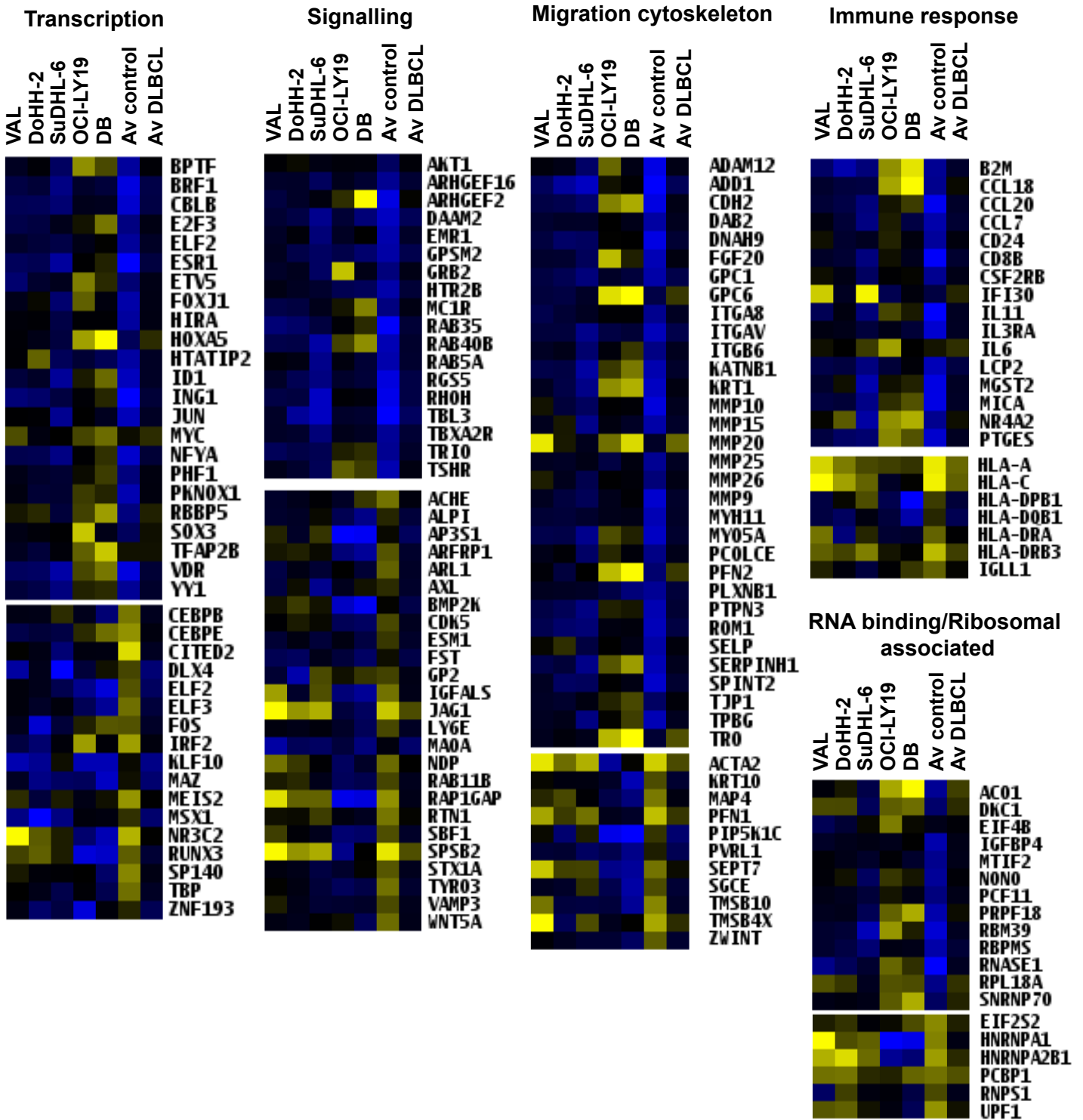


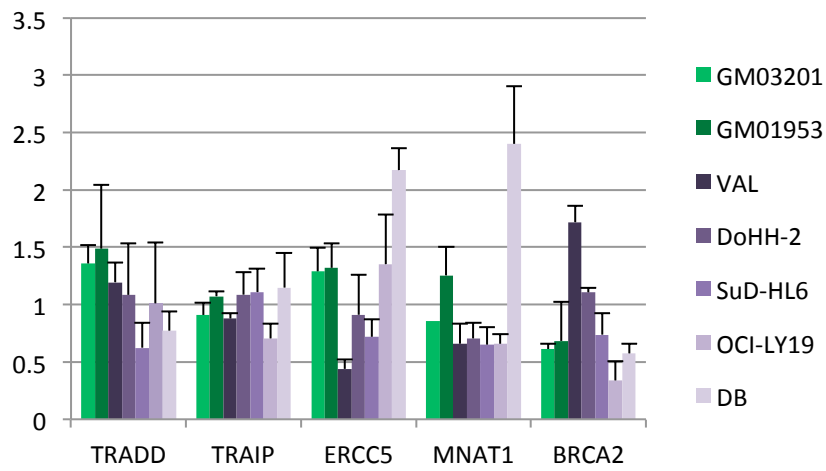
**Supplementary Figure 1: Gradient profiles of DLBCL cell lines**

Lysates of 5 DLBCL cell lines (Val, DoHH-2, SuDHL6, OCI-LY19 and DB) and 2 controls (GM03201 and GM01953) were applied on 10-60% (w/v) sucrose gradients. They were separated into 11 fractions and absorbance at 254nm was measured.

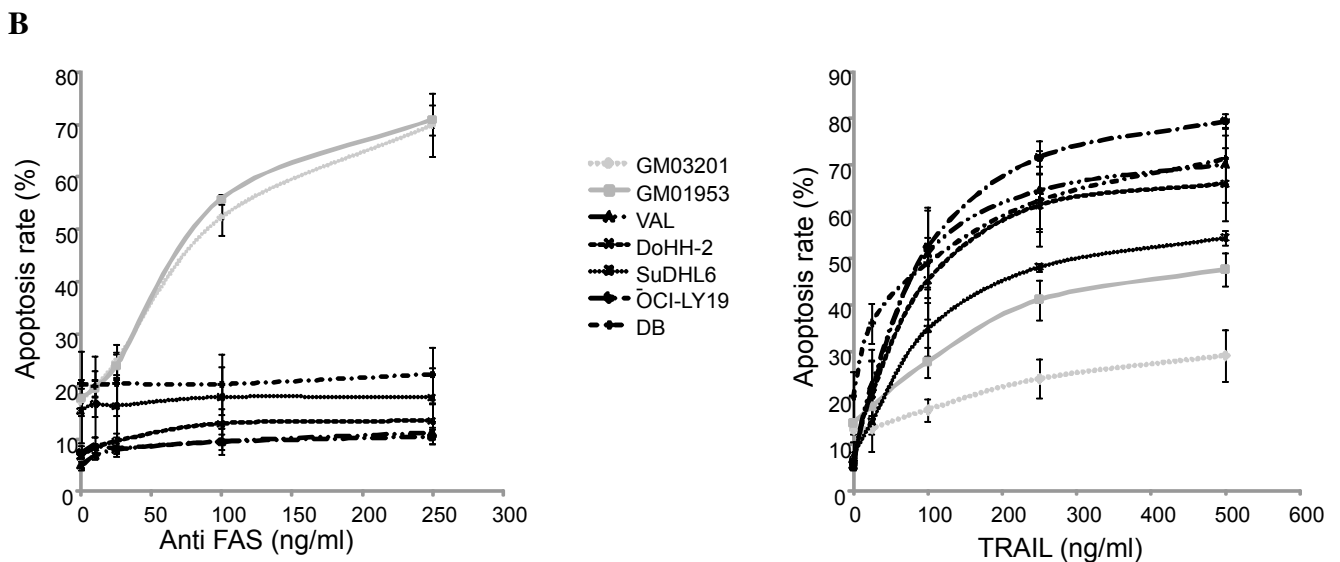
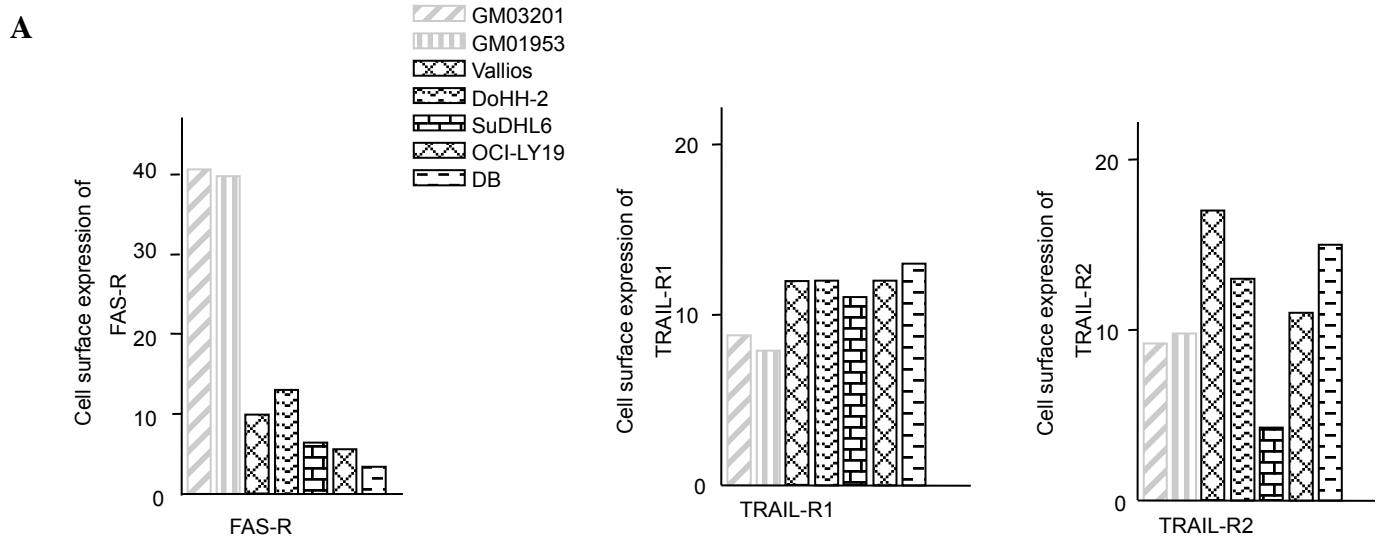


**Supplementary Figure 2: Heat map showing changes in RNA association with polysomes in DLBCL compared to controls**

Selected candidate mRNAs that displayed significantly increased quantile ranking DLBCL cell lines compared to control B-cells. Genes are clustered into functional groups. A colour scale has been used to represent the ratio of mRNA in subpolysome to polysome fractions. Transformed from the  $\log_2[\text{Polysome}:\text{Subpolysome}]$  where blue indicates subpolysome associated and yellow signifies that the mRNA is predominately polysome associated.



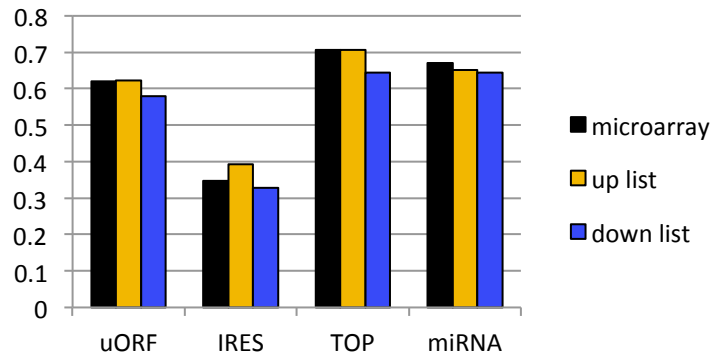
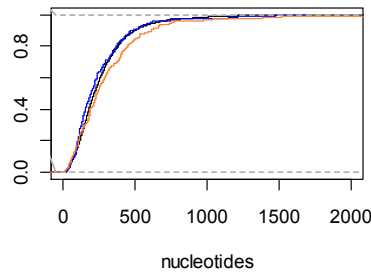
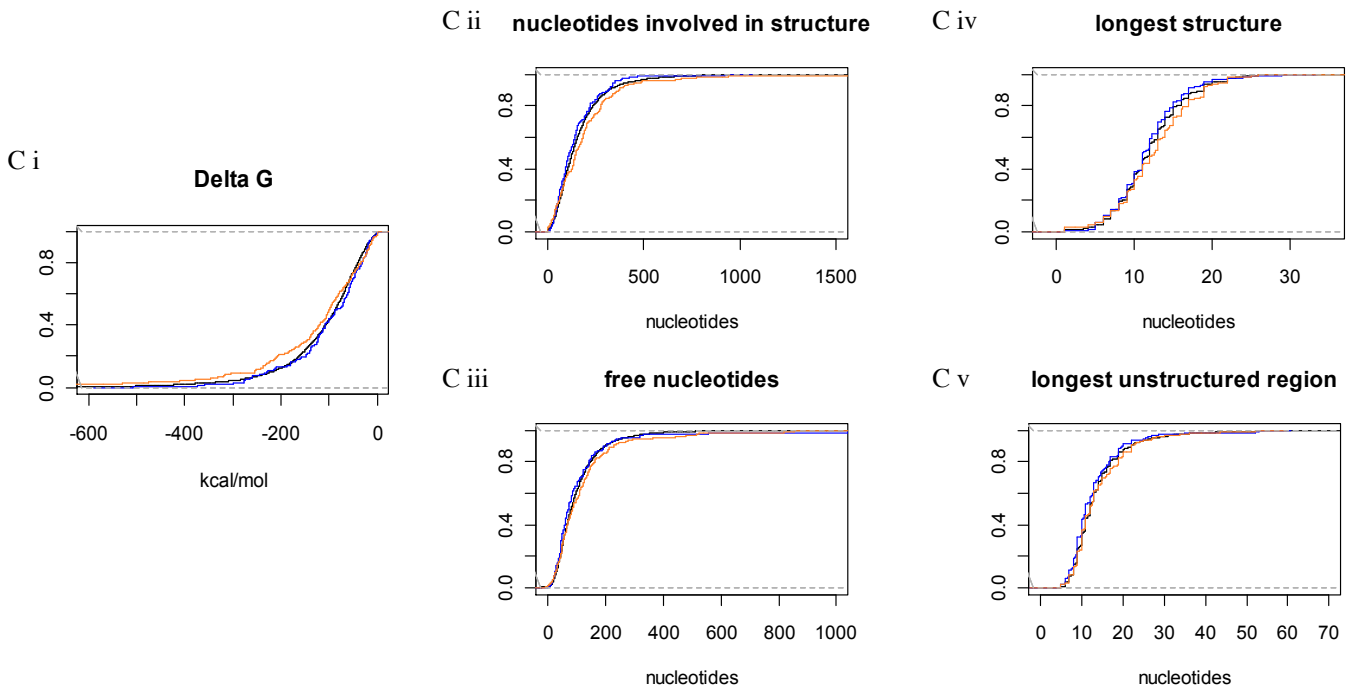
**Supplementary Figure 3: Evaluation of total RNA contents by quantitative RT-PCR**  
 Error bars represent standard deviations on 3 independent experiments.



**Supplementary Figure 4: Sensitivity of DLBCL derived cell lines to FAS-induced apoptosis**

**(A)** Surface expression of TRAIL receptors TRAIL-R1 and TRAIL-R2. TRAIL-R1 is slightly more expressed in DLBCL cell lines than in the controls.

**(B)** DLBCL (VAS, DoHH-2, SuDHL-6, OCI-LY19 and DB) and control (GM03201 and GM01953) were treated by increasing doses of TRAIL or an anti-FAS antibody, and apoptosis measured by flow cytometry following annexin/PI staining. DLBCL cell lines were almost completely resistant to Fas activation but as sensitive as the controls to TRAIL.

**A****B****5'UTR length****C****Supplementary Figure 5: Contribution of 5' UTR features to translation dysregulation****(A) Contribution of 5' UTR and 3' UTR features to translation dysregulation:**

The cDNA microarray data were analysed and the percentage of mRNA containing uORF, IRES and TOP-like sequences in the 5' UTR (in-house Perl scripts) and predicted miRNA target sites in the 3' UTR (conserved targets of conserved miRNA families from TargetScan; <http://www.targetscan.org>) were calculated for those mRNAs in the "up" and "down" lists and those in the full microarray set. No significant changes between the full microarray set and the lists were seen ( $\chi^2$  tests; p-values ranging from 0.1 to 0.99).

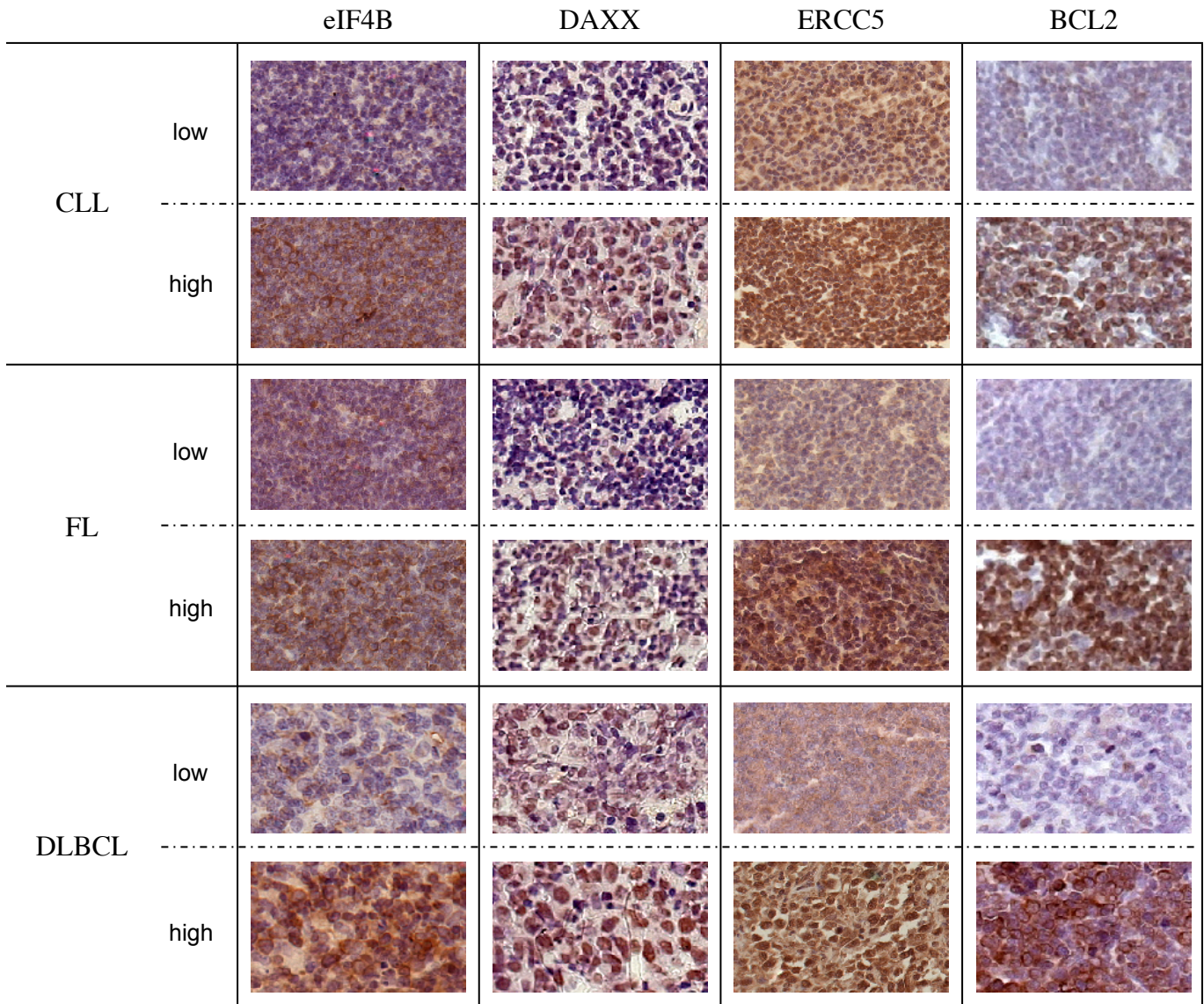
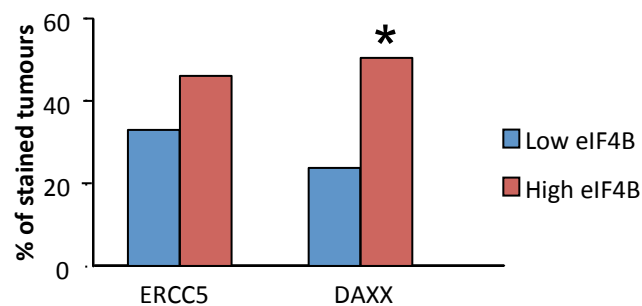
**(B) Cumulative density plot showing the distribution of the 5'UTR length** in the "up list" (in yellow), the "down list" (in blue) and the rest of mRNA in the microarray (in black).

**(C) Analysis of the most stable structure for 5'UTR (as given by mfold)**

(Ci) shows the cumulative distribution of the delta G of this structure in the "up list" (in yellow), the "down list" (in blue) and the rest of mRNA in the microarray (in black).

(Cii) and (Ciii) show respectively the distribution of number of paired nucleotide and the number of free nucleotide in those structures.

(Civ) and (Cv) show respectively the distribution of the size of the longest string of nucleotides involved in a hairpin and the size of the longest string of nucleotides in an unstructured region.

**A****B****Supplementary Figure 6: Tissue microarray analysis****(A) Section examples**

Tumours sections stained with different antibodies on the tissue microarrays.

Tissue microarrays were hybridized with primary antibodies against eIF4B, DAXX, ERCC5 or BCL2, then with a biotinylated secondary, streptavidin peroxydase and a DAB reaction was performed (brown staining). Nuclei were counterstained with haematoxylin (blue). For each antibodies, examples of CLL, FL and DLBCL tumours expressing low or high levels of the protein are shown.

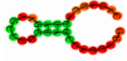
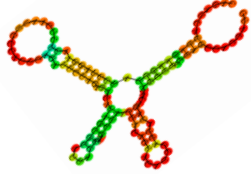
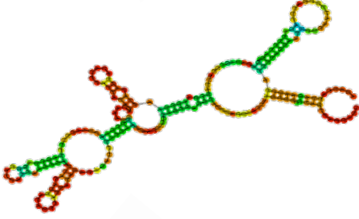
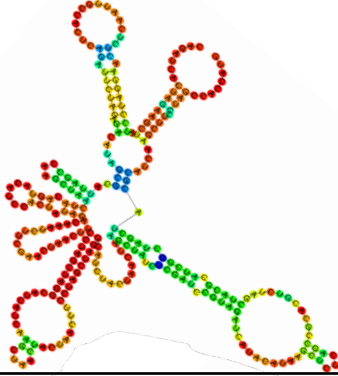
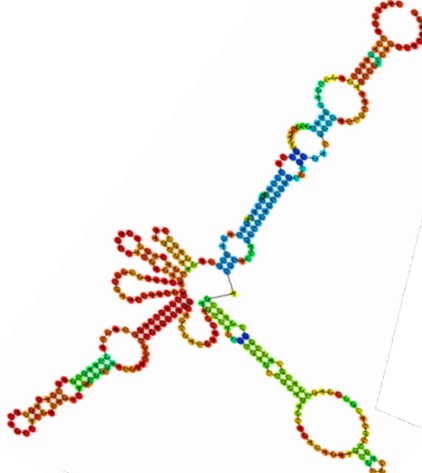
**(B) Histogram showing the connection between eIF4B expression and ERCC5 and DAXX.**

The proportion of tumours expressing high levels of ERCC5 and DAXX is higher in the sections that express eIF4B. Chi-square tests were performed and showed that the connexion between DAXX and eIF4B expression is statistically significant (\*,  $p < 0.05$ )

	<b>brand</b>	<b>reference</b>	<b>dilution for Western blot</b>	<b>dilution for immunohistochemistry</b>
<b>4EBP1</b>	cell signaling	9644	1/1000	
<b>4EBP1 (P)</b>	cell signaling	9459	1/1000	
<b>eIF2 alpha</b>	cell signaling	9722	1/1000	
<b>eIF2 alpha (P)</b>	cell signaling	3597	1/1000	
<b>eIF4B</b>	cell signalling	3592	1/1000	
<b>eIF4E</b>	cell signaling	4952	1/1000	
<b>eIF4E (P)</b>	cell signaling	9741	1/1000	
<b>RPS6</b>	cell signaling	2217	1/1000	
<b>FAS</b>	cell signaling	4233	1/1000	
<b>BCL2</b>	cell signaling	2872	1/1000	
<b>BCLxL</b>	cell signaling	2762	1/1000	
<b>β-Tubulin</b>	cell signaling	2146	(1/5000)	
<b>actin</b>	Sigma	clone AC15	1/10000	
<b>MNAT1</b>	abcam	ab65125	(1/1000)	1/25
<b>ERCC5</b>	abcam	ab46	(1/500)	
<b>TRAIP</b>	abcam	ab47543	(1/1000)	
<b>c-Myc</b>	Epitomics	1472	1/1000	
<b>eIF4B</b>	Epitomics	clone EP2299Y		1/150
<b>DAXX</b>	Upstate	07-471	1/1000	1/300

**Supplementary Table 1: Provenance of antibodies and dilutions used**



Insert length (bases)	SEQUENCE 5' ⇒ 3' (encompassing AUG)	FREE ENERGY	PREDICTED STRUCTURE
27	CAGATCACTAGAAAGCTTGCTAGCC ACCATG	-2.39 kcal/mol.	
115	CAGATCACTAGAAAGCTATCCTAGG AACTCTCAATTGCCACTCAGATTCT AGAGACATAGCGCATTAGCCAAGC TAACTACAGTACATCCACTATAGAC AAAGCTTCCTAGCCACCATG	-22,23 kcal/mol	
217	CAGATCACTAGAAAGCTATCCTAGG AACTCTCAATTGCCACTCAGATTCT AGAGACATAGCGCATTAGCCAAGC TAACTACAGTACATCCACTATAGAC AAATCTTCGAACTAACTTCCTAGCT AGGCATCATCAAGCTAACTACAGTA CATCCACTATAGACAGATCTTCGAA CTAACTTCCTAGCTAGGCATCTACT AACTAAGCTTCCTAGCCACCATG	-44,92 kcal/mol	
265	CAGATCACTAGAAAGCTATCCTAGG AACTCTCAATTGCCACTCAGATTCT AGAGACATAGCGCATTAGCCAAGC TAACTACAGTACATCCACTATAGAC AAATCTTCGAACTAACTTCCTAGCT AGGCATCATCAAGCTAACTACTAAC TTCCTAGCTAGGCATCTACTAACTA AGCTATCTCGATCCGTAGATCATA ATAAGCTCTCAGCCGCACGTCTAG CTACGCATCGGCTAGCTACGCATC AAGCTTCCTAGCCACCATG	-58.30 kcal/mol.	
327	CAGATCACTAGAAAGCTATCCTAGG AACTCTCAATTGCCACTCAGATTCT AGAGACATAGCGCATTAGCCAAGC TAACTACAGTACATCCACTATAGAC AAATCTTCGAACTAACTTCCTAGCT AGGCATCATCAAGCTAACTACAGTA CATCCACTATAGACAGATCTTCGAA CTAACTTCCTAGCTAGGCATCTACT AACTAAGCTATCTCGATCCGTAGAT CATAcataagctctcagccgcacg TCTAGCTACGCATCGGCTAGCTAC GCATCAGTCTAGCTGAGCTCGCT ACGTTACCCGCAAAGCTTCCTAGC CACCATG	-71.95 kcal/mol	

### Supplementary Table 2: Length and structure of the 5'UTRs subcloned in pRL vector

Reporter vectors with long 5'UTRs were derived from a modified pRL-CMV (Promega) presenting an HA tag at the 5' end of the luciferase coding region.

To generate pRL27, a deletion was performed between NheI and HindIII sites using the Quikchange XL site directed mutagenesis kit (Stratagene) and oligonucleotides DEL1-F

(5'GTTTAGTGAACCGTCAGATCACTAGAAAGCTTGCTAGCCACCATGGCTTACCCCG3') and DEL1-R (5'GGGTAAGCCATGGTGGCTAGCAAGCTTCTAGTGATCTGACGGTTCATAAAC3'). Oligonucleotide DeL1-F introduces a NcoI site at the luciferase AUG initiation codon. NcoI / HindIII digestion of pRL27 and double strand oligonucleotides insertion generated reporter constructs harboring variable 5' untranslated region from 115 to 350 nucleotides. The 17 nucleotides region upstream the luciferase AUG start codon remained unchanged in all vectors. Resulting plasmids namely pRL115, pRL217, pRL265 or pRL327 were checked by DNA sequencing. Sequences, folding and free energy of the thermodynamic prediction of the variable 5' UTRs are provided. The empty pGL3 vector expressing *Firefly luciferase* was use as an internal control in this case.



	Apoptosis					DNA repair				Validations in tumour samples				
	TRADD	FAS	DAXX	BCL-2	TRAIP	c-MYC	ERCC5	BRCA2	MNAT1		eIF4B	BCL-2	DAXX	ERCC5
GM03201	4.246	1.622	0.011	0.029	0.085	0.352	0.238	0.032	0.357	Tonsil 1	0.252	0.352	0.420	0.632
GM01953	2.416	1.418	0.018	0.243	0.486	0.308	0.173	0.007	0.825	Tonsil 2	0.146	0.312	0.197	0.368
VAL	0.094	0.457	0.436	1.915	0.637	1.014	1.138	0.790	0.890	DLBCL 1	2.119	1.214	2.301	1.253
DoHH-2	0.065	0.414	1.169	2.158	0.871	1.678	1.312	1.771	0.711	DLBCL 2	2.219	0.909	1.575	1.463
SuD-HL6	0.042	1.129	2.457	0.222	1.783	1.206	1.800	1.774	1.109	DLBCL 3	0.290	1.077	0.421	1.016
OCI-LY19	0.023	0.975	1.558	1.019	2.479	1.450	1.998	2.076	1.489	DLBCL 4	0.888	1.910	1.340	1.425
DB	0.114	0.984	1.353	1.414	0.658	0.992	0.341	0.549	1.619	DLBCL 5	1.087	1.225	0.747	0.843
<b>p-value</b>	<b>0.001</b>	<b>0.017</b>	<b>0.026</b>	<b>0.045</b>	<b>0.084</b>	<b>0.004</b>	<b>0.035</b>	<b>0.019</b>	<b>0.064</b>	<b>p-value</b>	<b>0.019</b>	<b>0.003</b>	<b>0.020</b>	<b>0.016</b>

#### translation initiation

	eIF4B		eIF4B-P/		eIF4E		eIF4B-P/		eIF2α P/			
	eIF4G	total	eIF4B-P	total	eIF4A	total	eIF4E-P	total	eIF4H	eIF2α	eIF2α-P	total
GM03201	0.377	0.472	0.431	0.913	0.415	0.783	0.855	1.092	0.805	0.836	0.816	0.976
GM01953	0.819	0.303	0.325	1.074	0.367	0.883	1.009	1.143	0.677	0.623	0.511	0.819
VAL	1.380	1.185	1.701	1.436	0.498	1.148	1.174	1.023	1.566	1.003	1.005	1.002
DoHH-2	1.727	1.360	0.863	0.635	0.473	1.150	1.159	1.008	1.167	1.414	0.983	0.695
SuD-HL6	1.379	1.252	0.941	0.751	4.195	0.686	0.756	1.102	1.033	1.268	0.702	0.554
OCI-LY19	0.704	1.202	0.941	0.783	0.491	1.111	0.818	0.736	0.667	0.963	1.065	1.105
DB	0.614	1.227	1.798	1.466	0.560	1.239	1.229	0.992	1.086	0.892	1.918	2.150
<b>p-value</b>	<b>0.098</b>	<b>0.00003</b>	<b>0.026</b>	<b>0.474</b>	<b>0.260</b>	<b>0.108</b>	<b>0.302</b>	<b>0.111</b>	<b>0.098</b>	<b>0.042</b>	<b>0.120</b>	<b>0.342</b>

#### mTOR signaling

	PI3K			PKB-P/		4EBP1		4EBP-P/	
	PI3K	PKB total	PKB-P	total	mTOR	total	4EBP1-P	total	
GM03201	0.254	0.500	0.013	0.025	0.193	0.453	0.172	0.380	
GM01953	0.225	0.612	0.018	0.030	0.319	0.796	0.321	0.403	
VAL	0.428	0.768	0.353	0.459	0.902	0.493	0.475	0.962	
DoHH-2	0.425	0.625	0.661	1.058	1.490	1.651	1.561	0.945	
SuD-HL6	0.388	0.579	0.877	1.515	0.870	0.868	0.914	1.053	
OCI-LY19	0.461	0.878	0.776	0.884	1.389	1.811	2.017	1.114	
DB	0.322	0.725	0.697	0.961	0.935	1.017	0.801	0.788	
<b>p-value</b>	<b>0.005</b>	<b>0.075</b>	<b>0.003</b>	<b>0.010</b>	<b>0.006</b>	<b>0.127</b>	<b>0.055</b>	<b>0.001</b>	

#### Supplementary Table 3: Quantification of Western blots from figures 2, 3D and 5A

The blots were quantified with Image J software. The values obtained were normalised first to tubulin, then to the average value for the 7 cell lines. P-values were obtained by performing a unpaired t.test comparing the 5 DLBCL cell lines (or patient samples) to the 2 controls. For phosphorylated proteins, the relative ratio between phosphorylated and total proteins (p/total) was also calculated.

	eIF4B			DAXX			ERCC5			p value		
	analysed	negative	positive	p-value	analysed	negative	positive	p-value	analysed		negative	positive
<b>DLBCL</b>	<b>153</b>	<b>41 (26.8%)</b>	<b>112 (73.2%)</b>		<b>153</b>	<b>80 (52.3%)</b>	<b>73 (47.7%)</b>		<b>134</b>	<b>70 (52.2%)</b>	<b>64 (47.8%)</b>	
Age at diagnosis												
<65 years	65	20 (30.8%)	45 (69.2%)	0.47	66	39 (59.1%)	27 (40.9%)	0.27	54	26 (48.1%)	28 (51.9%)	0.55
≥65 years	87	21 (24.1%)	66 (75.9%)		87	41 (47.1%)	46 (52.9%)		77	44 (57.1%)	33 (42.9%)	
<b>Gender</b>												
male	87	23 (26.4%)	64 (73.6%)	0.94	86	41 (47.7%)	45 (52.3%)	0.39	74	40 (54.1%)	34 (45.9%)	0.75
female	65	18 (27.7%)	47 (72.3%)		67	39 (58.2%)	28 (41.8%)		57	30 (52.6%)	27 (47.4%)	
<b>International prognosis index</b>												
≤2	41	10 (24.4%)	31 (75.6%)	0.73	45	29 (64.4%)	16 (35.6%)	0.10	31	18 (58.1%)	13 (41.9%)	0.52
>=3	33	8 (24.2%)	25 (75.8%)		35	12 (34.3%)	23 (65.7%)		28	13 (46.4%)	15 (53.6%)	
<b>cell origin (HANS classification)</b>												
GC-like	40	6 (15%)	34 (85%)	0.09	42	22 (52.4%)	20 (47.6%)	0.99	35	16 (45.7%)	19 (54.3%)	0.44
non GC-like	85	26 (30.6%)	59 (69.4%)		80	45 (56.3%)	35 (43.8%)		74	40 (54.1%)	34 (45.9%)	
<b>FL</b>	<b>65</b>	<b>30 (46.2%)</b>	<b>35 (53.8%)</b>		<b>73</b>	<b>66 (90.4%)</b>	<b>7 (9.6%)</b>		<b>29</b>	<b>17 (58.6%)</b>	<b>12 (41.4%)</b>	
Age at diagnosis												
<65 years	44	20 (45.5%)	24 (54.5%)	0.93	53	50 (94.3%)	3 (5.7%)	0.33	20	12 (60%)	8 (40%)	0.09
≥65 years	20	9 (45%)	11 (55%)		19	15 (78.9%)	4 (21.1%)		8	0 (0%)	8 (100%)	
<b>Gender</b>												
male	21	11 (52.4%)	10 (47.6%)	0.57	27	25 (92.6%)	2 (7.4%)	0.70	10	3 (30%)	7 (70%)	0.47
female	44	19 (43.2%)	25 (56.8%)		46	41 (89.1%)	5 (10.9%)		19	9 (47.4%)	10 (52.6%)	
<b>grade</b>												
1	21	9 (42.9%)	12 (57.1%)		26	25 (96.2%)	1 (3.8%)		12	4 (33.3%)	8 (66.7%)	
2	33	15 (45.5%)	18 (54.5%)	0.63	34	30 (88.2%)	4 (11.8%)	0.43	13	8 (61.5%)	5 (38.5%)	0.07
3	11	6 (54.5%)	5 (45.5%)		13	11 (84.6%)	2 (15.4%)		4	0 (0%)	4 (100%)	
<b>CLL</b>	<b>46</b>	<b>21 (45.7%)</b>	<b>25 (54.3%)</b>		<b>44</b>	<b>40 (90.9%)</b>	<b>4 (9.1%)</b>		<b>30</b>	<b>22 (73.3%)</b>	<b>8 (26.7%)</b>	
Age at diagnosis												
<65 years	20	11 (55%)	9 (45%)	0.40	18	17 (94.4%)	1 (5.6%)	0.60	14	10 (71.4%)	4 (28.6%)	0.87
≥65 years	25	10 (40%)	15 (60%)		25	22 (88%)	3 (12%)		16	12 (75%)	4 (25%)	
<b>Gender</b>												
male	33	16 (48.5%)	17 (51.5%)	0.74	32	30 (93.8%)	2 (6.3%)	0.58	21	15 (71.4%)	6 (28.6%)	0.84
female	12	5 (41.7%)	7 (58.3%)		11	9 (81.8%)	2 (18.2%)		8	6 (75%)	2 (25%)	

**Supplementary Table 4: Composition of the tissue microarrays**

The table shows the number of tumours sections immunostained with anti-ERCC5, anti-eIF4B and anti-DAXX antibodies that could be analysed for each tumour type: Diffuse Large B-cell lymphoma (DLBCL), Follicular Lymphoma (FL) and Chronic Lymphocytic leukemia (CLL). Clinical features such as gender or age do not impact on the expression for the studied proteins. ERCC5, eIF4B and DAXX do not significantly correlate either with the grade of FL, the International Prognosis Index for DLBCL or the cell or origin classification in Ganglionic Cell like (GC) and non GC DLBCL. Chi-square tests were used to generate p-values.