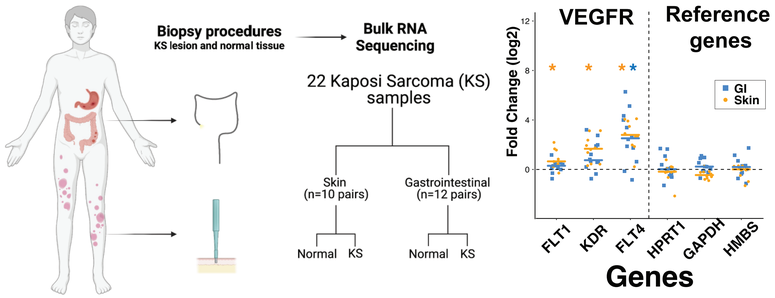
[2]Department of Microbiology & Immunology, Georgetown University

KSHV is an oncogenic gammaherpesvirus

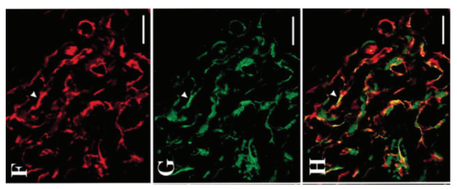
- Large dsDNA virus: 170 kb, Endcodes >100 genes
- Tropsim: mainly endothelial and B cells
- Latency: silent, persistent infection
- Lytic: productive infection



VEGF Receptors are upregulated in Kaposi sarcoma (KS) clinical samples



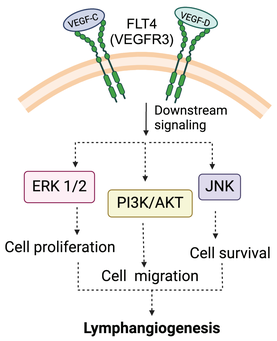
KS is a highly vascularized tumor, VEGFRs drive pro-angiogenic pathways



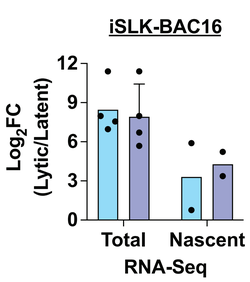
FLT4 | CD31 (endothelial cell) | Merge

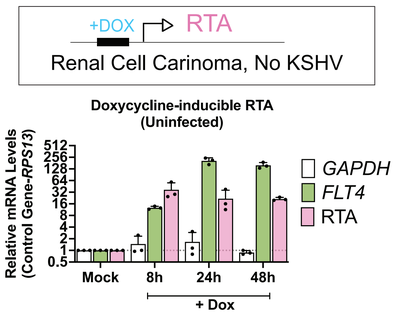
KS tissue Immunohistochemistry

Skobe *et al. J Invest Derm,* 1999



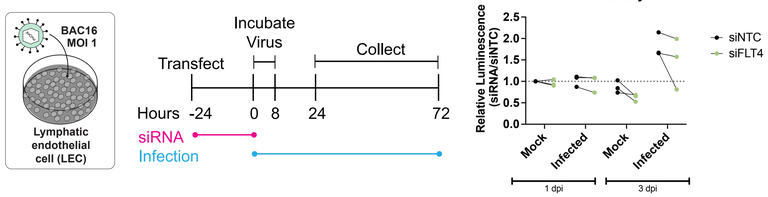
KSHV transcription factor RTA induces *FLT4*



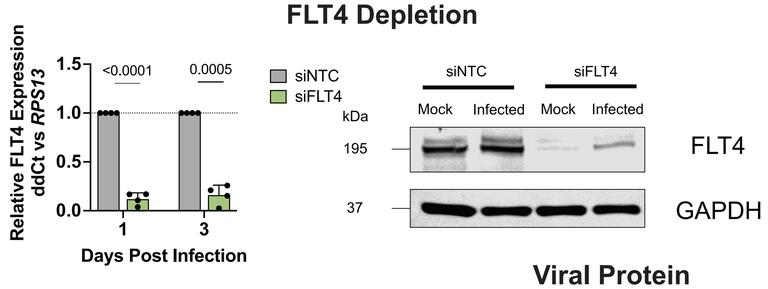


FLT4 decreases viral replication

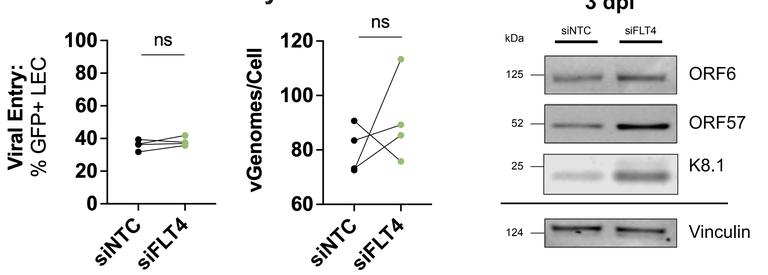
Experimental Methods



FLT4 Depletion

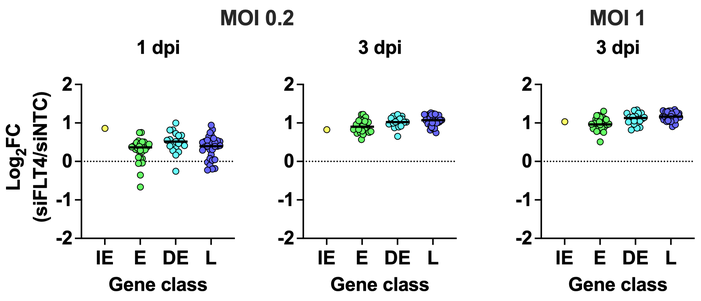


Viral Entry

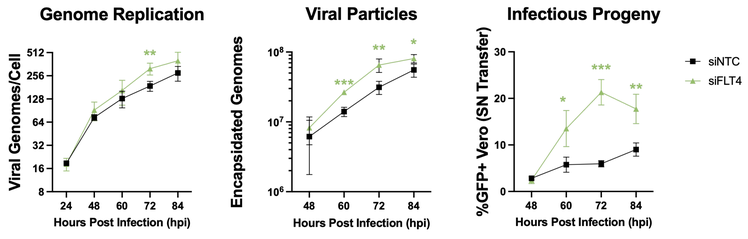


Viral Protein

Viral Transcripts (RNA-seq, MOI 0.2: n=2, MOI 1: n=3)

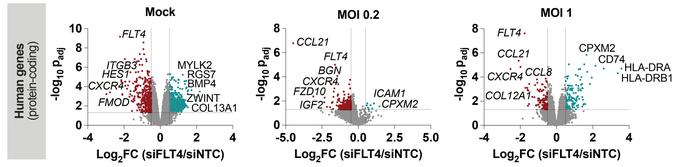


Viral Replication Kinetics

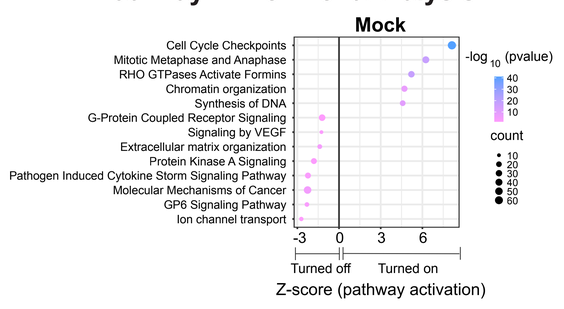


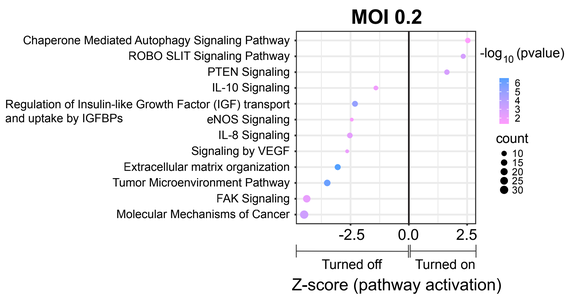
FLT4 promotes pro-cancer and anti-immune gene expression

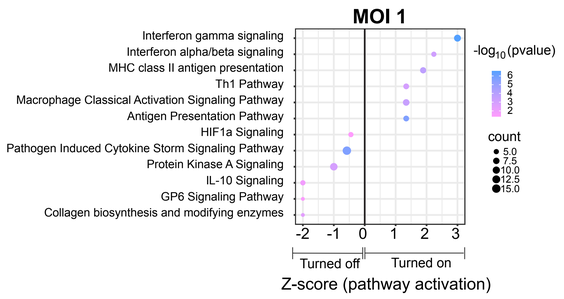
Differential Expression Analysis



Pathway Enrichment Analysis







Proposed Model

