



Data in Brief

Genomic analysis of xCT-regulatory network in KSHV + primary effusion lymphomas

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ABSTRACT

Kaposi's sarcoma-associated herpesvirus (KSHV) is the etiological agent of primary effusion lymphoma (PEL), a rapidly progressing malignancy mostly arising in HIV-infected patients Chen et al. (2007) [1]. Even under conventional chemotherapy, PEL continues to portend nearly 100% mortality within several months, which urgently requires novel therapeutic strategies. We have previously demonstrated that targeting xCT, an amino acid transporter for cystine/glutamate exchange, induces significant PEL cell apoptosis through regulation of multiple host and viral factors [2]. More importantly, one of xCT selective inhibitors, Sulfasalazine (SASP), effectively prevents PEL tumor progression in an immune-deficient xenograft model [2]. In the current study, we use Illumina microarray to explore the profile of genes altered by SASP treatment within 3 KSHV + PEL cell-lines, and discover that many genes involved in oxidative stress/antioxidant defense system, apoptosis/anti-apoptosis/cell death, and cellular response to unfolded proteins/topologically incorrect proteins are potentially regulated by xCT Dai et al. (2015) [3]. The microarray original data have been submitted to Gene Expression Omnibus (GEO) database (Accession number: GSE65418).

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Specifications

Organism/cell line/tissue	Homo sapiens/KSHV + primary effusion lymphoma cell lines, BC-1, BCP-1 and BCBL-1
Sex	Male
Sequencer or array type	Illumina BeadStation 500 and BeadScan
Data format	Raw data: FASTAQ file
Experimental factors	Cells were treated with vehicle or the xCT selective inhibitor SASP (0.5 mM) for 48 h
Experimental features	Microarray gene expression profiling to identify transcripts that are regulated by SASP
Consent	Data are publicly available
Sample source location	LSUHSC, New Orleans, Louisiana

2. Experimental design, materials and methods

2.1. Cell culture and reagents

The PEL cell-line BCBL-1 (KSHV⁺/EBV^{neg}) was maintained in RPMI 1640 medium (Gibco) with supplements as described previously [1,2]. The other PEL cell-lines BC-1 (KSHV⁺/EBV⁺) and BCP-1 (KSHV⁺/EBV^{neg}) were purchased from American Type Culture Collection (ATCC) and maintained in complete RPMI 1640 medium (ATCC) supplemented with 20% FBS. All cells were cultured at 37 °C in 5% CO₂. All experiments were carried out using cells harvested at low (<20) passages. Sulfasalazine (SASP) was purchased from Sigma.

2.2. Microarray and data analysis

Microarray analysis was performed and analyzed at the Stanley S. Scott Cancer Center's Translational Genomics Core at LSUHSC. BC-1, BCP-1 and BCBL-1 cells were treated with vehicle or the xCT selective inhibitor SASP (0.5 mM) for 48 h, respectively. Total RNA was isolated using Qiagen RNeasy kit (Qiagen), and 500 ng of total RNA was used to synthesize dscDNA. Biotin-labeled RNA was generated using the TargetAmp-Nano Labeling Kit for Illumina Expression BeadChip

1. Direct link to deposited data

<http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE65418>.

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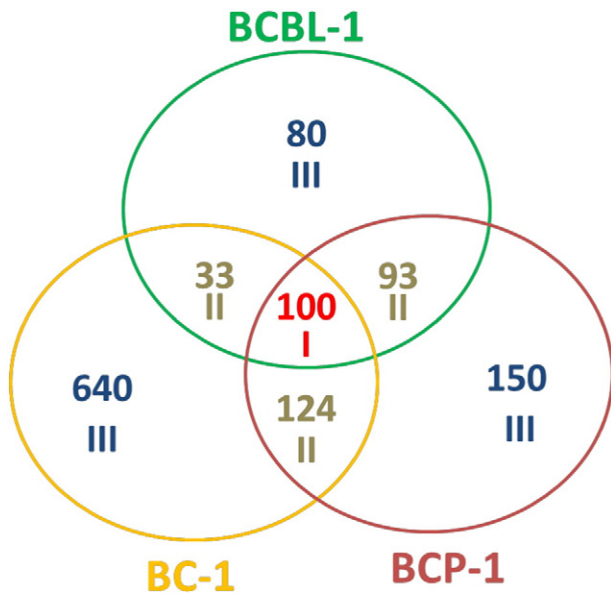


Fig. 1. Intersection analysis of gene profile altered within SASP-treated KSHV + PEL cell-lines. The HumanHT-12 v4 Expression BeadChip (Illumina) was used to detect genomic gene profile altered within 3 SASP-treated KSHV + PEL cell-lines (BCBL-1, BC-1 and BCP-1) when compared with vehicle-treated controls. Intersection analysis of significantly altered genes (up/down ≥ 2 folds and $p < 0.05$) was performed using the Illumina GenomeStudio Software. Set I: Common genes altered in all the 3 cell-lines; Set II: Similar genes altered in every 2 cell-lines; Set III: Unique genes altered in each cell-line.

(Epicenter), according to the manufacturers' instructions, and hybridized to the HumanHT-12 v4 Expression BeadChip (Illumina) which contains more than 47,000 probes derived from the NCBI RefSeq Release 38 and other sources, at 58 °C for 16 h. The chip was washed, stained with streptavidin-Cy3, and scanned with the Illumina BeadStation 500 and BeadScan.

Using the Illumina's GenomeStudio software, we normalized the signals using the "cubic spline algorithm" that assumes that the distribution of the transcript abundance is similar in all samples. The background

signal was removed using the "detection p-value algorithm" to remove targets with signal intensities equal or lower than that of irrelevant probes (with no known targets in the human genome but thermodynamically similar to the relevant probes). The microarray experiments were performed twice for each group and the average values were used for analysis. Common, similar, and unique sets of genes and enrichment analysis were performed using the MetaCore Software (Thompson Reuters), and the results were summarized in Fig. 1. Enrichment analysis shows that several major cellular functions were affected within SASP-treated PEL cells, including oxidative stress/antioxidant defense system, apoptosis/anti-apoptosis/cell death, and cellular response to unfolded proteins/topologically incorrect proteins, which is consistent with the SASP-induced apoptosis phenotype that we recently observed in KSHV + PEL cell-lines [2,3]. Therefore, our microarray data indicate that xCT as well as downstream controlled genes may represent new "drug targets" for better PEL treatment.

Conflict of interest

The authors declare no conflict of interests.

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