Statistical analyses.
In Figure 1D, IHC staining scores for BCL6 and PY-STAT3, calculated as described in the following section, were tabulated for GCB and non-GCB groups. Chi-square analysis was performed to evaluate whether the observed distribution deviate significantly from a random pattern. P-values <0.05 were considered significant. In Figure 2B, the signal values of the *BCL6, STAT3* and *cyclin D2* genes were $\log_2$ transformed and compared using a Wilcoxon-Mann-Whitney non-parametric test between ABC-DLBCL and GCB-DLBCL groups. *P*-values <0.05 were considered significant.

IHC analysis of BCL6 and PY-STAT3 expression on TMA
Tissue microarrays (TMA) were constructed using a Beecher Instruments microarrayer (Silver Spring, MD) as previously described.[1] Each case was represented by three 1 mm cores. The percentage and intensity of staining of neoplastic B cells were independently scored in the TMA, each using a 10-tiered scale (0-9).[2] The product of both was used as a case score and a value of 10 or greater was considered positive for chi-square calculations (equal or greater than 50% positive tumor B cells with intensity of 2 or 20% positive cells with intensity of 5). P-values <0.05 were considered significant. Because each of the TMA DLBCL cases randomly lost 2.7% ± 1.3% of the triplicate cores from the TMA, for analytical purposes, the missing score was replaced with the mean value for the whole group. Cases with greater than 10% core loss were previously excluded from the analysis. In Figure 2C and Table S2, the BCL6 positive cases were further divided into 2 groups: moderate = score 10-39, strong = score 40 and greater. In Table S3, the PY-STAT3 positive cases were divided as: moderate = score 10-20, strong = score 21 and above.

Electrophoretic mobility shift assay (EMSA).
Methods for preparation of nuclear extracts and EMSA procedures for BCL6 have been described previously[3]. Core sequences of the BCL6-like sites in *STAT3* are given in Figure 4B. Sequences of the canonical BCL6 probe as well as probes corresponding to the candidate BCL6 sites in *STAT3* promoter region are listed in **Table S4**.

Northern and Western Blots.
Total RNA samples were prepared with the Trizol reagent (Invitrogen). Ten micrograms of RNA per sample were separated on 0.9% formaldehyde-agarose gel and transferred and hybridized using standard methods. Probes (human BCL6 or STAT3 cDNA and a rat GAPDH probe) were labeled with α-^{32}P dCTP using the Ready-to-go kit (Amersham/Pharmacia Biotech.). For Western Blots, whole-cell lysates were prepared in NP40 buffer supplemented with a protease inhibitor cocktail (Roche) and phosphatase inhibitors (17 mM sodium pyrophosphate, 100 mM sodium fluoride, 4 mM sodium orthovanadate and 0.12 M okadaic acid). Equivalent amounts of protein were separated on 7~12% SDS-PAGE gels, transferred to nitrocellulose membranes, and processed according to standard methods. The results were visualized by the ECL system (Amersham). Antibodies to guanine nucleotide dissociation inhibitor (GDI) or GAPDH were used as internal controls for protein loading.

Chromatin Immunoprecipitation (ChIP).
ChIP was performed using the ChIP assay kit (Upstate Biotechnology) following the manufacturer's instructions with the following modifications: 10×10^6 Ly1 cells were used for each ChIP reaction; chromatin was sheared to an average length of 600 bp; 2 µg of anti-BCL6 LN-3 antibody or normal rabbit IgG (Santa Cruz), or 10 µl of MTA3 antibody was used. PCR products obtained after 30 cycles of amplification were resolved on 1.5% agarose gels. Sequences for the PCR primers are: STAT3 site B (5 -AGTGATGGAACGGAGTACGG-3 and 5 -ACGCGGGAATCAGCTAGTTA-3); site D (5 -TGTAGACTTAGACAGGCTTCAGG-3 and 5 -TTTAGAAAATGCAGACCGTTCA-3); -20 kb site (5 -GAACGAAGTGAGGGAGCAAG-3 and 5 -TTCATTCCCCTGCTCAAAAC-3).

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