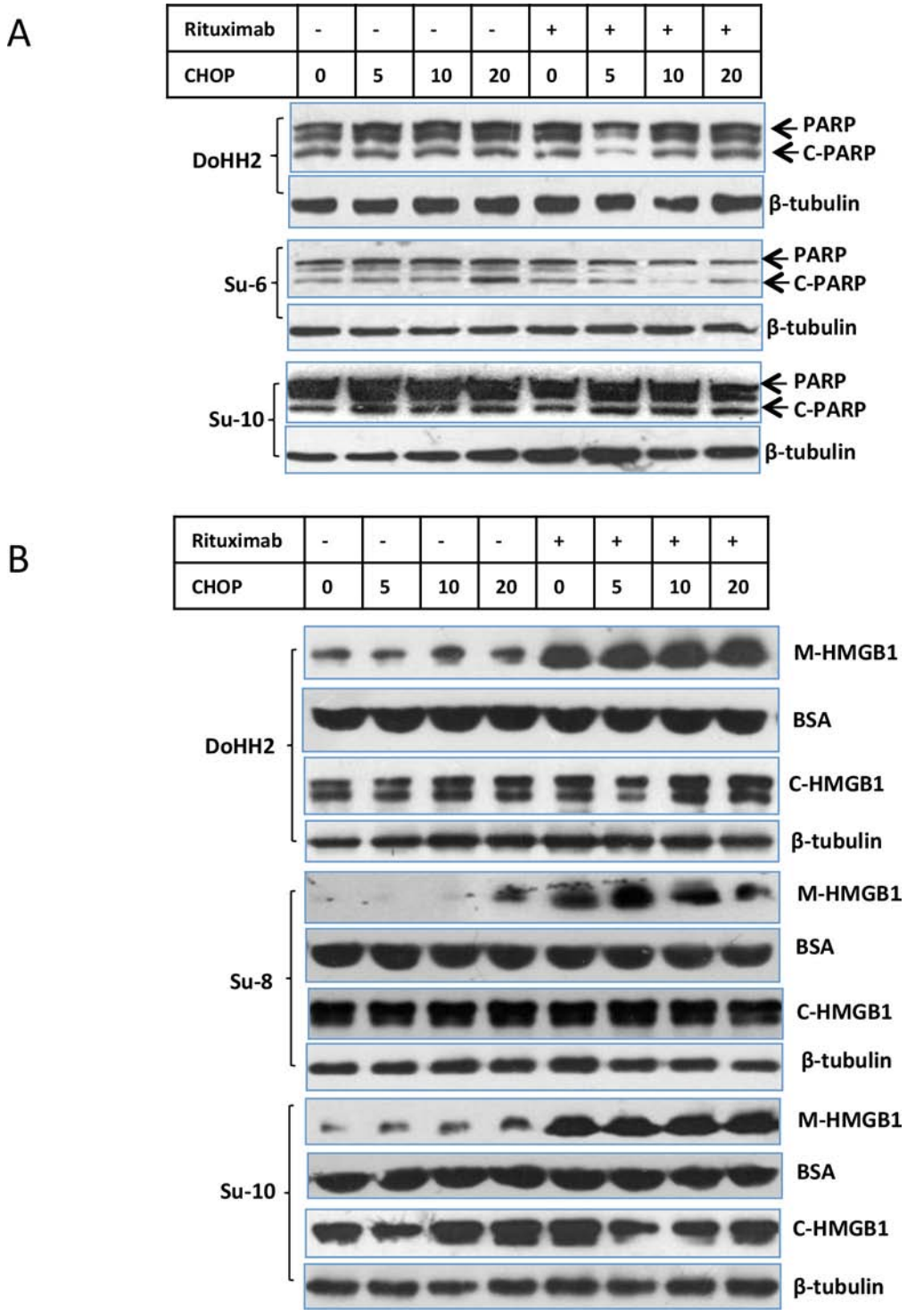
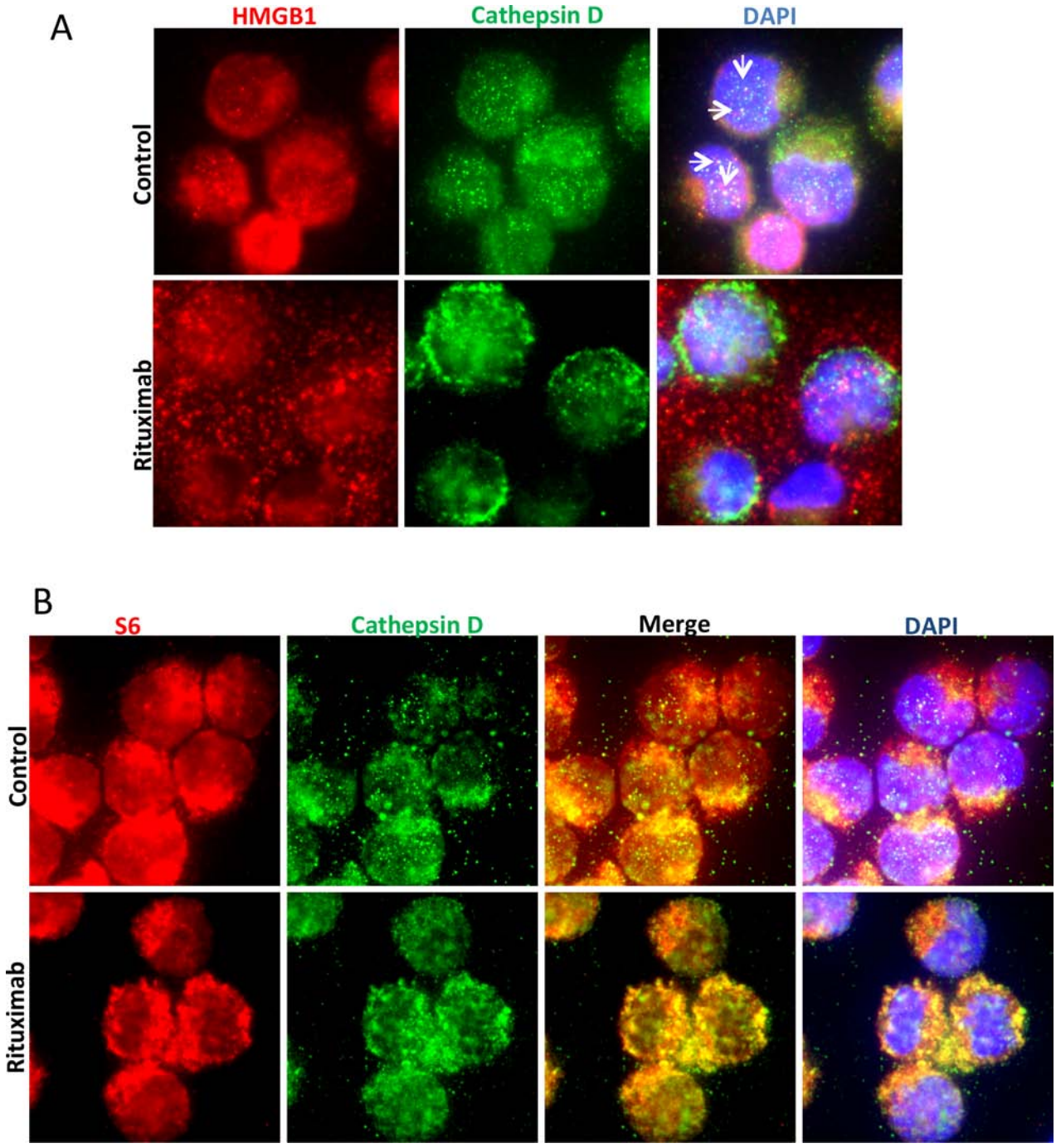
SUPPLEMENTARY FIGURES AND TABLES

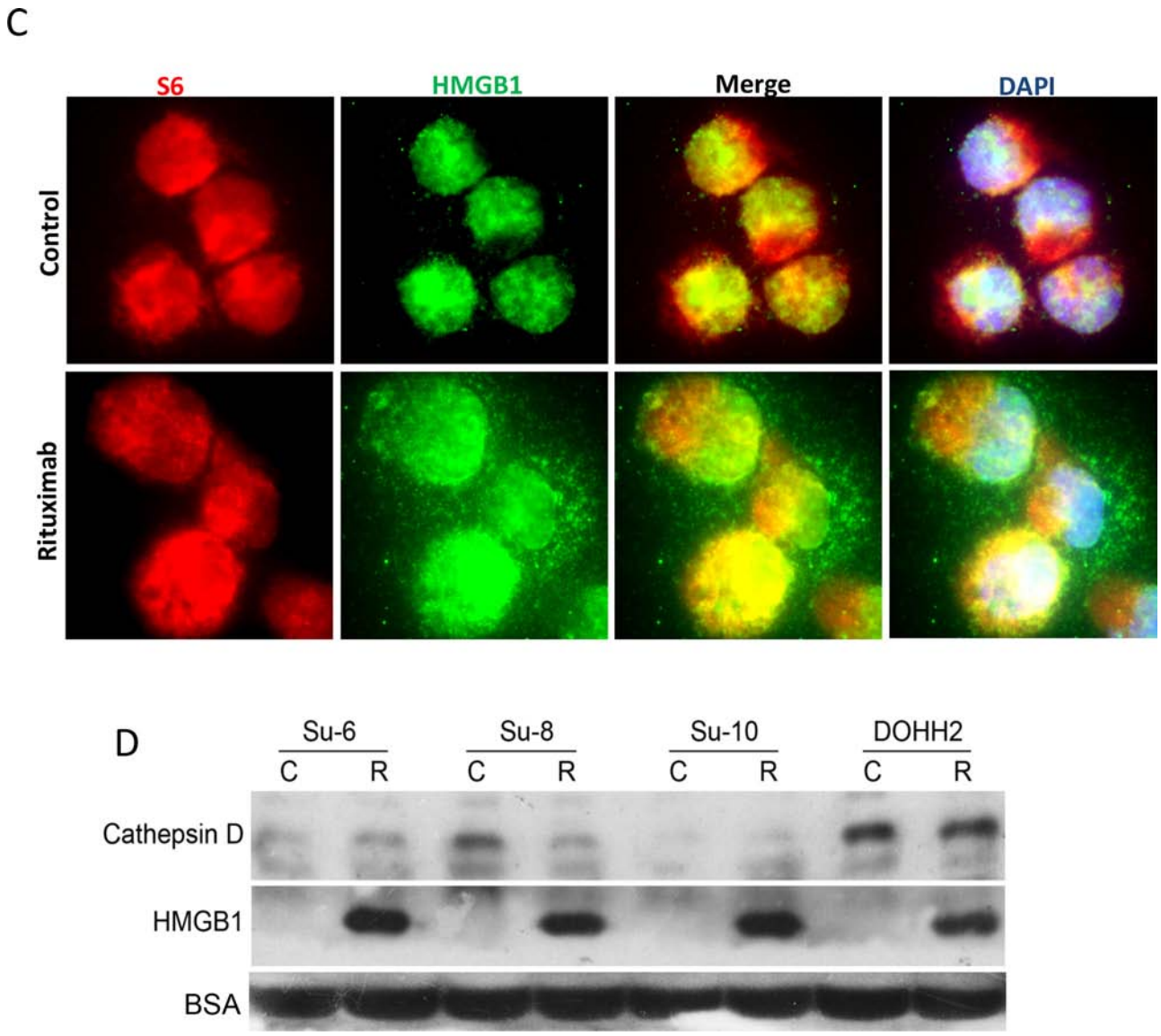


Supplementary Figure S1: Comparison of CHOP and R-CHOP-induced PARP cleavage and HMGB1 release. DLBCL cell lines were treated with CHOP or R-CHOP for 24 hours. Cytosolic proteins were used to test PARP Cleavage **A.** and HMGB1 expression (C-HMGB1) **B.** Conditioned medium (50 µl) was used to determine HMGB1 release (M-HMGB1) (B) BSA and β-tubulin were used as loading controls for conditioned medium Cytosolic proteins, respectively.

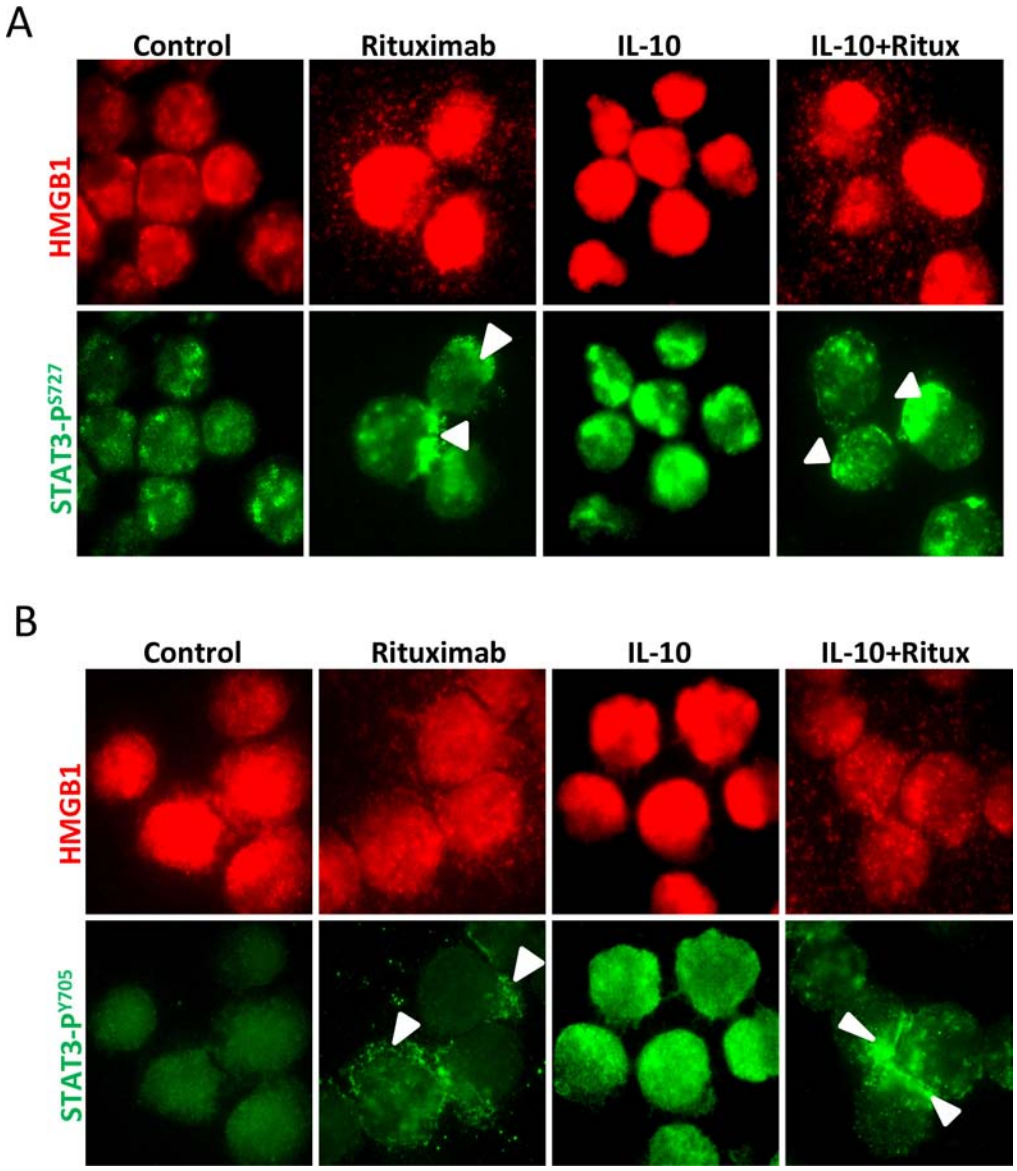


Supplementary Figure S2: The association between HMGB1 and cathepsin D release. DoHH2 cells were treated with Rituximab for 4 hours. Cells on slides were fixed/permeabilized and stained with rabbit anti-HMGB1/mouse anti-cathepsin D **A.** rabbit anti-S6/mouse anti-cathepsin D **B.** and rabbit anti-S6/mouse HMGB1

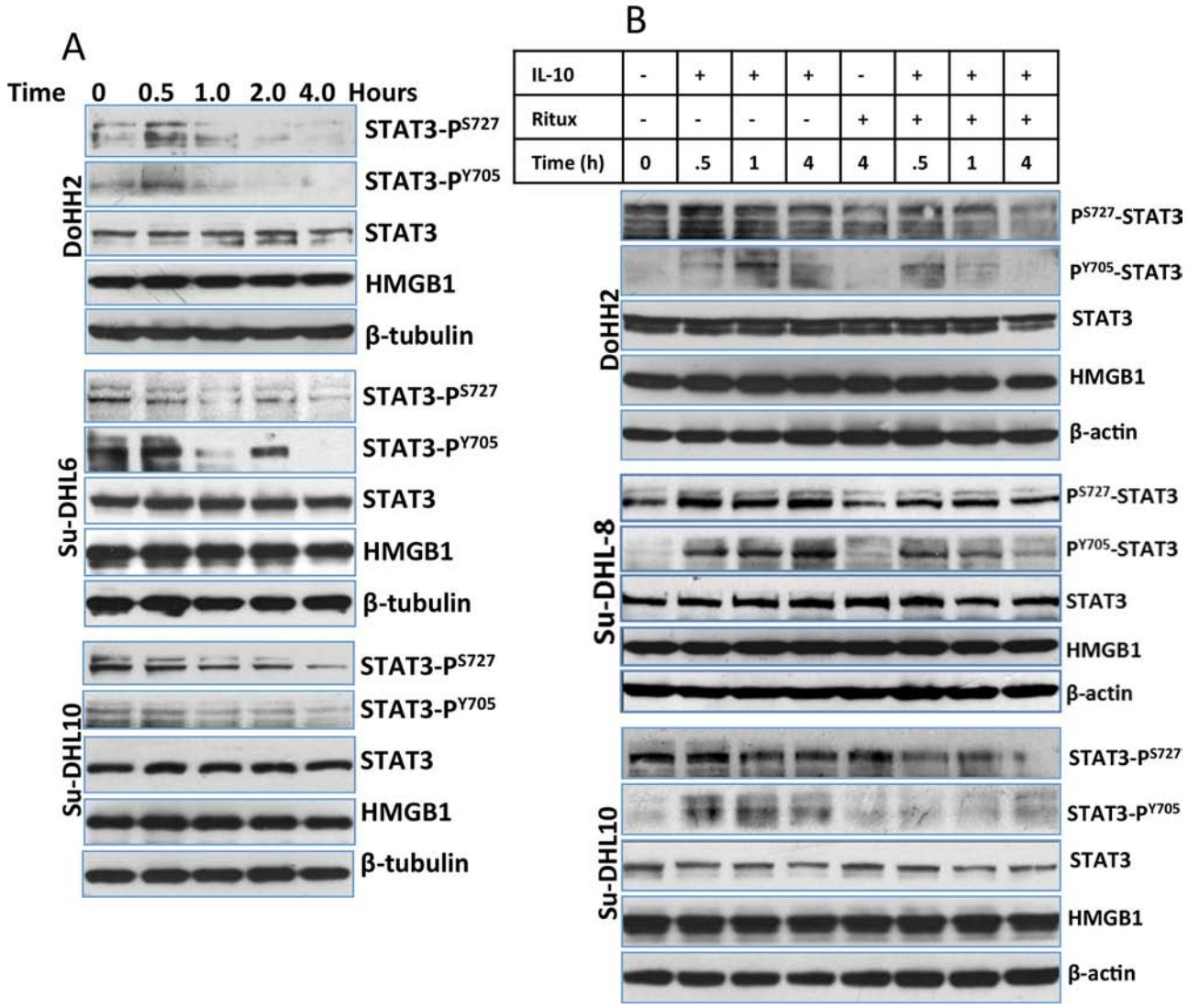
(*Continued*)



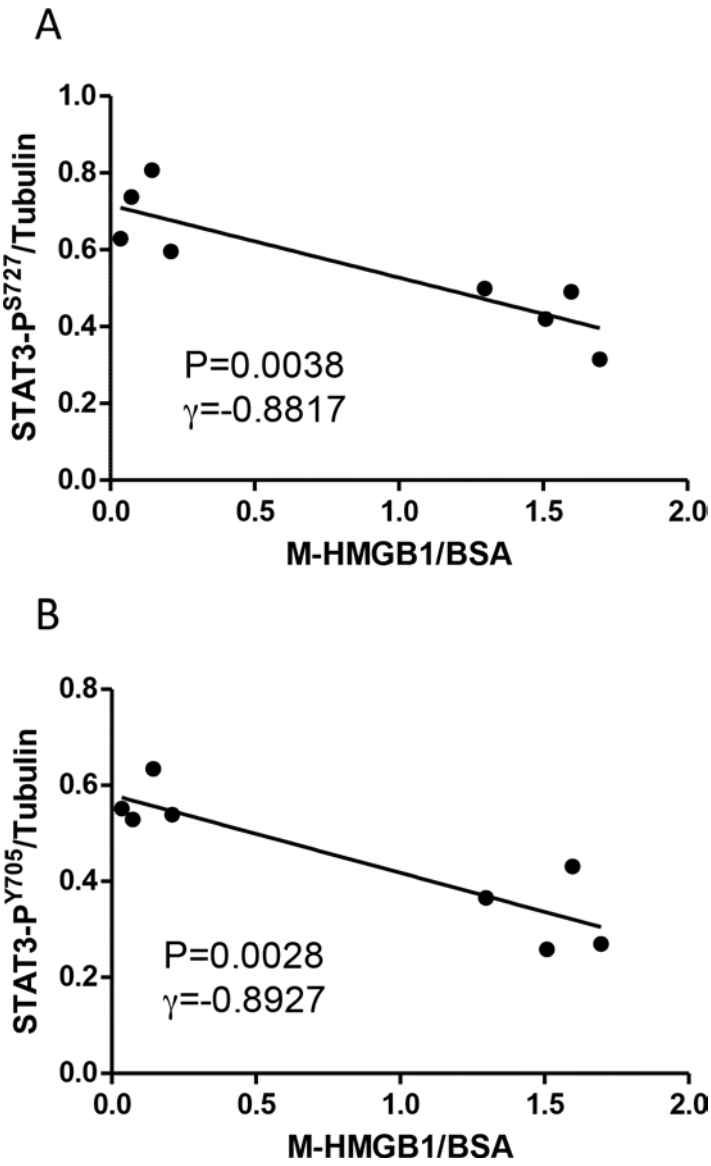
Supplementary Figure S2: (*Continued*) C, D. Four DLBCL cell lines were treated with rituximab for 4 hours. 50 μl of conditioned medium was used for Western Blotting. BSA was used as a loading control. 'C' means control and 'R' indicates Rituximab.



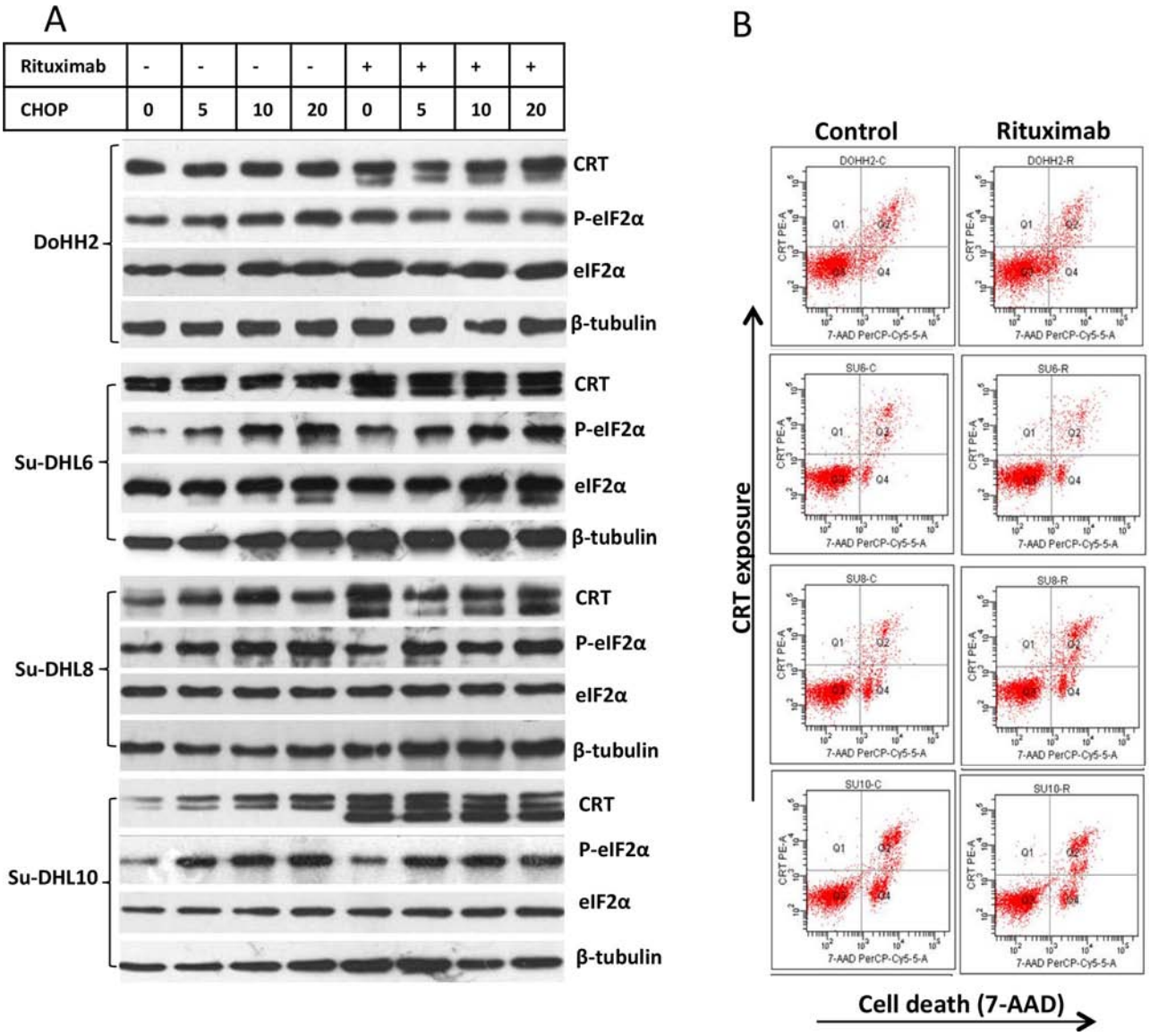
Supplementary Figure S3: Single color images of rituximab induced intracellular shuttling of STAT3 (green) and HMGB1 (red). **A.** STAT3-P^{S727} and **B.** STAT3-P^{Y705}. Arrow head indicate cytoplasmic localization of STAT3.



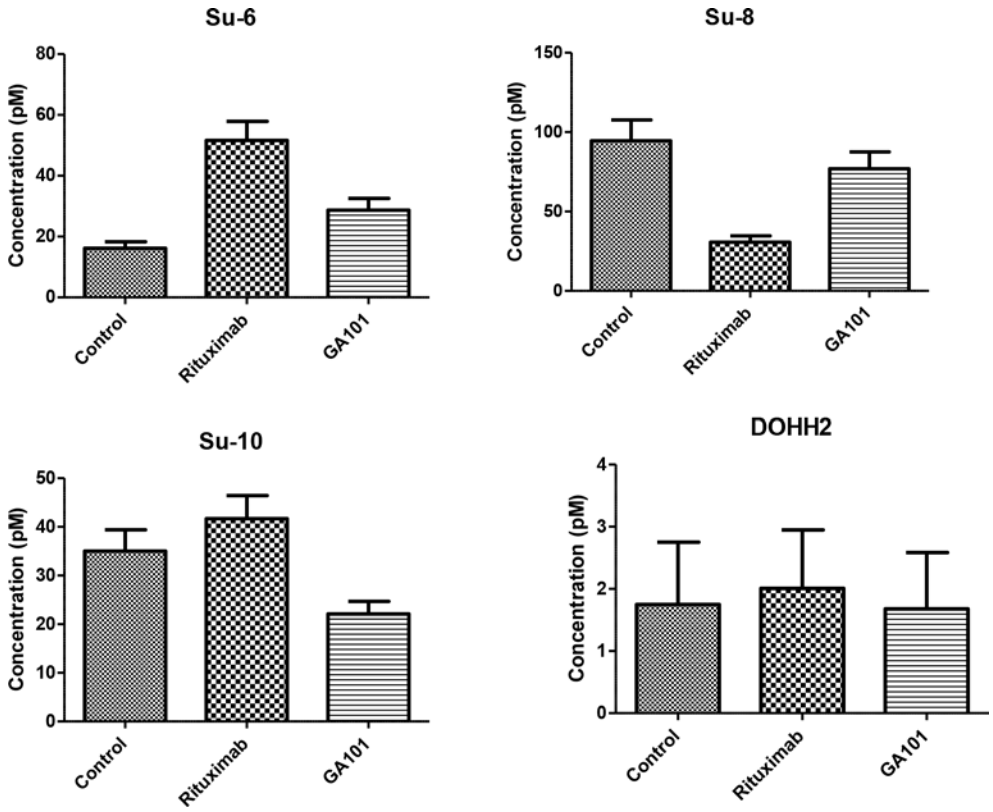
Supplementary Figure S4: Rituximab-induced STAT3 inhibition. A. Time dependent course of rituximab-induced inhibition of STAT3. **B.** Rituximab-induced STAT3 inhibition on IL-10 treated cells.



Supplementary Figure S5: Correlation between STAT3 activity and HMGB1 release. A. STAT3-P^{727}; **B.** STAT3-P^{Y705}. Data shown are mean values from Figure 4 D, 4E and 4G and analyzed by Pearson's Correlation using Prism Software.



Supplementary Figure S6: Effect of CHOP or R-CHOP in inducing eIF2α phosphorylation (A) and CRT exposure (B). **A.** DLBCL cells were treated with CHOP or R-CHOP for 24 hours. Expression of CRT, P-eIF2α and P-eIF2α were determined by Western blotting. **B.** DLBCL cells were treated with rituximab for 4 hours. After fixation, cells were stained with CRT-PE and 7-AAD. Cells with CRT exposure were defined as 7-AAD negative and CRT-PE positive. We were not be able to identify CHOP-induced CRT exposure due to the auto-fluorescence of CHOP.



Supplementary Figure S7: Rituximab or GA101-induced ATP release. DLBCL cells were treated with 10 μg/ml of rituximab or GA101 for 4 hours. ATP concentration in the conditioned medium (10 μl) was determined using ATP chemiluminescence ELISA kit.

Supplementary Table S1: Summary of clinical characteristics of DLBCL patients' plasma used for ELISA

	No of patients	Percentage
Total No	40	100%
Age		
>50	26	65%
<50	14	35%
Gender		
Male	25	62.5%
Female	15	37.5%
Stage at diagnosis		
I	4	10%
II	18	45%
III	6	15%
IV	12	30%
IPI score		
0	11	27.5%
1	18	45%
2	7	17.5%
3	4	10%
Treatment with		
CHOP	24	60%
R-CHOP	16	40%
Treatment response		
No response	0	0%
CHOP-PR	24	100%*
CHOP-CR	0	0%*
R-CHOP-PR	12	75%**
R-CHOP-CR	4	25%**

Note: * indicates percentages of patients who were treated with CHOP and ** means percentages of patients who were treated with R-CHOP.

Supplementary Table S2: Preparation of CHOP

Drug (supplier)	Clinical Dose (mg/m^2)	Calculated ratio	Concentration* (mg/ml)	Amount of drug added to make CHOP, ml (mg)
Cyclophosphamide (Sigma)	750	83.20	20	4.16 (83.2)
Doxorubicin (Sigma)	50	5.55	2	2.75 (5.5)
Vincristine (Sigma)	1.4	0.16	1	0.16 (0.16)
Prednisolone (Sigma)	100	11.09	20	0.55 (11.1)
Total Dose	901.4	100	10	made up to 10

Note: The final concentration of CHOP is 10 mg/ml. The aliquots were stored at −80°C.
* indicates the concentration of each drug prepared in DMSO.

Supplementary Table S3: List of primary antibodies

Name of antibody	Type	Company	Cat No	Application	Dilution
β-actin	Mouse	Sigma	A5316	WB	1:10,000
BSA	Mouse	Sigma	B2901	WB	1:5000
Cathepsin D	Rabbit	Abcam	ab72915	WB	1:1000
Cathepsin D	Mouse	Sigma	C0715	IF	1:100
CD80-PE	Mouse	Biolegend	305208	FC	1:20
CD83-PE	Mouse	Biolegend	305308	FC	1:20
CRT-PE	Mouse	Enzo	ADI-SPA-601PE	FC	5 μg/ml
CRT	Rabbit	Cell Signalling	12238	WB	1:1000
GA-101	Human	Roche		Treatment	10 μg/ml
eIF2α	Rabbit	Cell Signalling	9722	WB	1:1000
eIF2α-P^{S51}	Rabbit	Cell Signalling	9721	WB	1:1000
HMGB1	Rabbit	Abcam	ab18256	IP	1:100
				IF	1:200
HMGB1	Mouse	Sigma	WH0003146M8	WB	1:1000
				IF	1:200
OKT3	Mouse	Abcam	ab86883	Treatment	10 μg/ml
Rituximab	Chimeric	Roche		Treatment	10 μg/ml
S6-ribosome protein	Rabbit	Cell Signalling	2217	IF	1:100
STAT3	Mouse	Cell Signalling	9139	WB	1:1000
STAT3-P^{S727}	Rabbit	ImmunoWay	YP0250	WB	1:1000
				IP	1:100
STAT3-P^{S727}	Rabbit	Cell Signalling	9134	IF	1:100
STAT3-P^{Y705}	Mouse	Cell Signalling	9138	WB	1:1000
				IP	1:100
STAT3-P^{Y705}	Rabbit	Cell Signalling	9145	WB	1:1000
				IP	1:100
				IF	1:100
PARP	Rabbit	Beyotime Biotec	AP102	WB	1:1000
β-tubulin	Mouse	Abmart	M 20005	WB	1:1000

Note: FC = flow cytometry; IF = Immuno-fluorescent staining; IP = Immuno-precipitation; WB = Western blotting.

Supplementary Table S4: List of secondary antibodies

Name of antibody	Type	Company	Cat No.	Application	Dilution
Anti-mouse IgG -HRP	Goat	Santa Cruz	sc-2005	WB	1:5000
Anti-rabbit IgG -HRP	Goat	Santa Cruz	sc-2004	WB	1:5000
Alexa Fluor® 488 Anti-Rabbit IgG	Goat	Invitrogen	A11034	IF, FC	1:100
Alexa Fluor® 546 Anti-rabbit IgG	Goat	Invitrogen	A11035	IF, FC	1:100
Alexa Fluor® 488 Anti-Mouse IgG	Donkey	Invitrogen	A21202	IF, FC	1:100
Alexa Fluor® 546 Anti-Mouse IgG	Donkey	Invitrogen	A10036	IF, FC	1:100