Supplementary Methods

Flow Cytometry

First, cells were stained with live/dead reactive amine dyes as follows: cells were washed once with flow buffer (PBS with 5% FBS and 0.5% sodium azide), decanted and resuspended in 100μL of PBS with violet fluorescent reactive dye (Thermo Fisher Scientific, catalog # L34955) or near IR fluorescent reactive dye (Thermo Fisher Scientific, catalog # L34976) at a concentration of 0.3μL per 100μL of PBS. Cells were stained for 15 minutes at room temperature in the dark, washed once with flow buffer, and decanted.

Second, all other stains were applied in 100μL of flow buffer, and stained for 15 minutes at room temperature in the dark. To assess purity of selection, stains used were: CD45 (5μL) (BD Pharmingen, catalog #), CD19 (5μL) (BD Pharmingen, catalog #), and CD3 (5μL) (Thermo Fisher Scientific, catalog #5016228). Other flow antibodies include: PD-L1 (5μL) (Thermo Fisher Scientific, catalog #5011055), CD69 (2.5μL) (Beckman Coulter, catalog #6607110), PD-L2 (5μL) (Thermo Fisher Scientific, catalog #12-2799-42), CTLA-4 (5μL) (Thermo Fisher Scientific, catalog #25-1529-42), LAG-3 (5μL) (Thermo Fisher Scientific, catalog #25-2239-42), PD-1 (5μL) (Thermo Fisher Scientific, catalog # 12-2799-42). Flow cytometry data were analysed using Kaluza Analysis Software version 1.5 (Beckman Coulter).

Other Reagents

IFNγ was blocked by application of anti-IFNγ antibody (Peprotech, catalog #500-P32-100ug) to the co-culture immediately after plating at a concentration of 2ug/mL. Recombinant human IFNγ (R&D Systems, catalog #285-IF-100) was used at the indicated concentrations for

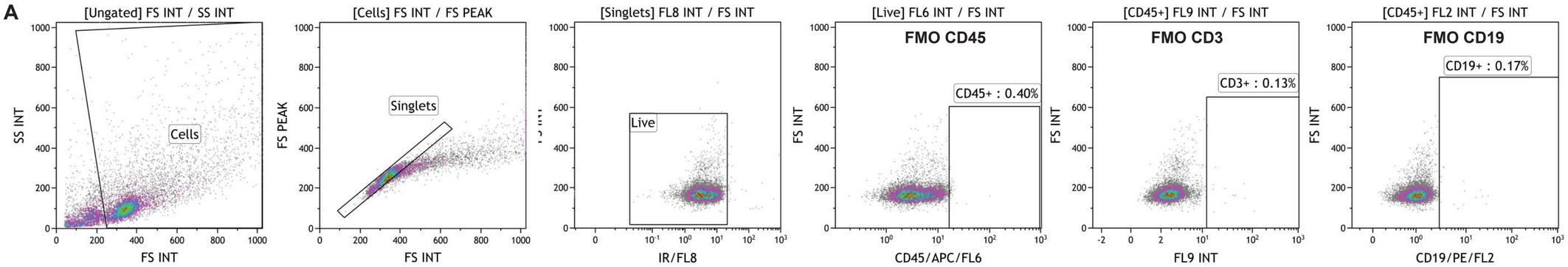
the indicated timepoints. Ibrutinib was provided by Pharmacyclics, Inc., acalabrutinib was provided by AstraZeneca (formerly Acerta Pharma), and duvelisib was purchased through the Ohio State pharmacy. CD40 was blocked by application of lucatumumab (HCD-122) to the culture media immediately after plating at a concentration of 10ug/mL. RNA polymerase II was inhibited with α-amanitin (Sigma-Aldrich, catalog #A2263) in a 1mg/mL suspension with DMSO. α-amanitin was applied to MCL cells only for 3 hours at a concentration of 30ug/mL. Following incubation, cells were washed twice with PBS prior to plating with T-cells.

Patient Number	Sex	Age	MCL Variant	Prior therapy or Treatment Naïve (P or N)	Previous Treatment
1	M	55	NA	N	none
2	M	62	Classical	P	FCR, BR, EPOCH
3	M	66	Classical	P	RCHOP, bortezomib, BR, lenalidomide, RICE
4	M	66	Classical	P	cyclophosphamide, BR, bortezomib, RCHOP
5	M	50	Classical	P	BR and ASCT
6	Unknown				
7	M	81	Classical	N	None
8	F	55	Classical	N	None
9	M	71	Classical	P	CHOP, BR
10	F	79	Classical	P	CVP,FCR,PCR
11	M	60	Classical	P	CVAD
12	M	75	unknown	P	RCHOP, ASCT
13	Unknown				
14	Unknown				
15	M	66	unknown	P	R-BAC
16	Unknown				

Key

CHOP=Cyclophosphamide, doxorubicin, vincristine, prednisone
RCHOP=Rituximab and CHOP
BR=Bendamustine, rituximab
ASCT= Autologous stem cell transplant
FCR=Fludarabine, cyclophosphamide and rituximab
EPOCH=Etoposide, prednisone, vincristine, cyclophosphamide and doxorubicin
RICE=Rituximab, ifosfamide, carboplatin, etoposide
RBAC=Rituximab, bendamustine, cytarabine

A



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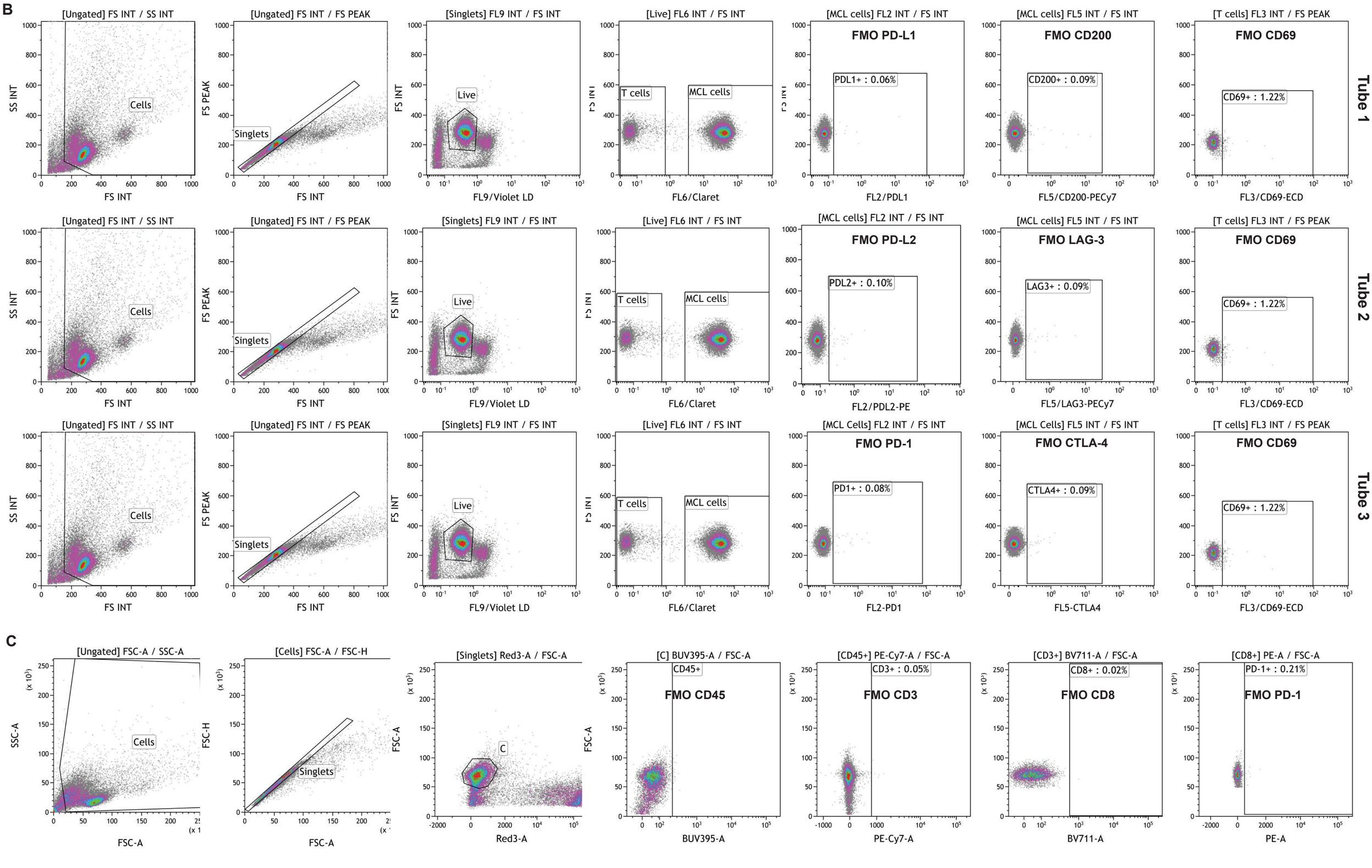
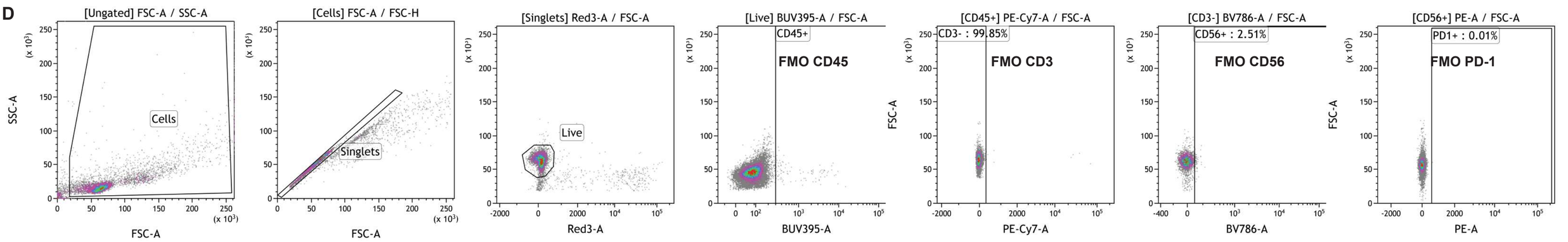


C

D



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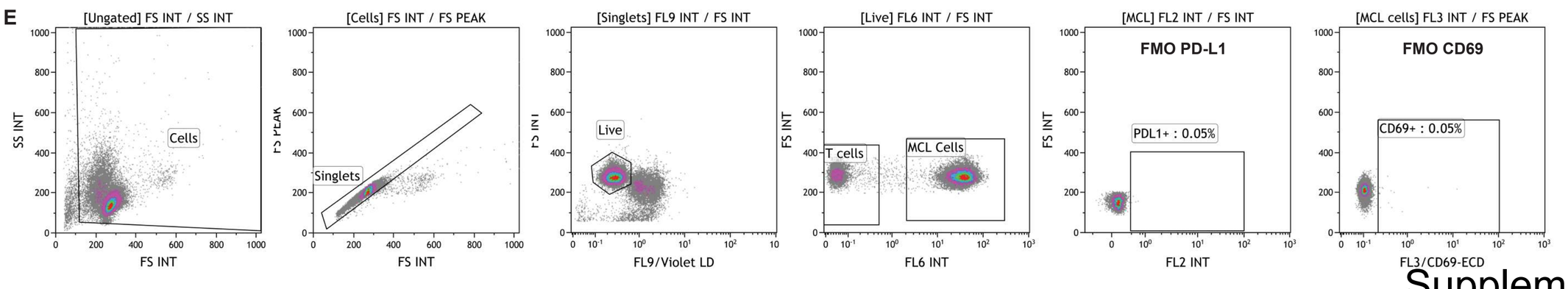
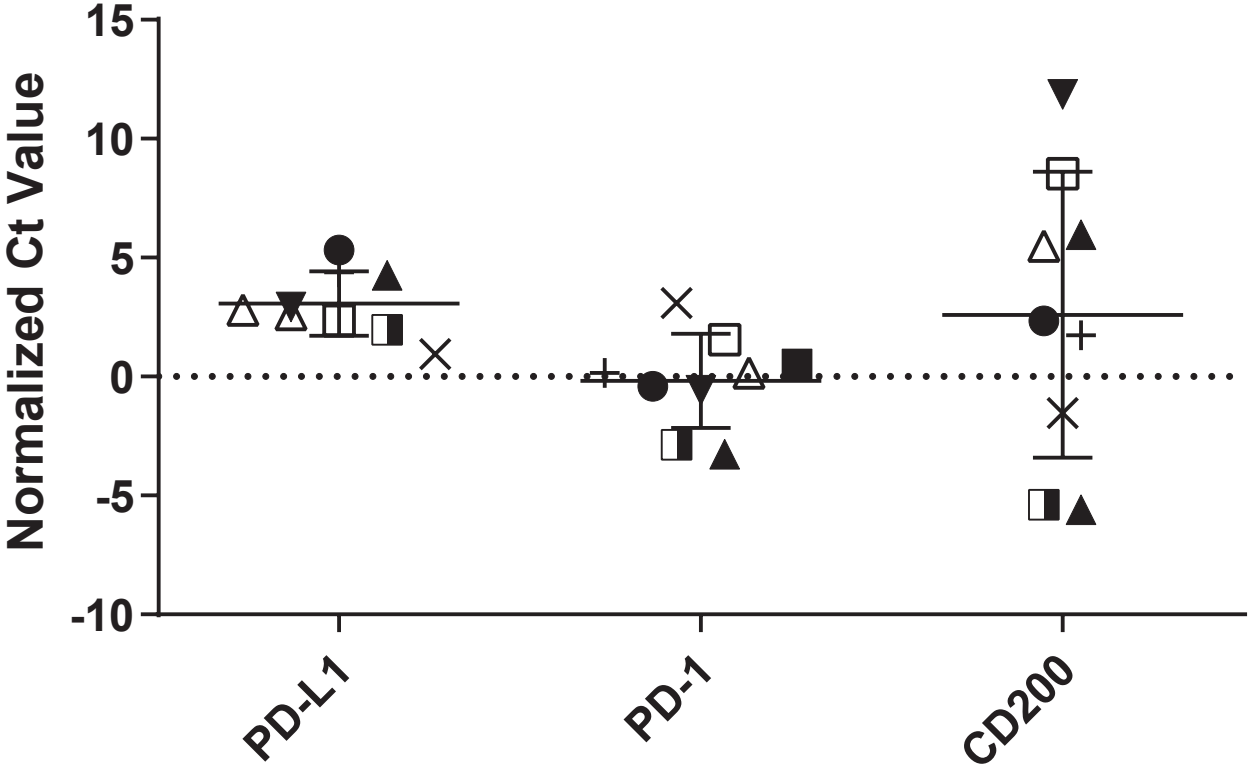
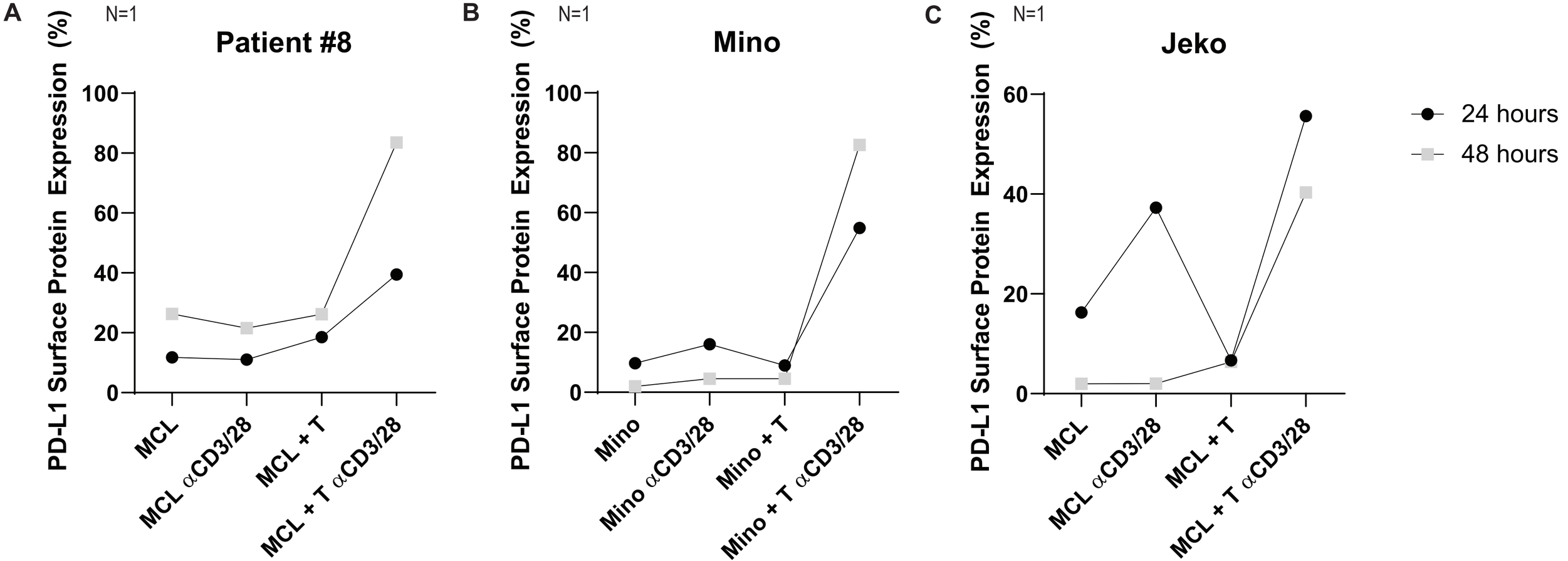


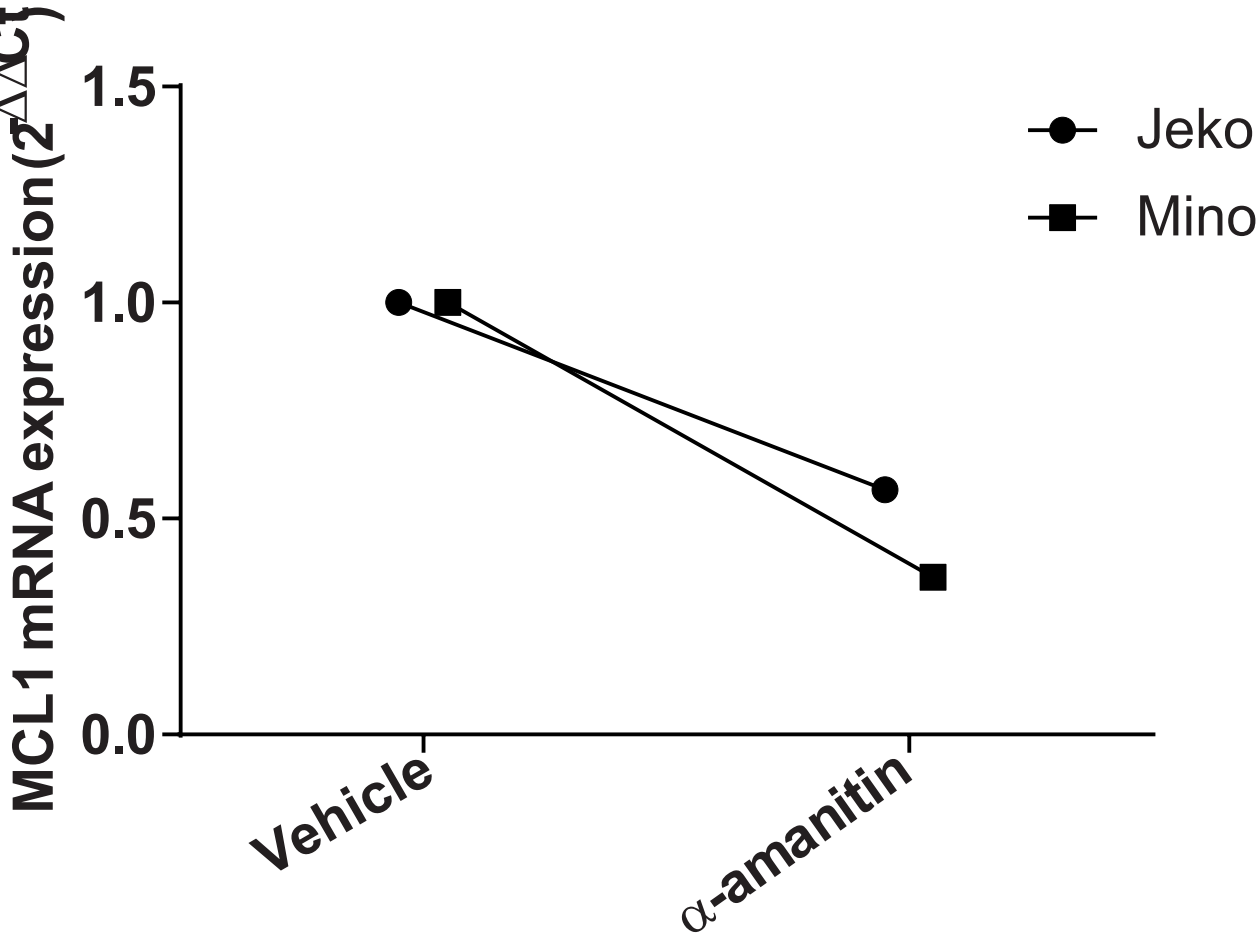
Supplementary Figure 1



Supplementary Figure 2



Supplementary Figure 3



Supplementary Figure 4