

![](_page_0_Figure_1.jpeg)

![](_page_0_Figure_2.jpeg)

**Supplementary figure 1** RNA-seq reads aligned to the wild type EBV genome confirm extensive transcription from the *Bam*HI-A region (highlighted by red square).

![](_page_1_Figure_0.jpeg)

**Supplementary figure 2** (A) RT-qPCR validation of differentially expressed genes from four groups identified by GO enrichment analysis which may play a role in EBV infection and NPC tumor progression. (B) RT-qPCR validation of *GAPLINC*, *DTX3* and *ELF3*, which are upregulated by knockdown of BART IncRNA. Gene expression is shown as fold change in mRNA expression relative to that of *GAPDH*. C<sub>P</sub> values >35 were considered unreliable. The average and SEM of three independent experiments are shown. \**P*<0.05, \*\**P*<0.01, \*\*\**P*<0.001.

![](_page_2_Figure_0.jpeg)

**Supplementary figure 3** Relative gene expression of *IKZF3* (A) and *F3* (B *p66*<sup>*Shc*</sup> (B) in EBV-positive cell lines AGS-Bx1, HeLa-Bx1, C666-1, Mutu I and Mutu III analyzed by RT-qPCR. Gene expression is shown as mRNA expression relative to that of *ACTB*. The average and SEM of at least two independent experiments are shown.

## Supplementary table 1 RNA-seq reads.

Α

| Sample             | Raw reads   | Filtered reads | Mapped to<br>human genome |
|--------------------|-------------|----------------|---------------------------|
| C666-1 Gap-CTL #1  | 130,320,036 | 128,896,420    | 122,357,404               |
| C666-1 Gap-CTL #2  | 130,811,438 | 129,743,974    | 123,449,754               |
| C666-1 Gap-BART #1 | 133,609,546 | 132,380,916    | 126,378,620               |
| C666-1 Gap-BART #2 | 126,998,364 | 125,875,392    | 119,540,534               |

В

| Sample             | Unmapped<br>reads | Mapped to<br>EBV genome |
|--------------------|-------------------|-------------------------|
| C666-1 Gap-CTL #1  | 6,539,016         | 384,110                 |
| C666-1 Gap-CTL #2  | 6,002,296         | 167,628                 |
| C666-1 Gap-BART #1 | 6,294,220         | 257,428                 |
| C666-1 Gap-BART #2 | 6,334,858         | 143,578                 |

| Oligo             | Sequence (5'-3')                      | Reference                        |
|-------------------|---------------------------------------|----------------------------------|
| V(A/B)-F          | TCTTCTAGAGGACGCAGGATATCTGCAGGATCAGAGG | Yamamoto <i>et al</i> . 2012(1)  |
| VII(A/B)-R        | AGGGGATCCGCACCCCAGTACCGGGCCATCCG      | Yamamoto <i>et al</i> . 2012 (1) |
| V-F               | GAAAAGCTTGGGATTAATGCCTGGACCCTCACCAG   | Yamamoto <i>et al</i> . 2012 (1) |
| VII(D)-R          | AGGGGATCCCCCGCCACCACGGTGCAGCCTAC      | Yamamoto <i>et al</i> . 2012 (1) |
| Gap-CTL           | A*A*C*A*C*G*T*C*T*A*T*A*C*G*C*        | N/A                              |
| Gap-BART_exon III | C*G*G*A*C*C*T*G*A*A*A*C*G*A*G*A*      | N/A                              |
| Gap-BART_exon V   | T*C*A*T*T*C*C*A*T*C*G*G*A*T*A*A*      | N/A                              |
| Gap-BART_exon VII | T*A*C*A*C*C*T*T*C*A*T*C*A*C*G*G*      | N/A                              |
| BART_ exon III-F  | GGGGTTGTAACGGAAGGCAA                  | N/A                              |
| BART_exon III-R   | TGTCCGGTAAACGCCATACG                  | N/A                              |
| BART_exon V-F     | CGGCCCAGTAGCTTGATGAC                  | N/A                              |
| BART_exon V-R     | GGTGTACACGCACGAGAAATG                 | N/A                              |
| BART_exon VII-F   | AAGTCAGGAATGCCTTCTGGTG                | N/A                              |
| BART_exon VII-R   | CACACCTGTTTACCCAGACC                  | N/A                              |
| ACTB-F            | CACTCTTCCAGCCTTCCTTC                  | Cao <i>et al.</i> 2015 (2)       |
| ACTB-R            | GTACAGGTCTTTGCGGATGT                  | Cao <i>et al.</i> 2015 (2)       |
| AIFM3-F           | TCCCATTGTGTCCAAGGTCG                  | N/A                              |
| AIFM3-R           | AGGACATGTCGCCAGTCTTG                  | N/A                              |
| ALDH1A3-F         | ATAAGCCCGACGTGGACAAG                  | N/A                              |
| ALDH1A3-R         | GAACCCGGCGGCCAAG                      | N/A                              |
| AOX1-F            | TCATCTAAGGGTCTGGGAGAGT                | N/A                              |
| AOX1-R            | TCCAGGTTCATCTCTCGGAA                  | N/A                              |
| CD274-F           | TGCAGGGCATTCCAGAAAGA                  | N/A                              |
| CD274-R           | TAGGTCCTTGGGAACCGTGA                  | N/A                              |
| CD7-F             | CCTGTAGACCCAGAGAGGCT                  | N/A                              |
| CD7-R             | GGAGACTGCTGCACCTCTT                   | N/A                              |
| CDH1-F            | TGCCCAGAAAATGAAAAAGG                  | Albino <i>et al</i> . 2012 (3)   |
| CDH1-R            | GTGTATGTGGCAATGCGTTC                  | Albino et al. 2012 (3)           |

| CDH16-F   | TGCAGAGCTGTCTGTGGAAG    | Sancisi <i>et al</i> . 2013 (4) |
|-----------|-------------------------|---------------------------------|
| CDH16-R   | CCCCTGACAGCACGATCT      | Sancisi <i>et al</i> . 2013 (4) |
| CDK8-F    | CAGAGGCTGTGACAATGGACT   | N/A                             |
| CDK8-R    | ATCCTTCCCATCTTTCCTCTTGG | N/A                             |
| CLDN11-F  | CTCATCCTGCCGGGCTAC      | N/A                             |
| CLDN11-R  | CGGATGCAGGGAAGAACAGT    | N/A                             |
| CLDN14-F  | TCTTGCACATGGGAGCTGGA    | N/A                             |
| CLDN14-R  | CTTCCAGGCATGCAGAAAACCT  | N/A                             |
| CLDN18-F  | TTCCATCCCAGTACCAAAGC    | Ito <i>et al</i> . 2011 (5)     |
| CLDN18-R  | CCGTTCTTTCCCCAGACATA    | Ito <i>et al</i> . 2011 (5)     |
| CXCL10-F  | TTCAAGGAGTACCTCTCTAG    | N/A                             |
| CXCL10-R  | CTGGATTCAGACATCTCTTCTC  | N/A                             |
| CXCL8-F   | TCCTGATTTCTGCAGCTCTGT   | N/A                             |
| CXCL8-R   | AAATTTGGGGTGGAAAGGTT    | N/A                             |
| CXCR2-F   | TGGATTTCCCCCTTGCAACC    | N/A                             |
| CXCR2-R   | AAATCCTGACTGGGTCGCTG    | N/A                             |
| DDX58-F   | GTGCAAAGCCTTGGCATGT     | N/A                             |
| DDX58-R   | TGGCTTGGGATGTGGTCTACTC  | N/A                             |
| DEFB4A-F  | GCTTGATGTCCTCCCCAGACT   | N/A                             |
| DEFB4A-R  | CAGGATCGCCTATACCACCAAA  | N/A                             |
| DTX3-F    | TTCCATGGGCTTTCCAGGTC    | N/A                             |
| DTX3-R    | GCCATTCTGGACAGGACGAA    | N/A                             |
| ECM1-F    | GGTGGGCTGCTCACACATTC    | N/A                             |
| ECM1-R    | AGGGGGACCCACTTCCTTTT    | N/A                             |
| ELF3-F    | CCTGGCGGAACTGGATTTCT    | N/A                             |
| ELF3-R    | CATGAGGCTACCGGAGTGG     | N/A                             |
| GAPDH-F   | GAAGGTGAAGGTCGGAGTA     | N/A                             |
| GAPDH-R   | GAAGATGGTGATGGGATTTC    | N/A                             |
| GAPLINC-F | TGGACTCAGGCACGTTTACA    | N/A                             |
| GAPLINC-R | TGGCACAATCAGGGCTCTTG    | N/A                             |

| GP1BA-F    | TGTGAGGTCTCCAAAGTGGC    | N/A                              |
|------------|-------------------------|----------------------------------|
| GP1BA-R    | TAAGGCATCAGGGTTGCCAG    | N/A                              |
| GP5-F      | GCTTGCAAGTGTGTCTTCCG    | N/A                              |
| GP5-R      | GGCTGTCGGAGATCATGAGG    | N/A                              |
| HSD17B12-F | GGAGCAGCGCCTATTAGTGT    | N/A                              |
| HSD17B12-R | CGAAATACGCAGGGCTAGGT    | N/A                              |
| IFIH1-F    | GTTGAAAAGGCTGGCTGAAAAC  | N/A                              |
| IFIH1-R    | TCGATAACTCCTGAACCACTG   | N/A                              |
| IFIT1-F    | TAGCCAACATGTCCTCACAGAC  | N/A                              |
| IFIT1-R    | TCTTCTACCACTGGTTTCATGC  | N/A                              |
| IFIT2-F    | GGTCTCTTCAGCATTTATTGGTG | Imaizumi <i>et al</i> . 2014 (6) |
| IFIT2-R    | TGCCGTAGGCTGCTCTCCA     | Imaizumi <i>et al</i> . 2014 (6) |
| IFNA1-F    | CAGTTCCAGAAGGCTCCAGC    | Li et <i>et al.</i> 2014 (7)     |
| IFNA1-R    | TCCTCATCCCAAGCAGCAG     | Li et <i>et al.</i> 2014 (7)     |
| IFNB1-F    | TTGAATGGGAGGCTTGAATA    | N/A                              |
| IFNB1-R    | CTATGGTCCAGGCACAGTGA    | N/A                              |
| IFNL1-F    | CGCCTTGGAAGAGTCACTCA    | Bayer <i>et al.</i> 2016 (8)     |
| IFNL1-R    | GAAGCCTCAGGTCCCAATTC    | Bayer <i>et al.</i> 2016 (8)     |
| IFNL2-F    | ACATAGCCCAGTTCAAGTC     | Bayer <i>et al</i> . 2016 (8)    |
| IFNL2-R    | GACTCTTCTAAGGCATCTTTG   | Bayer <i>et al</i> . 2016 (8)    |
| IL10-F     | CGAGATGCCTTCAGCAGAGT    | N/A                              |
| IL10-R     | CGCCTTGATGTCTGGGTCTT    | N/A                              |
| IL13-F     | TGAGGAGCTGGTCAACATCA    | Stellato <i>et al.</i> 2011 (9)  |
| IL13-R     | CAGGTTGATGCTCCATACCAT   | Stellato <i>et al.</i> 2011 (9)  |
| IL5-F      | GAGACCTTGGCACTGCTTTC    | N/A                              |
| IL5-R      | CCCCTTGCACAGTTTGACTC    | N/A                              |
| IL6-F      | CCCTGAGAAAGGAGACATGTAA  | N/A                              |
| IL6-R      | TCTTTTTCAGCCATCTTTGGA   | N/A                              |
| IL7R-F     | CCAACCGGCAGCAATGTATG    | N/A                              |
| IL7R-R     | AGGATCCATCTCCCCTGAGC    | N/A                              |

| IKZF3-F               | AGAGAAGTTCCCTTGAGGAG       | Veistinen <i>et al</i> . 2002 (10)      |
|-----------------------|----------------------------|---|
| IKZF3-R               | TAGCTGATGGCGTTATTGATGG     | Veistinen <i>et al</i> . 2002 (10)      |
| IRF7-F                | GCAGCGTGAGGGTGTGTCTT       | Li et al. 2011 (11)                     |
| IRF7-R                | GCTCCATAAGGAAGCACTCGAT     | Li <i>et al</i> . 2011 (11)             |
| ISG20-F               | CTCCACGAACGTCAAATGCG       | N/A                                     |
| ISG20-R               | ATCAAGTGAAGTCAGGGGCG       | N/A                                     |
| ITGA10-F              | CTGACAGGTCTCTGCTCCCCC      | Mertens-Walker <i>et al</i> . 2015 (12) |
| ITGA10-R              | CCATCGCTGTCCACCCCCAA       | Mertens-Walker <i>et al</i> . 2015 (12) |
| ITGA5-F               | CAAAGGGCCTGGAGTTGGAT       | N/A                                     |
| ITGA5-R               | AGCCTGAAACACTCAGCCTC       | N/A                                     |
| ITGA9-F               | CAAAGGCATCGGCAAGGTTT       | N/A                                     |
| ITGA9-R               | TCCCCATTCAGGTCAACTGC       | N/A                                     |
| ITGB7-F               | TGCCGTCTCCCAGATCAGTA       | N/A                                     |
| ITGB7-R               | GTTTCCACATAGGTGCGTGC       | N/A                                     |
| KCNQ10T1-F            | TACCGGATCCAGGTTTGCAGTACA   | Cao <i>et al.</i> 2015 (2)              |
| KCNQ10T1-R            | GCTGATAAAGGCACCGGAAGGAAA   | Cao <i>et al.</i> 2015 (2)              |
| KDM1B-F               | ACAGAATTGGAGGCCGAGTC       | N/A                                     |
| KDM1B-R               | GAGCGAGCAGATACTTGTTCA      | N/A                                     |
| LPP-F                 | AGACAAGATCGGCCTGAAGAA      | N/A                                     |
| LPP-R                 | CCTCTGATGAGCGTCCAGTG       | N/A                                     |
| OAS1-F                | CGTTGGTGTTGGCATCTTCT       | N/A                                     |
| OAS1-R                | TGTCTGCATTGTCGGCACTT       | N/A                                     |
| OLR1-F                | GAGTAGCAAATTGTTCAGCTCCT    | N/A                                     |
| OLR1-R                | CTCGGACTCTAAATCAGATCAGC    | N/A                                     |
| ORM1-F                | CACCACCTACCTGAATGTCCAGC    | Porez et <i>et al</i> . 2013 (13)       |
| ORM1-R                | GATCAGCAAGTGAGCGAAATGC     | Porez et <i>et al</i> . 2013 (13)       |
| p66 <sup>Shc</sup> -F | AATGAGTCTCTGTCATCGCTGGAG   | Li et <i>et al.</i> 2014 (14)           |
| p66 <sup>Shc</sup> -R | GGCGATGATCTGTTTGCAGTCTGCGG | Li et <i>et al.</i> 2014 (14)           |
| PCDHAC2-F             | CTGGGGAGCTGATAGCCAGA       | N/A                                     |
| PCDHAC2-R             | CCCCTGCTTAACGGGTCTTT       | N/A                                     |

| PDPN-F             | CAACAGTGACCCTGGTTGGA               | N/A                             |
|--------------------|------------------------------------|---------------------------------|
| PDPN-R             | GGCGTAACCCTTCAGCTCTT               | N/A                             |
| SCARF1-F           | ACAGTCTCACATCACGACCC               | N/A                             |
| SCARF1-R           | CTTGGGGTGGCACACAGTAG               | N/A                             |
| SCCPDH-F           | AGCTGGGAAGACCAACACTG               | N/A                             |
| SCCPDH-R           | TCAAGCGAGGCTGGATTAGC               | N/A                             |
| SELE-F             | GGCAGTGGACACAGCAAATC               | N/A                             |
| SELE-R             | TGGACAGCATCGCATCTCA                | N/A                             |
| SEPT9-F            | TGAAGAAGTCTTACTCAGGAGGC            | N/A                             |
| SEPT9-R            | TGGAATTTCTGGGTGGAGCTG              | N/A                             |
| TINAG-F            | GTTCCAAGGAGAAGCCCACA               | N/A                             |
| TINAG-R            | CCGGTCCACATTCTCTGGAA               | N/A                             |
| TLR3-F             | TGTCTGGAAGAAAGGGACTTTGA            | N/A                             |
| TLR3-R             | GTTGAACTGCATGATGTACCTTGA           | N/A                             |
| TNF-F              | TCTTCTCCTTCCTGATCGTG               | N/A                             |
| TNF-R              | GCCAGAGGGCTGATTAGAGA               | N/A                             |
| TNFAIP6-F          | AGCACGGTCTGGCAAATACA               | N/A                             |
| TNFAIP6-R          | ATCCATCCAGCAGCACAGAC               | N/A                             |
| WISP1-F            | GTAAGATGTGCGCTCAGCAG               | N/A                             |
| WISP1-R            | GAAGGACTGGCCGTTGTTGT               | N/A                             |
| oriPtL_BamHI-F     | CGGGGATCCCGTTGCACCCACAACATGTAAGGGC | N/A                             |
| oriPtL-KpnI-R      | GGGGTACCCCTGACACGGGGGGGGGGCCAAAC   | N/A                             |
| ChIP_IFNB141-F     | AGGACCATCTCATATAAATAGGCCATACCC     | Li et <i>et al.</i> 2011(15)    |
| ChIP_IFNB141-R     | ACTGAAAATTGCTGCTTCTTTGTAGGAATC     | Li et <i>et al</i> . 2011 (15)  |
| ChIP_IFNB1_+644-F  | CTCCTAGCCTGTGCCTCTGG               | N/A                             |
| ChIP_IFNB1_+644-R  | ATGCAGTACATTAGCCATCAGTCA           | N/A                             |
| ChIP_CXCL849-F     | GEGCCATCAGTTGCAAATC                | Imamura <i>et al.</i> 2014 (16) |
| ChIP_CXCL849-R     | TTCCTTCCGGTGGTTTCTTC               | Imamura <i>et al.</i> 2014 (16) |
| ChIP_CXCL8_+2918-F | CCAGCTGTGTTGGTAGTGCT               | N/A                             |
| ChIP_CXCL8_+2918-R | AAACAAGTTTCAACCAGCAAGAA            | N/A                             |

A star indicates that the nucleotide has a phosphorothioate backbone and an undisclosed number of flanking nucleotides are LNA nucleotides. N/A; not applicable.

## Supplementary table 2 references

- 1. **Yamamoto T, Iwatsuki K.** 2012. Diversity of Epstein-Barr virus BamHI-A rightward transcripts and their expression patterns in lytic and latent infections. Journal of medical microbiology **61**:1445-1453.
- Cao S, Moss W, O'Grady T, Concha M, Strong MJ, Wang X, Yu Y, Baddoo M, Zhang K, Fewell C, Lin Z, Dong Y, Flemington EK. 2015. New Noncoding Lytic Transcripts Derived from the Epstein-Barr Virus Latency Origin of Replication, oriP, Are Hyperedited, Bind the Paraspeckle Protein, NONO/p54nrb, and Support Viral Lytic Transcription. J Virol 89:7120-7132.
- Albino D, Longoni N, Curti L, Mello-Grand M, Pinton S, Civenni G, Thalmann G, D'Ambrosio G, Sarti M, Sessa F, Chiorino G, Catapano CV, Carbone GM. 2012. ESE3/EHF controls epithelial cell differentiation and its loss leads to prostate tumors with mesenchymal and stem-like features. Cancer Res 72:2889-2900.
- 4. Sancisi V, Gandolfi G, Ragazzi M, Nicoli D, Tamagnini I, Piana S, Ciarrocchi A. 2013. Cadherin 6 is a new RUNX2 target in TGF-beta signalling pathway. PLoS One 8:e75489.
- Ito T, Kojima T, Yamaguchi H, Kyuno D, Kimura Y, Imamura M, Takasawa A, Murata M, Tanaka S, Hirata K, Sawada N. 2011. Transcriptional regulation of claudin-18 via specific protein kinase C signaling pathways and modification of DNA methylation in human pancreatic cancer cells. J Cell Biochem 112:1761-1772.
- Imaizumi T, Numata A, Yano C, Yoshida H, Meng P, Hayakari R, Xing F, Wang L, Matsumiya T, Tanji K, Tatsuta T, Murakami M, Tanaka H. 2014. ISG54 and ISG56 are induced by TLR3 signaling in U373MG human astrocytoma cells: possible involvement in CXCL10 expression. Neurosci Res 84:34-42.
- Li YF, Lee KG, Ou X, Lam KP. 2014. Bruton's tyrosine kinase and protein kinase C micro are required for TLR7/9-induced IKKalpha and IRF-1 activation and interferon-beta production in conventional dendritic cells. PLoS One 9:e105420.
- Bayer A, Lennemann NJ, Ouyang Y, Bramley JC, Morosky S, Marques ET, Jr., Cherry S, Sadovsky Y, Coyne CB. 2016. Type III Interferons Produced by Human Placental Trophoblasts Confer Protection against Zika Virus Infection. Cell Host Microbe 19:705-712.
- Stellato C, Gubin MM, Magee JD, Fang X, Fan J, Tartar DM, Chen J, Dahm GM, Calaluce R, Mori F, Jackson GA, Casolaro V, Franklin CL, Atasoy U. 2011. Coordinate regulation of GATA-3 and Th2 cytokine gene expression by the RNA-binding protein HuR. J Immunol 187:441-449.

- 10. Veistinen E, Liippo J, Lassila O. 2002. Quantification of human Aiolos splice variants by real-time PCR. J Immunol Methods **271:**113-123.
- 11. Li Q, Tainsky MA. 2011. Epigenetic silencing of IRF7 and/or IRF5 in lung cancer cells leads to increased sensitivity to oncolytic viruses. PLoS One 6:e28683.
- Mertens-Walker I, Fernandini BC, Maharaj MS, Rockstroh A, Nelson CC, Herington AC, Stephenson SA. 2015. The tumour-promoting receptor tyrosine kinase, EphB4, regulates expression of integrin-beta8 in prostate cancer cells. BMC Cancer 15:164.
- Porez G, Gross B, Prawitt J, Gheeraert C, Berrabah W, Alexandre J, Staels B, Lefebvre
  P. 2013. The hepatic orosomucoid/alpha1-acid glycoprotein gene cluster is regulated by the nuclear bile acid receptor FXR. Endocrinology 154:3690-3701.
- Li X, Xu Z, Du W, Zhang Z, Wei Y, Wang H, Zhu Z, Qin L, Wang L, Niu Q, Zhao X, Girard L, Gong Y, Ma Z, Sun B, Yao Z, Minna JD, Terada LS, Liu Z. 2014. Aiolos promotes anchorage independence by silencing p66Shc transcription in cancer cells. Cancer Cell 25:575-589.
- Li P, Wong JJ, Sum C, Sin WX, Ng KQ, Koh MB, Chin KC. 2011. IRF8 and IRF3 cooperatively regulate rapid interferon-beta induction in human blood monocytes. Blood 117:2847-2854.
- 16. Imamura K, Imamachi N, Akizuki G, Kumakura M, Kawaguchi A, Nagata K, Kato A, Kawaguchi Y, Sato H, Yoneda M, Kai C, Yada T, Suzuki Y, Yamada T, Ozawa T, Kaneki K, Inoue T, Kobayashi M, Kodama T, Wada Y, Sekimizu K, Akimitsu N. 2014. Long noncoding RNA NEAT1-dependent SFPQ relocation from promoter region to paraspeckle mediates IL8 expression upon immune stimuli. Mol Cell 53:393-406.