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Profiling viral and host microRNA expression in cells infected with KSHV and EBV

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MicroRNAs are small non-coding RNAs of around 22 nucleotides that post-transcriptionally regulate gene expression. MicroRNAs have important functions in embryogenesis, hematapoiesis and carcinogenesis. Virally encoded microRNAs have been identified in EBV and KSHV and recent data suggest a role for both viral and host microRNAs in pathogenesis. We have developed a custom microarray to detect expression of all human and viral microRNAs. Probes are 60 mer oligonucleotides containing a 40 nucleotide non genomic linker sequence. Four replicates of each probe are represented on the array and eight arrays are printed on each slide. The arrays are printed by Agilent ensuring excellent quality control. We have used this array to profile viral and host microRNAs in KSHV in primary effusion lymphoma (PEL) cells infected with KSHV alone or KSHV and EBV, and in KSHV infected and uninfected endothelial cells. The effect of KSHV reactivation on viral and host microRNA expression was determined by induction of viral replication by an adenovirus vector expressing KSHV ORF 50, the master switch of lytic replication.

KSHV encoded microRNAs were detected in PEL cell lines during latency and levels of expression did not substantially change after reactivation. The EBV co-infected PEL cell lines also expressed high levels of the EBV encoded BART2 microRNAs but not the BHRF1–3 microRNAs. Interestingly, KSHV reactivation caused an increase of EBV encoded microRNAs. PEL lines display a unique cellular microRNA expression pattern which may contribute to their post-germinal center arrested phenotype.

In addition, we detected for the first time viral and cellular microRNA expression patterns in two different endothelial cell lines (TIVE and SLK) latently infected with KSHV. KSHV infection leads to a marked induction of human microRNA expression including several microRNAs with known roles in carcinogenesis. Ongoing studies include microRNA profiling of EBV infected B cells and lymphoma cell lines as well as KSHV infected primary B cells.

Viral microRNAs are expressed in infected cells and likely modulate both viral and host genes relevant to lymphomagenesis. EBV and KSHV infection also up-regulate expression of host microRNAs previously shown to play a role in tumorogenesis.