# Validation of LymphGen classification on a 400-gene clinical next-generation sequencing panel in diffuse large B-cell lymphoma: real-world experience from a cancer center

## Authors

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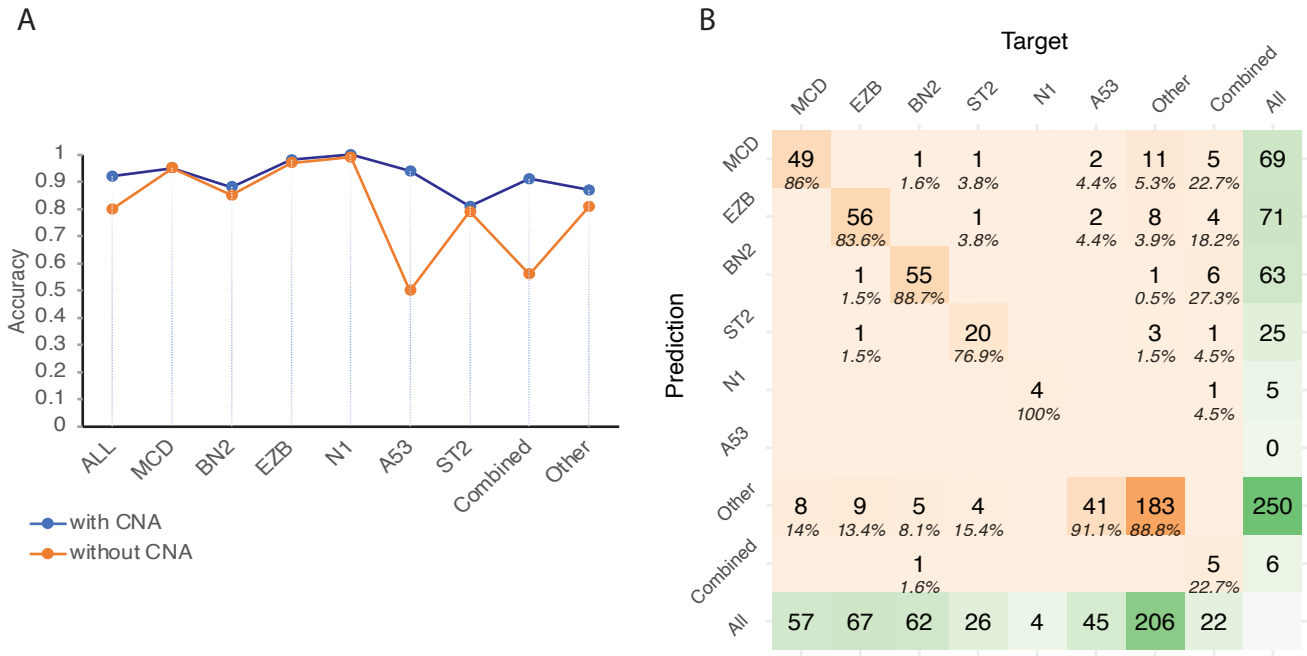
Supplementary Figure 1

# MSK-HEME IMPACT - a 400 gene targeted NGS panel designed for hematopoietic malignancy

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| ABL1 | BCL2 | CEBPA | ETV6 | HGF | JUN | MSH2 | PHF6 | RPTOR | SRSF2 | ZRSR2 |
| ACTG1 | BCL6 | CHEK1 | EZH2 | HIF1A | KDM5A | MSH6 | PIGA | RRAGC | STAG1 | H1B |
| AKT1 | BCOR | CHEK2 | FAM46C | HIST1H1B | KDM5C | MTOR | PIK3C2G | RTEL1 | STAG2 | H1-2 |
| AKT2 | BCORL1 | CIC | FANCA | HIST1H1C | KDM6A | MUTYH | PIK3C3 | RUNX1 | STAT3 | H1D |
| AKT3 | BCR | CIITA | FANCC | HIST1H1D | KDR | MYC | PIK3CA | RUNX1T1 | STAT5A | H1E |
| ALK | BIRC3 | CRBN | FANCD2 | HIST1H1E | KEAP1 | MYCL1 | PIK3CG | SAMHD1 | STAT5B | H2AC |
| ALOX12B | BLM | CREBBP | FAS | HIST1H2AC | KIT | MYCN | PIK3R1 | SDHA | STAT6 | H2AG |
| AMER1 | BRAF | CRKL | FAT1 | HIST1H2AG | KMT2A | MYD88 | PIK3R2 | SDHB | STK11 | H2AL |
| APC | BRCA1 | CRLF2 | FBXO11 | HIST1H2AL | KMT2B | NBN | PIM1 | SDHC | SUFU | H2AM |
| AR | BRCA2 | CSF1R | FBXW7 | HIST1H2AM | KMT2C | NCOR1 | PLCG1 | SDHD | SUZ12 | H2BC |
| ARAF | BRD4 | CSF3R | FGF19 | HIST1H2BC | KMT2D | NCOR2 | PLCG2 | SETBP1 | SYK | H2BC5 |
| ARHGEF28 | BRIP1 | CTCF | FGF3 | HIST1H2BD | KRAS | NCSTN | PMS2 | SETD1A | TBL1XR1 | H2BG |
| ARID1A | BTG1 | CTNNB1 | FGF4 | HIST1H2BG | KSR2 | NF1 | PNRC1 | SETD1B | TBX3 | H2BJ |
| ARID1B | BTK | CUX1 | FGFR1 | HIST1H2BJ | LCK | NF2 | POT1 | SETD2 | TERT | H2BK |
| ARID2 | CALR | CXCR4 | FGFR2 | HIST1H2BK | LMO1 | NFE2 | PPP2R1A | SETD3 | TET1 | H2BO |
| ARID3A | CARD11 | CYLD | FGFR3 | HIST1H2BO | LTB | NFE2L2 | PRDM1 | SETD4 | TET2 | H3C2 |
| ARID3B | CASP8 | DAXX | FGFR4 | HIST1H3B | MALT1 | NKX2-1 | PRKAR1A | SETD5 | TET3 | H3C8 |
| ARID3C | CBFB | DDR2 | FLCN | HIST1H3G | MAP2K1 | NOTCH1 | PTCH1 | SETD6 | TGFBR2 | |
| ARID4A | CBL | DDX3X | FLT1 | HLA-A | MAP2K2 | NOTCH2 | PTEN | SETD7 | TNFAIP3 | |
| ARID4B | CCND1 | DIS3 | FLT3 | HNF1A | MAP2K4 | NOTCH3 | PTPN1 | SETD8 | TNFRSF14 | |
| ARID5A | CCND2 | DNMT3A | FLT4 | HRAS | MAP3K1 | NOTCH4 | PTPN11 | SETDB1 | TOP1 | |
| ARID5B | CCND3 | DOT1L | FOXL2 | ID3 | MAP3K13 | NPM1 | PTPN2 | SETDB2 | TP53 | |
| ASXL1 | CCNE1 | DTX1 | FOXO1 | IDH1 | MAP3K14 | NRAS | RAD21 | SF3B1 | TP63 | |
| ASXL2 | CD274 | DUSP22 | FOXP1 | IDH2 | MAPK1 | NSD1 | RAD50 | SGK1 | TRAF2 | |
| ATM | CD28 | EED | FURIN | IGF1 | MAPK3 | NT5C2 | RAD51 | SH2B3 | TRAF3 | |
| ATP6AP1 | CD58 | EGFR | FYN | IGF1R | MCL1 | NTRK1 | RAD51B | SMAD2 | TRAF5 | |
| ATP6V1B2 | CD79A | EGR1 | GATA1 | IGF2 | MDM2 | NTRK2 | RAD51C | SMAD4 | TSC1 | |
| ATR | CD79B | EP300 | GATA2 | IKBKE | MDM4 | NTRK3 | RAD51D | SMARCA4 | TSC2 | |
| ATRX | CDC73 | EP400 | GATA3 | IKZF1 | MED12 | P2RY8 | RAD52 | SMARCB1 | TSHR | |
| ATXN2 | CDH1 | EPHA3 | GNA11 | IKZF3 | MEF2B | PAK7 | RAD54L | SMARCD1 | TYK2 | |
| AURKA | CDK12 | EPHA5 | GNA12 | IL7R | MEN1 | PALB2 | RAF1 | SMC1A | U2AF1 | |
| AURKB | CDK4 | EPHA7 | GNA13 | INPP4B | MET | PARP1 | RARA | SMC3 | U2AF2 | |
| AXIN1 | CDK6 | EPHB1 | GNAQ | IRF1 | MGA | PAX5 | RB1 | SMG1 | UBR5 | |
| AXL | CDK8 | ERBB2 | GNAS | IRF4 | MGAM | PBRM1 | REL | SMO | VAV1 | |
| B2M | CDKN1B | ERBB3 | GNB1 | IRF8 | MITF | PCBP1 | RET | SOCS1 | VAV2 | |
| BACH2 | CDKN2A | ERBB4 | GRIN2A | IRS2 | MLH1 | PDCD1 | RHOA | SOX2 | VHL | |
| BAP1 | CDKN2Ap14ARF | ERG | GSK3B | JAK1 | MOB3B | PDGFRA | RICTOR | SP140 | WHSC1 | |
| BARD1 | CDKN2Ap16INK4A | ESCO2 | HDAC1 | JAK2 | MPEG1 | PDGFRB | RNF43 | SPEN | WT1 | |
| BCL10 | CDKN2B | ESR1 | HDAC4 | JAK3 | MPL | PDPK1 | ROBO1 | SPOP | XBP1 | |
| BCL11B | CDKN2C | ETNK1 | HDAC7 | JARID2 | MRE11A | PDS5B | ROS1 | SRC | XPO1 | |

Supplementary Figure 1: Gene list of MSK IMPACT HEME, a 400 gene targeted NGS panel designed for hematopoitic malignancy.

Supplementary Figure 2



Supplementary Figure 3

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| Gene | Enriched in | A53 | BN2 | EZB | MCD | N1 | ST2 | p-Value |
|---|---|---|---|---|---|---|---|---|
| ACTG1 | ST2 | 0.0% | 7.7% | 5.8% | 7.5% | 0.0% | 40.7% | 8.68E-06 |
| TET2 | ST2 | 28.6% | 2.6% | 7.0% | 5.0% | 0.0% | 33.3% | 1.04E-04 |
| SOCS1 | ST2 | 14.3% | 15.4% | 24.4% | 25.0% | 9.1% | 63.0% | 2.97E-04 |
| HIST1H1D | ST2 | 0.0% | 5.1% | 8.1% | 0.0% | 0.0% | 25.9% | 2.93E-03 |
| STAT3 | ST2 | 14.3% | 15.4% | 9.3% | 0.0% | 0.0% | 29.6% | 4.43E-03 |
| NOTCH1 | N1 | 14.3% | 2.6% | 2.3% | 5.0% | 100.0% | 0.0% | 0 |
| EPHB1 | N1 | 0.0% | 0.0% | 0.0% | 0.0% | 18.2% | 0.0% | 7.44E-07 |
| ASXL1 | N1 | 0.0% | 0.0% | 1.2% | 5.0% | 27.3% | 0.0% | 4.93E-05 |
| AKT2 | N1 | 0.0% | 0.0% | 0.0% | 0.0% | 9.1% | 0.0% | 2.73E-03 |
| PTPN11 | N1 | 0.0% | 0.0% | 0.0% | 0.0% | 9.1% | 0.0% | 2.73E-03 |
| KRAS | N1 | 0.0% | 0.0% | 1.2% | 2.5% | 18.2% | 0.0% | 3.89E-03 |
| MYD88 | MCD | 14.3% | 25.6% | 4.7% | 92.5% | 18.2% | 0.0% | 0 |
| PIM1 | MCD | 28.6% | 25.6% | 12.8% | 95.0% | 9.1% | 33.3% | 0 |
| ETV6 | MCD | 14.3% | 0.0% | 5.8% | 57.5% | 9.1% | 0.0% | 3.11E-15 |
| CD79B | MCD | 0.0% | 28.2% | 4.7% | 57.5% | 0.0% | 3.7% | 5.81E-12 |
| MPEG1 | MCD | 0.0% | 10.3% | 0.0% | 40.0% | 9.1% | 7.4% | 7.35E-09 |
| CDKN2A | MCD | 28.6% | 35.9% | 12.8% | 67.5% | 36.4% | 11.1% | 1.38E-08 |
| CDKN2B | MCD | 28.6% | 20.5% | 8.1% | 55.0% | 9.1% | 7.4% | 5.87E-08 |
| SETD1B | MCD | 42.9% | 12.8% | 10.5% | 52.5% | 18.2% | 14.8% | 2.38E-06 |
| PPP2R1A | MCD | 0.0% | 0.0% | 1.2% | 20.0% | 0.0% | 0.0% | 1.55E-05 |
| U2AF2 | MCD | 0.0% | 0.0% | 0.0% | 20.0% | 0.0% | 7.4% | 3.56E-05 |
| TBL1XR1 | MCD | 0.0% | 7.7% | 9.3% | 40.0% | 0.0% | 11.1% | 3.72E-05 |
| HLA-A | MCD | 14.3% | 30.8% | 5.8% | 40.0% | 9.1% | 14.8% | 8.06E-05 |
| TNFRSF14 | EZB | 14.3% | 20.5% | 54.7% | 2.5% | 18.2% | 25.9% | 7.65E-08 |
| CREBBP | EZB | 0.0% | 18.0% | 54.7% | 15.0% | 27.3% | 11.1% | 3.30E-07 |
| EZH2 | EZB | 0.0% | 5.1% | 34.9% | 2.5% | 9.1% | 7.4% | 4.11E-06 |
| KMT2D | EZB | 28.6% | 28.2% | 59.3% | 25.0% | 18.2% | 14.8% | 2.07E-05 |
| MEF2B | EZB | 0.0% | 0.0% | 24.4% | 12.5% | 0.0% | 7.4% | 2.13E-03 |
| NOTCH2 | BN2 | 0.0% | 41.0% | 3.5% | 2.5% | 9.1% | 0.0% | 5.26E-10 |
| DTX1 | BN2 | 0.0% | 48.7% | 5.8% | 17.5% | 0.0% | 11.1% | 8.26E-08 |
| SPEN | BN2 | 14.3% | 35.9% | 2.3% | 2.5% | 0.0% | 11.1% | 2.87E-07 |
| BCL10 | BN2 | 0.0% | 25.6% | 0.0% | 7.5% | 9.1% | 0.0% | 8.23E-06 |
| TNFAIP3 | BN2 | 14.3% | 43.6% | 16.3% | 5.0% | 9.1% | 25.9% | 6.55E-04 |
| BCL2 | A53 | 57.1% | 5.1% | 57.0% | 15.0% | 9.1% | 11.1% | 2.23E-10 |
| IRF4 | A53 | 42.9% | 7.7% | 5.8% | 40.0% | 9.1% | 7.4% | 2.41E-06 |
| NCSTN | A53 | 28.6% | 5.1% | 0.0% | 0.0% | 0.0% | 0.0% | 5.96E-06 |
| SDHB | A53 | 14.3% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 2.18E-05 |
| PRDM1 | A53 | 28.6% | 18.0% | 1.2% | 22.5% | 0.0% | 3.7% | 3.13E-04 |
| RAD51 | A53 | 28.6% | 0.0% | 2.3% | 5.0% | 0.0% | 0.0% | 1.43E-03 |
| MAP2K2 | A53 | 28.6% | 7.7% | 1.2% | 5.0% | 0.0% | 0.0% | 5.28E-03 |

**Supplementary Figure 1:** Gene list of IMPACT, a 400 gene targeted NGS panel designed for hematopoietic malignancy.

**Supplementary Figure 2:** Contribution of copy number alteration: A) Performance of NCI samples filtered by IMPACT panel with or without copy number alterations. B) Confusion matrix comparing the performance with or without copy number alterations. The target represents the classification with copy number alteration; The prediction represents the classification without copy number alteration. The center number shows the number of cases; the percentage represents the portion of cases classified without copy number alteration for certain subtypes in the cases classified with copy number alteration for the same subtype (considered as ground truth in this comparison).

**Supplementary Figure 3:** List of important genes enriched in subtypes in the IMPACT panel. The genes with mutations significantly enriched in each subtype in IMPACT panel were identified. The percentage of cases carrying the specific mutation in each subtype is shown in the table. P-value represents the significance of the enrichment.