

Figure S1. Relative contribution of the most common base exchanges within our angioimmunoblastic T-cell lymphoma samples to the mutational profiles.

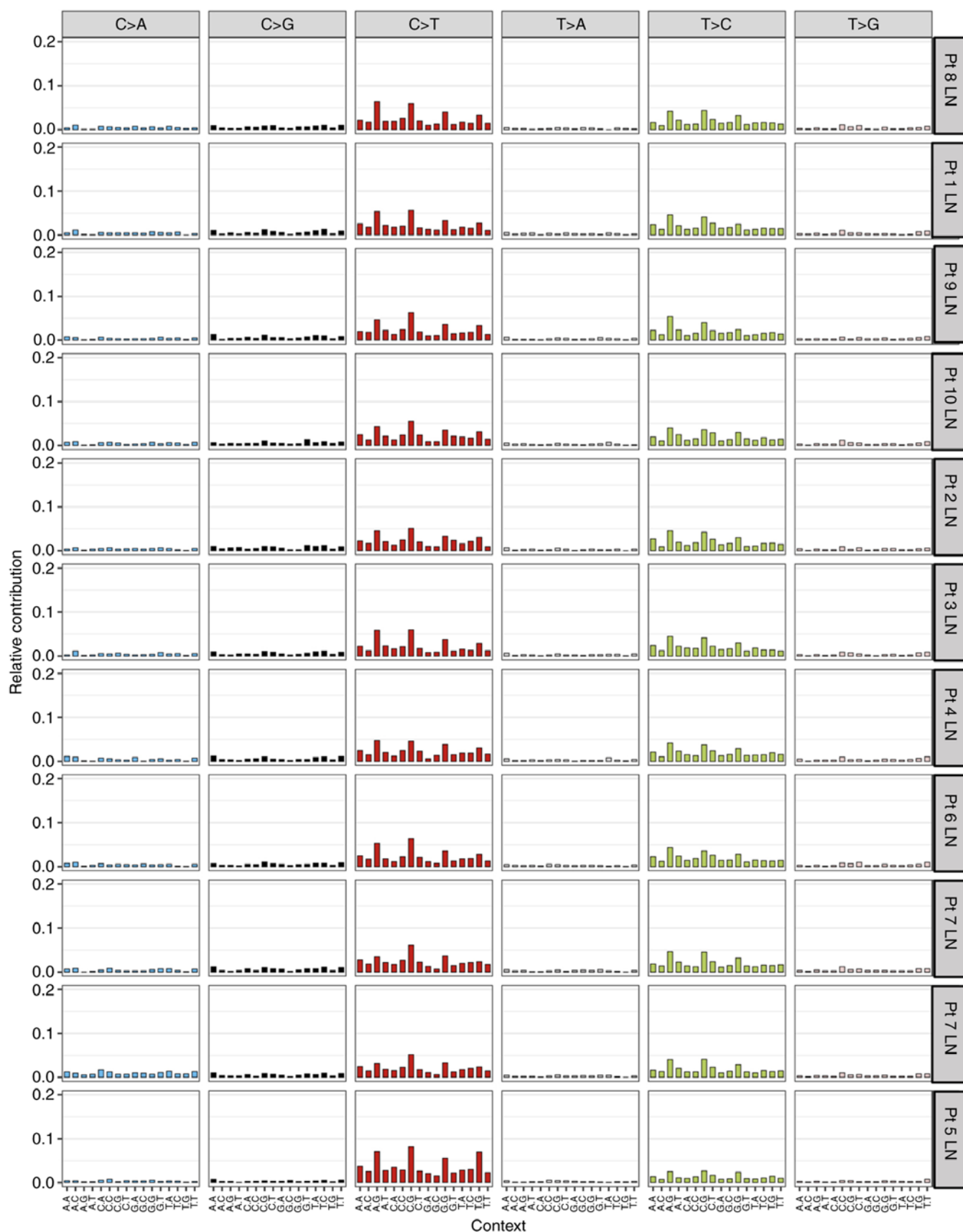


Figure S2. Kaplan-Meier survival plot of patients with angio-immunoblastic T-cell lymphoma. Red, EBV negative cases. Blue, EBV positive cases. EBV, Epstein Barr Virus; pos, positive; neg, negative.

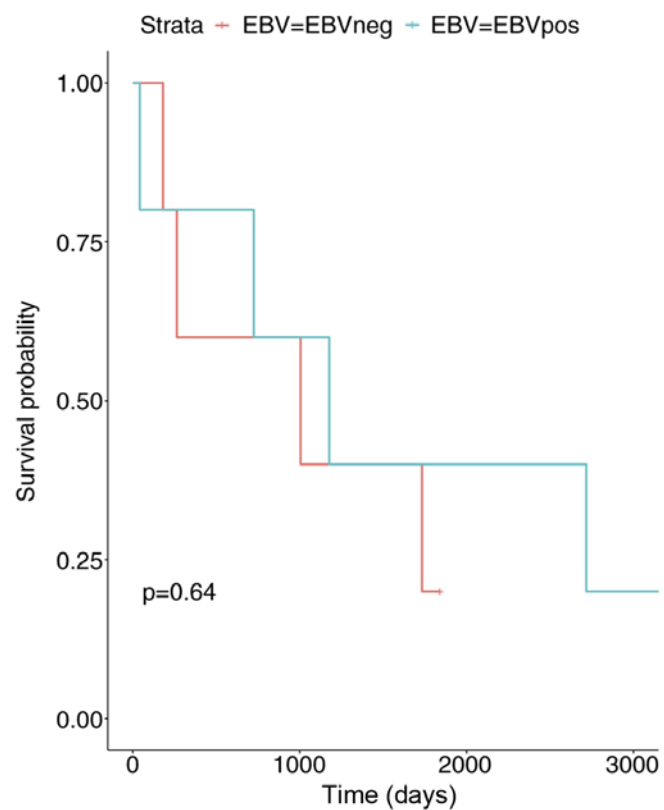


Figure S3. Principal component analysis of gene expression profile of angioimmunoblastic T-cell lymphoma. Shown is the PCA for *RHOA* mutational status and EBV infection status determined by NGS (see color key). EBV, Epstein Barr Virus; NGS, next generation sequencing; RHOA, ras homolog family member A.

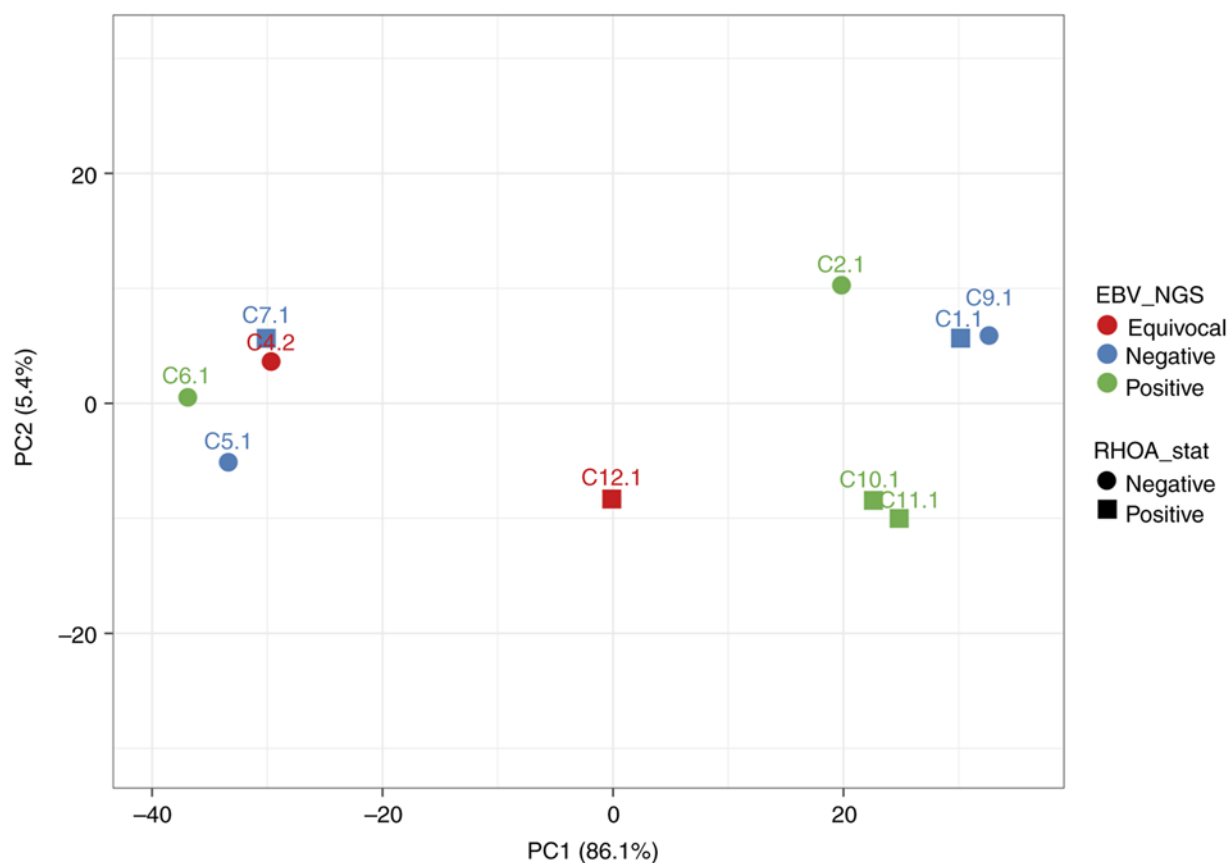


Figure S4. Heatmaps with hierarchical clustering by Euclidean distance for the relative contribution of cosmic signatures within the mutational pattern of angioimmunoblastic T-cell lymphoma cases. A, bone marrow tissues.

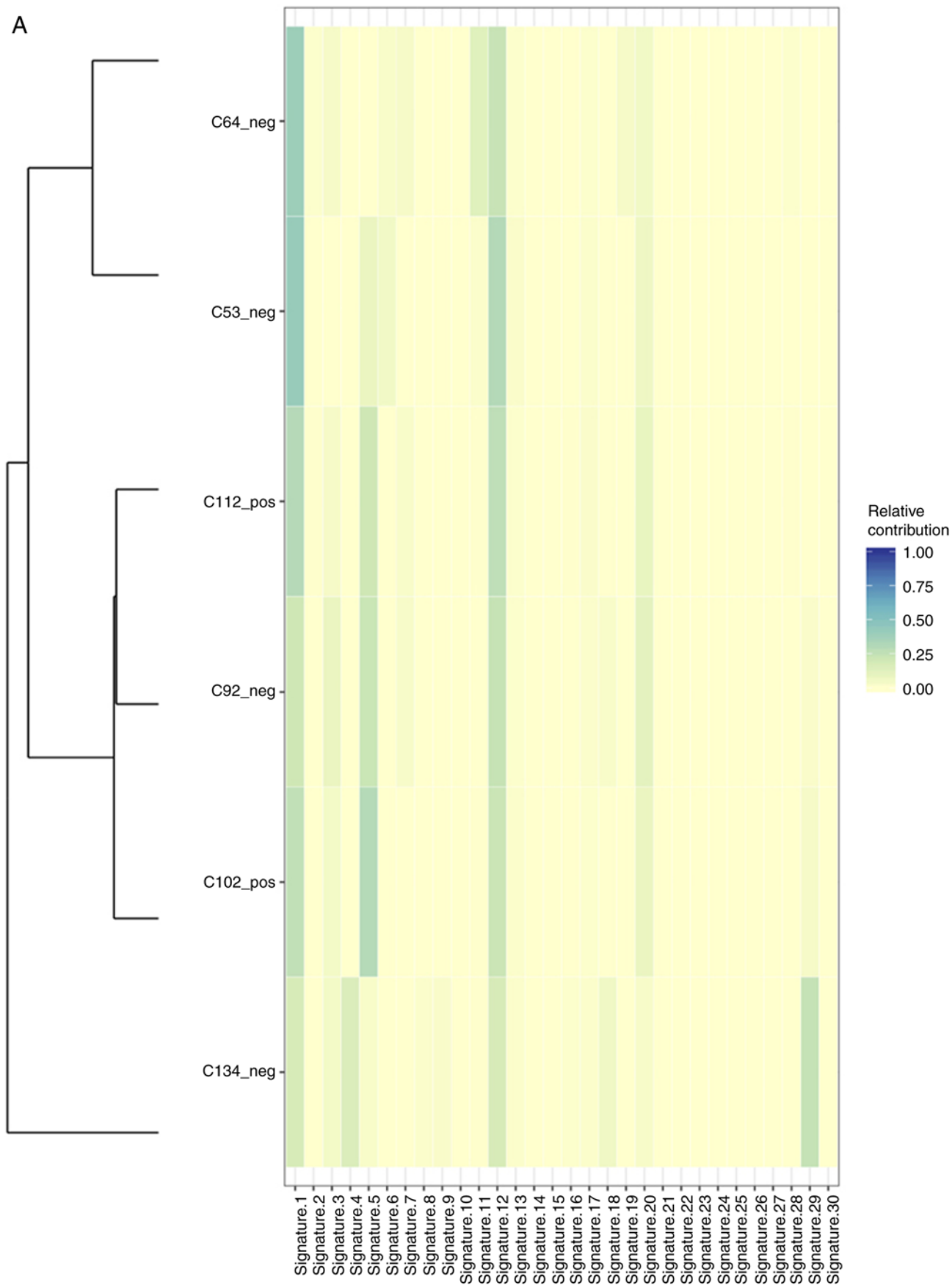


Figure S4 (Continued). Heatmaps with hierarchical clustering by Euclidean distance for the relative contribution of cosmic signatures within the mutational pattern of angioimmunoblastic T-cell lymphoma cases. B, lymph node tissues. Case numbers are tagged with 'pos' for *RHOA* positive mutational status and 'neg' for *RHOA* negative status. *RHOA*, ras homolog family member A.

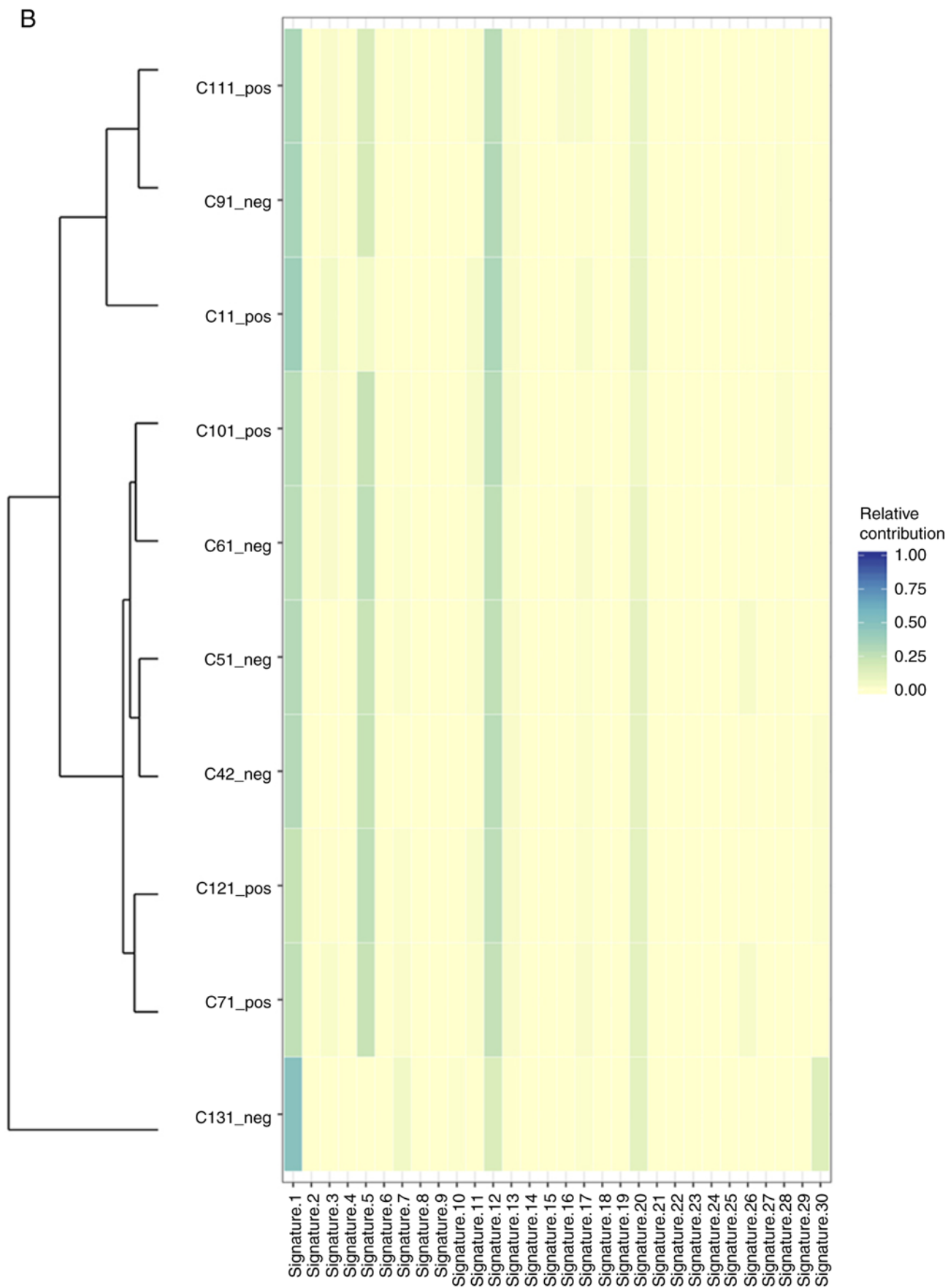


Table SI. Genes and microbes in Heme Malignancy Evaluation and Infectious Disease panel (HeME-ID).

|          |            |        |          |            |        |         |
|----------|------------|--------|----------|------------|--------|---------|
| ABL1     | CCND2      | DNAH5  | GATA3    | IRF4       | MKL1   | PHF6    |
| ABL2     | CCND3      | DNAH9  | GNA13    | IRF8       | MPL    | PIGA    |
| AKT1     | CCR4       | DNM2   | GNAI2    | IRS4       | MSH4   | PIK3CA  |
| ALK      | CCR7       | DNMT1  | GNAS     | ITK        | MSN    | PIK3CD  |
| ANKRD11  | CD274/PDL1 | DNMT3A | GNB1     | JAK1       | MTOR   | PIK3R4  |
| APLN     | CD28       | DUSP22 | GPRC5D   | JAK2       | MYC    | PIK3R5  |
| ARID1A   | CD58       | ECT2L  | GRM1     | JAK3       | MYD88  | PIM1    |
| ARID1B   | CD79A      | EED    | GTF2I    | JAKMIP2    | MYH11  | PIM3    |
| ARID2    | CD79B      | EIF4A1 | HMCN1    | KCNH5      | MYH9   | PLCG1   |
| ARID5B   | CDH10      | ELN    | HNRNPA1  | KCNH8      | NAV2   | PLCG2   |
| ASXL1    | CDH11      | EP300  | HNRNPR   | KDM6A      | NCKAP5 | PML     |
| ASXL3    | CDH18      | EPHA8  | HRAS     | KDM6B      | NCOR1  | POLE    |
| ATM      | CDKN2A     | EPHB3  | HSD17B13 | KIF23      | NF1    | POT1    |
| ATP2B3   | CDKN2B     | EPHB4  | ICOS     | KIT        | NFKB1  | PRDM1   |
| ATRX     | CDKN2C     | EPOR   | ID3      | KLF2       | NFKB2  | PRF1    |
| B2M      | CELSR2     | EPS8   | IDH1     | KLHL6      | NFKBIE | PRKCB   |
| BANK1    | CEPBA      | ERBB4  | IDH2     | KMT2A      | NKD1   | PTEN    |
| BCL11A   | CHD2       | ETNK1  | IGHA1    | KMT2C      | NLRP12 | PTPN1   |
| BCL11B   | CHD8       | ETV6   | IGHA2    | KMT2D      | NOL4   | PTPN11  |
| BCL2     | CIITA      | EZH2   | IGHG1    | KRAS       | NOTCH1 | PTPN2   |
| BCL6     | CNOT1      | FAS    | IGHG2    | LAMB1      | NOTCH2 | PTPRM   |
| BCOR     | CNOT3      | FAT1   | IGHG3    | LAMB2      | NPHS1  | PTPRT   |
| BCORL1   | COL22A1    | FAT2   | IGHG4    | LCK        | NPM1   | RAD21   |
| BCR      | CREBBP     | FAT4   | IGHJ1    | LCT        | NR4A3  | RARA    |
| BIRC3    | CRLF2      | FBXW10 | IGHJ2    | LIMCH1     | NRAS   | RB1     |
| BRAF     | CSF3R      | FBXW7  | IGHJ3    | LMO1       | NRP1   | RBM15   |
| BTG1     | CSMD3      | FGFR3  | IGHJ4    | LMO2       | NRSN1  | RELN    |
| BTK      | CTCF       | FLG2   | IGHJ5    | LPA        | NT5C2  | RHOA    |
| CACNA1C  | CTLA4      | FLT3   | IGHJ6    | LYL1       | NTRK3  | RHOB    |
| CACNA2D1 | CTNNB1     | FMNL2  | IGHM     | MALT1      | NUP214 | RHOT2   |
| CALR     | CUX1       | FOXA3  | IKZF1    | MAP2K1     | NUP98  | RIMS1   |
| CARD11   | CXCR4      | FOXO1  | IKZF2    | MAPK1      | PAX5   | RPL10   |
| CBL      | DCC        | FOXO3  | IKZF3    | MBNL1      | PCLO   | RPN1    |
| CBLB     | DDX31      | FOXO4  | IL7R     | EV11/MECOM | PCM1   | RPS15   |
| CBL      | DDX3X      | FYN    | INO80    | MEF2B      | PDCD1  | RTF1    |
| CCDC85A  | DDX58      | GATA1  | INTS8    | MEGF6      | PDGFRA | RUNX1   |
| CCND1    | DDX60      | GATA2  | IQGAP2   | MGA        | PDGFRB | RUNX1T1 |
| RYR3     | SIL1       |        |          |            |        |         |
| S1PR1    | TRGV1      |        |          |            |        |         |
| S1PR2    | TRGV2      |        |          |            |        |         |
| SALL3    | TRGV8      |        |          |            |        |         |
| SAMD9    | TRGV11     |        |          |            |        |         |
| SCN2A    | TRAF1      |        |          |            |        |         |
| SEC24D   | U2AF1      |        |          |            |        |         |
| SEPT5    | U2AF2      |        |          |            |        |         |
| SEPT6    | UBP1       |        |          |            |        |         |
| SEPT9    | UBR5       |        |          |            |        |         |
| SET      | ULK4       |        |          |            |        |         |
| SETBP1   | UNC5D      |        |          |            |        |         |
| SETD2    | VAV1       |        |          |            |        |         |
| SF3B1    | WAS        |        |          |            |        |         |
| SGK1     | WHSC1/NSD2 |        |          |            |        |         |
| SH2B3    | WT1        |        |          |            |        |         |
| SLFN5    | XPO1       |        |          |            |        |         |
| SMARCA2  | YTHDF2     |        |          |            |        |         |
| SMARCB1  | ZAP70      |        |          |            |        |         |
| SMC1A    | ZEB1       |        |          |            |        |         |
| SMC3     | ZFHX2      |        |          |            |        |         |
| SOCS1    | ZFHX3      |        |          |            |        |         |

Table SI. Continued.

|                     |       |
|---------------------|-------|
| SOCS3               | ZRSR2 |
| SPEG                |       |
| SPEN                |       |
| SRF                 |       |
| SRGAP3              |       |
| SRSF2               |       |
| STAG1               |       |
| STAG2               |       |
| STAG3               |       |
| STAT1               |       |
| STAT3               |       |
| STAT5A              |       |
| STAT5B              |       |
| STAT6               |       |
| Microbe             |       |
| EBV                 |       |
| HHV8                |       |
| HTLV-1              |       |
| HTLV-2              |       |
| CMV                 |       |
| HIV1                |       |
| HIV2                |       |
| HSV1                |       |
| HSV2                |       |
| B19                 |       |
| Helicobacter Pylori |       |
| Bartonella henselae |       |
| Treponema pallidum  |       |

Table SII. Quantitative sequencing results showing Epstein Barr Virus detection only.

| Case    | Tissue | Region | Coverage,<br>% | Sequencing<br>depth |
|---------|--------|--------|----------------|---------------------|
| Case1   | LN     | 1      | 11.5           | 0.8                 |
|         |        | 2      | 0              | 0.07                |
|         |        | 3      | 5.7            | 0.5                 |
| Case 2  | LN     | 1      | 64.1           | 4.0                 |
|         |        | 2      | 13.2           | 1.4                 |
|         |        | 3      | 39.6           | 2.8                 |
| Case 3  | LN     | 1      | 0              | 0.13                |
|         |        | 2      | 0              | 0.13                |
|         |        | 3      | 0              | 0.19                |
|         | BM     | 1      | 0              | 0.06                |
|         |        | 2      | 0              | 0.06                |
|         |        | 3      | 0              | 0.07                |
| Case 4  | LN     | 1      | 100            | 448                 |
|         |        | 2      | 100            | 402                 |
|         |        | 3      | 100            | 406                 |
|         | BM     | 1      | 8.5            | 0.5                 |
|         |        | 2      | 0              | 0.2                 |
|         |        | 3      | 6              | 0.5                 |
| Case 5  | LN     | 1      | 0              | 0.03                |
|         |        | 2      | 0              | 0                   |
|         |        | 3      | 5.3            | 0.85                |
| Case 6  | LN     | 1      | 0              | 0.15                |
|         |        | 2      | 5.4            | 0.53                |
|         |        | 3      | 0              | 0.2                 |
|         | BM     | 1      | 0              | 0                   |
|         |        | 2      | 0              | 0                   |
|         |        | 3      | 0              | 0                   |
| Case 7  | LN     | 1      | 87             | 9.2                 |
|         |        | 2      | 88             | 9.2                 |
|         |        | 3      | 87             | 10.2                |
|         | BM     | 1      | 0              | 0                   |
|         |        | 2      | 0              | 0                   |
|         |        | 3      | 0              | 0                   |
| Case 8  | LN     | 1      | 99.7           | 18.8                |
|         |        | 2      | 78.3           | 12.6                |
|         |        | 3      | 89.4           | 13.8                |
|         | BM     | 1      | 0              | 0                   |
|         |        | 2      | 0              | 0                   |
|         |        | 3      | 0              | 0                   |
| Case 9  |        | 1      | 51.8           | 3.8                 |
|         |        | 2      | 46.8           | 3.4                 |
|         |        | 3      | 53.8           | 3.5                 |
| Case 10 | LN     | 1      | 100            | 2117                |
|         |        | 2      | 89.7           | 1643                |
|         |        | 3      | 100            | 1842                |
|         | BM     | 1      | 8.8            | 0.5                 |
|         |        | 2      | 6.7            | 0.4                 |
|         |        | 3      | 8.6            | 0.7                 |
|         | BM     | 1      | 63.3           | 12.7                |
|         |        | 2      | 49.5           | 7                   |
|         |        | 3      | 59.4           | 10.6                |
|         | BM     | 1      | 10.2           | 0.6                 |
|         |        | 2      | 12.9           | 0.7                 |
|         |        | 3      | 6.6            | 0.5                 |

LN, lymph node; BM, bone marrow.