**Supplemental Table S4. Lists of the GSEA significant gene-sets across DLBCL cell lines according to higher (A) of lower (B) sensitivity to OTX015.** Up to the ten most significantly enriched gene-sets for each studied gene-sets collection are shown.

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| --- | --- | --- | --- | --- |
| **Table S4** |  |  |  |  |
| **MSigDB Collections** | **name** | **normalized enrichment score** | **Nominal p value** | **FDR q-val** |
| C2: Reactome | INTERFERON\_SIGNALING | 2.56E+00 | 0.00E+00 | 0.00E+00 |
| C2: Reactome | INTERFERON\_GAMMA\_SIGNALING | 2.49E+00 | 0.00E+00 | 0.00E+00 |
| C2: Reactome | INTERFERON\_ALPHA\_BETA\_SIGNALING | 2.48E+00 | 0.00E+00 | 0.00E+00 |
| C2: Reactome | CYTOKINE\_SIGNALING\_IN\_IMMUNE\_SYSTEM | 2.25E+00 | 0.00E+00 | 0.00E+00 |
| C2: Reactome | GLYCOLYSIS | 2.05E+00 | 0.00E+00 | 8.27E-04 |
| C2: Reactome | REGULATION\_OF\_IFNA\_SIGNALING | 1.92E+00 | 0.00E+00 | 8.60E-03 |
| C2: Reactome | ANTIVIRAL\_MECHANISM\_BY\_IFN\_STIMULATED\_GENES | 1.74E+00 | 0.00E+00 | 1.00E-01 |
| C2: Reactome | CHONDROITIN\_SULFATE\_BIOSYNTHESIS | 1.73E+00 | 2.13E-03 | 1.09E-01 |
| C2: Reactome | TRAF6\_MEDIATED\_IRF7\_ACTIVATION | 1.73E+00 | 4.16E-03 | 9.70E-02 |
| C2: Reactome | COSTIMULATION\_BY\_THE\_CD28\_FAMILY | 1.72E+00 | 4.04E-03 | 9.88E-02 |
| C2: BioCarta | IL6\_PATHWAY | 1.91E+00 | 0.00E+00 | 3.39E-02 |
| C2: BioCarta | INFLAM\_PATHWAY | 1.82E+00 | 0.00E+00 | 6.30E-02 |
| C2: BioCarta | IL10\_PATHWAY | 1.82E+00 | 0.00E+00 | 4.38E-02 |
| C2: BioCarta | ERYTH\_PATHWAY | 1.76E+00 | 0.00E+00 | 7.18E-02 |
| C2: BioCarta | IL22BP\_PATHWAY | 1.70E+00 | 6.20E-03 | 1.20E-01 |
| C2: BioCarta | DC\_PATHWAY | 1.70E+00 | 8.32E-03 | 1.04E-01 |
| C2: BioCarta | EGF\_PATHWAY | 1.67E+00 | 1.13E-02 | 1.19E-01 |
| C2: BioCarta | PDGF\_PATHWAY | 1.61E+00 | 2.11E-02 | 1.72E-01 |
| C2: BioCarta | IL12\_PATHWAY | 1.59E+00 | 3.20E-02 | 1.85E-01 |
| C2: BioCarta | PTEN\_PATHWAY | 1.56E+00 | 3.63E-02 | 2.15E-01 |
| C2: chemical and genetic perturbations | TAKEDA\_TARGETS\_OF\_NUP98\_HOXA9\_FUSION\_3D\_UP | 2.51E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | HECKER\_IFNB1\_TARGETS | 2.51E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | BROWNE\_INTERFERON\_RESPONSIVE\_GENES | 2.42E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | SANA\_RESPONSE\_TO\_IFNG\_UP | 2.40E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | DAUER\_STAT3\_TARGETS\_DN | 2.34E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | BROCKE\_APOPTOSIS\_REVERSED\_BY\_IL6 | 2.33E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | ICHIBA\_GRAFT\_VERSUS\_HOST\_DISEASE\_D7\_UP | 2.31E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | ELVIDGE\_HYPOXIA\_BY\_DMOG\_UP | 2.31E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | MOSERLE\_IFNA\_RESPONSE | 2.29E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | ELVIDGE\_HYPOXIA\_UP | 2.28E+00 | 0.00E+00 | 0.00E+00 |
| C2: KEGG | TYPE\_I\_DIABETES\_MELLITUS | 1.91E+00 | 0.00E+00 | 1.02E-02 |
| C2: KEGG | GRAFT\_VERSUS\_HOST\_DISEASE | 1.84E+00 | 0.00E+00 | 1.94E-02 |
| C2: KEGG | CYTOSOLIC\_DNA\_SENSING\_PATHWAY | 1.80E+00 | 2.01E-03 | 2.32E-02 |
| C2: KEGG | GLYCOSAMINOGLYCAN\_BIOSYNTHESIS\_CHONDROITIN\_SULFATE | 1.77E+00 | 2.00E-03 | 2.79E-02 |
| C2: KEGG | LEISHMANIA\_INFECTION | 1.76E+00 | 2.01E-03 | 3.02E-02 |
| C2: KEGG | ALLOGRAFT\_REJECTION | 1.71E+00 | 3.88E-03 | 4.64E-02 |
| C2: KEGG | TOLL\_LIKE\_RECEPTOR\_SIGNALING\_PATHWAY | 1.71E+00 | 0.00E+00 | 4.25E-02 |
| C2: KEGG | CELL\_ADHESION\_MOLECULES\_CAMS | 1.70E+00 | 0.00E+00 | 4.15E-02 |
| C2: KEGG | GLYCOLYSIS\_GLUCONEOGENESIS | 1.68E+00 | 4.05E-03 | 4.43E-02 |
| C2: KEGG | JAK\_STAT\_SIGNALING\_PATHWAY | 1.60E+00 | 0.00E+00 | 9.09E-02 |
| C3: transcription factor targets | V$AR\_01 | 1.83E+00 | 0.00E+00 | 1.61E-02 |
| C3: transcription factor targets | V$IRF1\_01 | 1.77E+00 | 0.00E+00 | 2.61E-02 |
| C3: transcription factor targets | V$AP1\_Q4 | 1.77E+00 | 0.00E+00 | 1.79E-02 |
| C3: transcription factor targets | YWATTWNNRGCT\_UNKNOWN | 1.76E+00 | 0.00E+00 | 1.34E-02 |
| C3: transcription factor targets | V$AP1FJ\_Q2 | 1.75E+00 | 0.00E+00 | 1.26E-02 |
| C3: transcription factor targets | V$IRF\_Q6 | 1.74E+00 | 0.00E+00 | 1.28E-02 |
| C3: transcription factor targets | YGACNNYACAR\_UNKNOWN | 1.72E+00 | 0.00E+00 | 1.89E-02 |
| C3: transcription factor targets | V$IRF2\_01 | 1.70E+00 | 0.00E+00 | 2.15E-02 |
| C3: transcription factor targets | V$AP1\_Q2 | 1.69E+00 | 0.00E+00 | 2.03E-02 |
| C3: transcription factor targets | V$IRF7\_01 | 1.69E+00 | 0.00E+00 | 1.96E-02 |
| C5: GO biological process | CARBOXYLIC\_ACID\_TRANSPORT | 1.78E+00 | 0.00E+00 | 4.53E-01 |
| C5: GO biological process | NEGATIVE\_REGULATION\_OF\_CELLULAR\_PROTEIN\_METABOLIC\_PROCESS | 1.78E+00 | 0.00E+00 | 2.41E-01 |
| C5: GO biological process | ORGANIC\_ACID\_TRANSPORT | 1.75E+00 | 3.89E-03 | 2.19E-01 |
| C5: GO cellular component | NUCLEOLAR\_PART | 1.77E+00 | 2.02E-03 | 1.67E-01 |
| C5: GO cellular component | DENDRITE | 1.68E+00 | 2.69E-02 | 2.28E-01 |
| C5: GO cellular component | CELL\_JUNCTION | 1.68E+00 | 4.16E-03 | 1.64E-01 |
| C5: GO cellular component | SECRETORY\_GRANULE | 1.65E+00 | 1.40E-02 | 1.54E-01 |
| C5: GO cellular component | TIGHT\_JUNCTION | 1.63E+00 | 6.07E-03 | 1.54E-01 |
| C5: GO cellular component | ENDOPLASMIC\_RETICULUM | 1.62E+00 | 0.00E+00 | 1.44E-01 |
| C5: GO cellular component | MICROSOME | 1.61E+00 | 8.08E-03 | 1.34E-01 |
| C5: GO cellular component | VESICULAR\_FRACTION | 1.61E+00 | 1.79E-02 | 1.20E-01 |
| C5: GO cellular component | INTERCELLULAR\_JUNCTION | 1.58E+00 | 4.04E-03 | 1.33E-01 |
| C5: GO cellular component | APICAL\_JUNCTION\_COMPLEX | 1.55E+00 | 2.12E-02 | 1.63E-01 |
| C5: GO molecular function | OXIDOREDUCTASE\_ACTIVITY\_GO\_0016705 | 1.80E+00 | 2.05E-03 | 2.00E-01 |
| C6: oncogenic signatures | LTE2\_UP.V1\_DN | 2.01E+00 | 0.00E+00 | 0.00E+00 |
| C6: oncogenic signatures | E2F1\_UP.V1\_DN | 1.95E+00 | 0.00E+00 | 5.53E-04 |
| C6: oncogenic signatures | EGFR\_UP.V1\_UP | 1.87E+00 | 0.00E+00 | 2.69E-03 |
| C6: oncogenic signatures | STK33\_UP | 1.87E+00 | 0.00E+00 | 2.01E-03 |
| C6: oncogenic signatures | STK33\_NOMO\_UP | 1.77E+00 | 0.00E+00 | 5.76E-03 |
| C6: oncogenic signatures | P53\_DN.V1\_DN | 1.74E+00 | 0.00E+00 | 7.05E-03 |
| C6: oncogenic signatures | MEK\_UP.V1\_DN | 1.71E+00 | 0.00E+00 | 7.36E-03 |
| C6: oncogenic signatures | STK33\_SKM\_UP | 1.70E+00 | 0.00E+00 | 7.89E-03 |
| C6: oncogenic signatures | WNT\_UP.V1\_DN | 1.69E+00 | 0.00E+00 | 7.67E-03 |
| C6: oncogenic signatures | RB\_P130\_DN.V1\_DN | 1.68E+00 | 0.00E+00 | 9.27E-03 |

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| **Table S4B** |  |  |  |  |
| **MSigDB Collections** | **Name** | **normalized enrichment score** | **Nominal p value** | **FDR q-val** |
| C2: Reactome | CELL\_CYCLE | -1.99E+00 | 0.00E+00 | 7.88E-03 |
| C2: Reactome | MITOTIC\_PROMETAPHASE | -1.96E+00 | 0.00E+00 | 1.23E-02 |
| C2: Reactome | CELL\_CYCLE\_MITOTIC | -1.94E+00 | 0.00E+00 | 1.10E-02 |
| C2: Reactome | DNA\_REPLICATION | -1.93E+00 | 0.00E+00 | 9.70E-03 |
| C2: Reactome | DOUBLE\_STRAND\_BREAK\_REPAIR | -1.92E+00 | 0.00E+00 | 9.74E-03 |
| C2: Reactome | G2\_M\_CHECKPOINTS | -1.91E+00 | 0.00E+00 | 8.76E-03 |
| C2: Reactome | G0\_AND\_EARLY\_G1 | -1.90E+00 | 0.00E+00 | 8.90E-03 |
| C2: Reactome | CHROMOSOME\_MAINTENANCE | -1.87E+00 | 0.00E+00 | 1.38E-02 |
| C2: Reactome | DNA\_STRAND\_ELONGATION | -1.87E+00 | 2.02E-03 | 1.23E-02 |
| C2: Reactome | G1\_S\_SPECIFIC\_TRANSCRIPTION | -1.87E+00 | 0.00E+00 | 1.11E-02 |
| C2: BioCarta | G2\_PATHWAY | -2.09E+00 | 0.00E+00 | 8.99E-04 |
| C2: BioCarta | MEF2D\_PATHWAY | -1.83E+00 | 2.01E-03 | 4.04E-02 |
| C2: BioCarta | ATM\_PATHWAY | -1.75E+00 | 5.95E-03 | 8.24E-02 |
| C2: BioCarta | ATRBRCA\_PATHWAY | -1.74E+00 | 1.99E-03 | 7.15E-02 |
| C2: BioCarta | PGC1A\_PATHWAY | -1.71E+00 | 8.11E-03 | 9.03E-02 |
| C2: BioCarta | NFAT\_PATHWAY | -1.62E+00 | 7.72E-03 | 1.88E-01 |
| C2: BioCarta | MITOCHONDRIA\_PATHWAY | -1.60E+00 | 2.71E-02 | 1.85E-01 |
| C2: BioCarta | CALCINEURIN\_PATHWAY | -1.58E+00 | 2.31E-02 | 2.02E-01 |
| C2: BioCarta | MPR\_PATHWAY | -1.58E+00 | 1.21E-02 | 1.82E-01 |
| C2: BioCarta | CHEMICAL\_PATHWAY | -1.57E+00 | 3.38E-02 | 1.72E-01 |
| C2: BioCarta | NOS1\_PATHWAY | -1.55E+00 | 2.73E-02 | 1.87E-01 |
| C2: chemical and genetic perturbations | ROSTY\_CERVICAL\_CANCER\_PROLIFERATION\_CLUSTER | -2.59E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | ZHOU\_CELL\_CYCLE\_GENES\_IN\_IR\_RESPONSE\_6HR | -2.45E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | SOTIRIOU\_BREAST\_CANCER\_GRADE\_1\_VS\_3\_UP | -2.36E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | ZHOU\_CELL\_CYCLE\_GENES\_IN\_IR\_RESPONSE\_24HR | -2.34E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | KONG\_E2F3\_TARGETS | -2.32E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | WHITFIELD\_CELL\_CYCLE\_LITERATURE | -2.32E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | PUJANA\_XPRSS\_INT\_NETWORK | -2.32E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | WINNEPENNINCKX\_MELANOMA\_METASTASIS\_UP | -2.31E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | KAUFFMANN\_MELANOMA\_RELAPSE\_UP | -2.31E+00 | 0.00E+00 | 0.00E+00 |
| C2: chemical and genetic perturbations | ISHIDA\_E2F\_TARGETS | -2.30E+00 | 0.00E+00 | 0.00E+00 |
| C2: KEGG | DNA\_REPLICATION | -1.98E+00 | 0.00E+00 | 9.65E-04 |
| C2: KEGG | CELL\_CYCLE | -1.92E+00 | 0.00E+00 | 2.24E-03 |
| C2: KEGG | MISMATCH\_REPAIR | -1.89E+00 | 0.00E+00 | 2.10E-03 |
| C2: KEGG | GLYCINE\_SERINE\_AND\_THREONINE\_METABOLISM | -1.84E+00 | 3.80E-03 | 8.35E-03 |
| C2: KEGG | P53\_SIGNALING\_PATHWAY | -1.74E+00 | 0.00E+00 | 2.95E-02 |
| C2: KEGG | HOMOLOGOUS\_RECOMBINATION | -1.69E+00 | 6.29E-03 | 4.64E-02 |
| C2: KEGG | PATHOGENIC\_ESCHERICHIA\_COLI\_INFECTION | -1.64E+00 | 8.20E-03 | 7.33E-02 |
| C3: transcription factor targets | V$E2F\_03 | -1.84E+00 | 0.00E+00 | 6.63E-03 |
| C3: transcription factor targets | V$E2F\_Q6\_01 | -1.77E+00 | 0.00E+00 | 1.04E-02 |
| C3: transcription factor targets | V$E2F1\_Q4\_01 | -1.77E+00 | 0.00E+00 | 8.50E-03 |
| C3: transcription factor targets | V$E2F\_Q4\_01 | -1.76E+00 | 0.00E+00 | 7.02E-03 |
| C3: transcription factor targets | V$E2F\_Q3 | -1.72E+00 | 0.00E+00 | 1.20E-02 |
| C3: transcription factor targets | V$E2F\_Q3\_01 | -1.71E+00 | 0.00E+00 | 1.18E-02 |
| C3: transcription factor targets | V$E2F1\_Q4 | -1.66E+00 | 0.00E+00 | 2.03E-02 |
| C5: GO biological process | CELL\_CYCLE\_CHECKPOINT\_GO\_0000075 | -1.90E+00 | 0.00E+00 | 5.96E-02 |
| C5: GO biological process | CELL\_DIVISION | -1.86E+00 | 0.00E+00 | 6.43E-02 |
| C5: GO biological process | CYTOKINESIS | -1.85E+00 | 2.05E-03 | 5.51E-02 |
| C5: GO biological process | MITOTIC\_CELL\_CYCLE\_CHECKPOINT | -1.81E+00 | 3.98E-03 | 7.10E-02 |
| C5: GO biological process | DNA\_RECOMBINATION | -1.78E+00 | 0.00E+00 | 8.77E-02 |
| C5: GO biological process | MEIOTIC\_CELL\_CYCLE | -1.74E+00 | 1.02E-02 | 1.37E-01 |
| C5: GO biological process | M\_PHASE | -1.73E+00 | 0.00E+00 | 1.22E-01 |
| C5: GO biological process | CHROMATIN\_ASSEMBLY\_OR\_DISASSEMBLY | -1.73E+00 | 7.80E-03 | 1.10E-01 |
| C5: GO biological process | DNA\_METABOLIC\_PROCESS | -1.73E+00 | 0.00E+00 | 1.04E-01 |
| C5: GO biological process | CELL\_CYCLE\_PROCESS | -1.71E+00 | 0.00E+00 | 1.09E-01 |
| C5: GO cellular component | CHROMOSOMEPERICENTRIC\_REGION | -1.87E+00 | 2.07E-03 | 2.55E-02 |
| C5: GO cellular component | CHROMOSOME | -1.84E+00 | 0.00E+00 | 2.38E-02 |
| C5: GO cellular component | CHROMOSOMAL\_PART | -1.81E+00 | 1.88E-03 | 2.58E-02 |
| C5: GO cellular component | KINETOCHORE | -1.79E+00 | 1.89E-03 | 2.42E-02 |
| C5: GO cellular component | SPINDLE\_POLE | -1.74E+00 | 3.91E-03 | 3.81E-02 |
| C5: GO cellular component | SPINDLE | -1.74E+00 | 9.78E-03 | 3.40E-02 |
| C5: GO cellular component | CENTROSOME | -1.73E+00 | 1.95E-03 | 3.01E-02 |
| C5: GO cellular component | SPINDLE\_MICROTUBULE | -1.67E+00 | 8.02E-03 | 5.86E-02 |
| C5: GO cellular component | CHROMATIN\_REMODELING\_COMPLEX | -1.66E+00 | 1.65E-02 | 5.50E-02 |
| C5: GO cellular component | MICROTUBULE\_CYTOSKELETON | -1.66E+00 | 0.00E+00 | 5.01E-02 |
| C6: oncogenic signatures | RB\_P107\_DN.V1\_UP | -1.80E+00 | 0.00E+00 | 6.14E-03 |
| C6: oncogenic signatures | GCNP\_SHH\_UP\_EARLY.V1\_UP | -1.70E+00 | 0.00E+00 | 2.07E-02 |
| C6: oncogenic signatures | E2F3\_UP.V1\_UP | -1.68E+00 | 0.00E+00 | 1.81E-02 |
| C6: oncogenic signatures | RB\_DN.V1\_UP | -1.68E+00 | 0.00E+00 | 1.45E-02 |
| C6: oncogenic signatures | KRAS.LUNG.BREAST\_UP.V1\_DN | -1.61E+00 | 0.00E+00 | 2.77E-02 |
| C6: oncogenic signatures | PRC2\_EZH2\_UP.V1\_UP | -1.58E+00 | 0.00E+00 | 3.48E-02 |
| C6: oncogenic signatures | BCAT\_BILD\_ET\_AL\_DN | -1.57E+00 | 1.36E-02 | 3.52E-02 |
| C6: oncogenic signatures | KRAS.50\_UP.V1\_DN | -1.55E+00 | 1.15E-02 | 3.64E-02 |
| C6: oncogenic signatures | P53\_DN.V1\_UP | -1.53E+00 | 0.00E+00 | 4.45E-02 |
| C6: oncogenic signatures | MTOR\_UP.N4.V1\_DN | -1.53E+00 | 5.95E-03 | 4.16E-02 |