

Our cohort

Under TKI first line N=100		PFS TKI (months)	P value	OS TKI (months)	P value
CXCL1	low	9	P=0.0418	32	P=0.0409
	high	3		18	
CXCL2	low	8	P=ns	32	P=0.08
	high	6		23	
CXCL3	low	8	P=ns	32	P=ns
	high	7		30	
CXCL5	low	10	P=0.0003	38	P=0.0046
	high	3		25	
CXCL7	low	10	P=0.008	37	P=ns
	high	3		23	
CXCL8	low	8	P=ns	34	P=0.0235
	high	4		18	

Supplementary Table S1

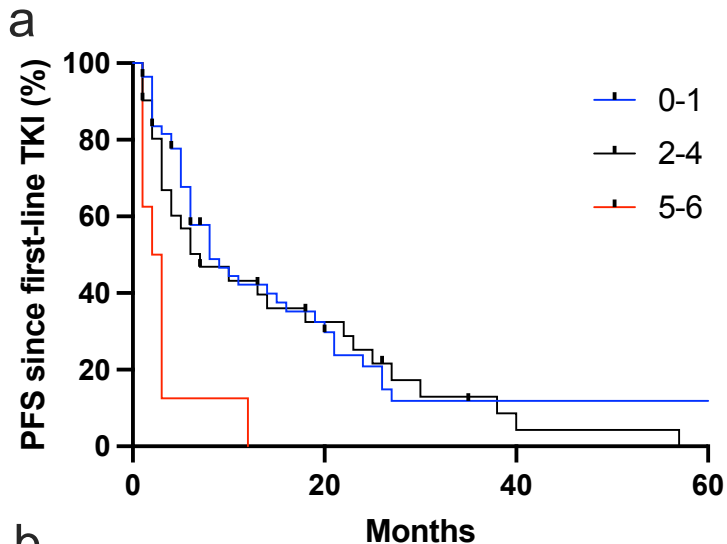
	Forward	Reverse
CCL17	5' TTCCCCTTAGAAAGCTGAAG	5' CTTCACTCTCTTGTTGTTGG
CCL18	5' CTATACCTCCTGGCAGATTC	5' CTCTCTTGGTTAGGAGGATG
CCL20	5' TATATTGTGCGTCTCCTCAG	5' GCTATGTCCAATTCCATTCC
CCL23	5' TGGAGAGTTACTTTGAAACG	5' ACAAGTTCAATTCTTCCTGG
CCL24	5' TAGTAACCAGCCTTCTGTTC	5' CTCAGGAATTCTCTTGAAAC
CXCL1	5' ATGCTGAACAGTGACAAATC	5' TCTTCTGTTCCCTATAAGGGC
CXCL11	5' CTACAGTTGTTCAAGGCTTC	5' CACTTTCCTGCTTTTACCC
CXCL5	5' GATGAGTACAAAAGTCCTGATCCA	5' CTGCAGCCACTGGTTCTGT
CXCL8	5' GTTTTTGAAGAGGGCTGAG	5' TTTGCTTGAAGTTTCACTGG
CXCR2	5' CCAGTCAGGATTTAAGTTTACC	5' GTTGATTTCCAGGGATTCTG
IL-1a	5' AGAGGAAGAAATCATCAAGC	5' TTATACTTTGATTGAGGGCG
mCCL17	5' CATTCCCTATCAGGAAGTTGG	5' CAGTCAGAAACACGATGG
mCCL22	5' CACATAACATCATGGCTACC	5' CAGAAGAACTCCTTCACTAAAC
mCXCR2	5' CTA CTGCAGGATTAAGTTTACC	5' GACGTATATTACAACCACAGC
mPD-L1	5' CAAGTGAGAATGCTAGATGTG	5' TCCATCTTGAGTCTTTGGAC
PD-L1	5'-ATGCCCCATACAACAAAATC	5'-GACATGTCAGTTCATGTTTCAG
TIMP3	5' CATGTGCAGTACATCCATAC	5' AGGTGATACCGATAGTTTCAG
VEFGA	5' TTTCTGCTGTCTTGGGTGCATTGG	5' ACCACTTCGTGATGATTCTGCCCT

Supplementary Table S2

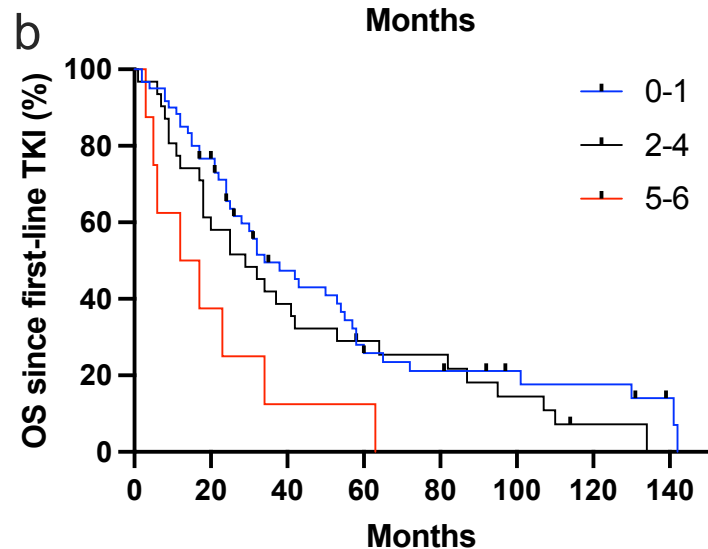
	Panel	Channel	Suppliers	References
CD107	1	FITC	Biolegend	121605
CD11b	2	BV605	Biolegend	101257
CD11c	2	BV785	Biolegend	117335
CD163	2	PE-eFluor 610	Invitrogen	61-1631-80
CD19	1	PE-CY7	Biolegend	104511
CD3	1	PercP-Cy5.5	Biolegend	100217
CD4	1	PE	BD	553730
CD45	1 & 2	AF700	Biolegend	103128
CD69	1	PE-CY7	Biolegend	104511
CD8	1	BV605	Biolegend	100743
F4/80	2	PE-Vio770	Miltenyi	130-118-459
Ly6C	2	APC-Vio770	Miltenyi	130-111-919
Ly6G	2	PerCP-Vio700	Miltenyi	130-117-500
MCHII	2	VioBlue	Miltenyi	130-112-394
NK1.1	1	APC	Biolegend	108709
Viability	1 & 2	405/520 Fixable Dye	Miltenyi	130-110-206

Supplementary Table S3

Our cohort



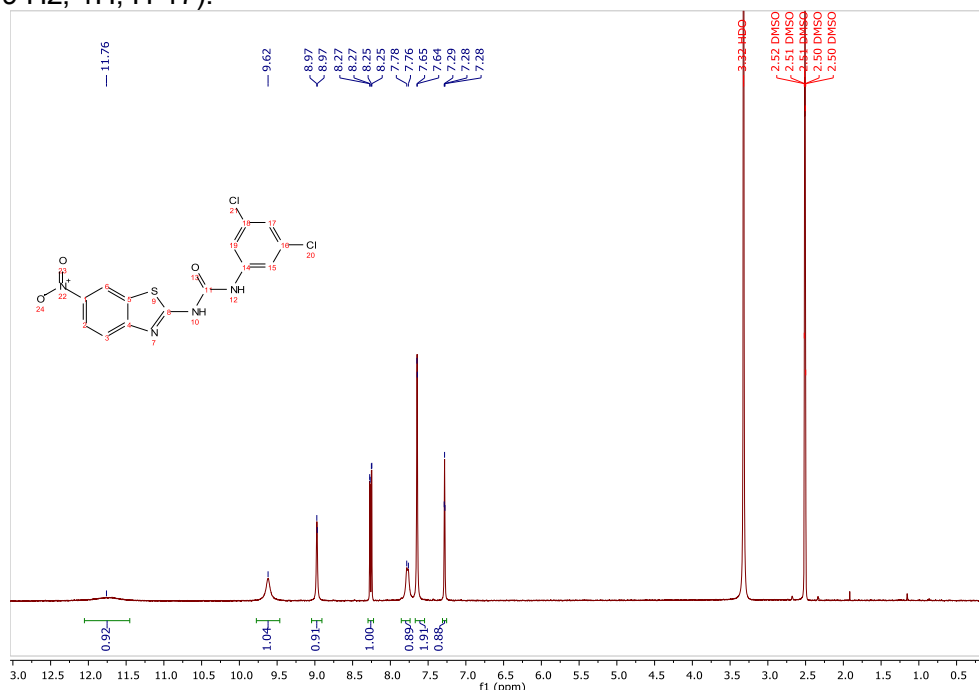
Under TKI N=98	score	PFS (months)	P value
CXCL1 + CXCL2 + CXCL3 + CXCL5 + CXCL7 + CXCL8	0	8	P=0.0097
	2-4	7	
	5-6	2.5	



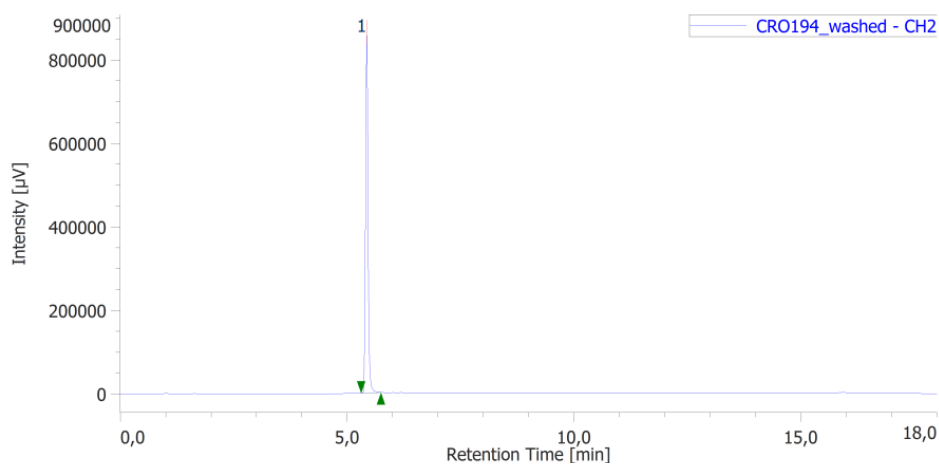
Under TKI N=98	score	OS (months)	P value
CXCL1 + CXCL2 + CXCL3 + CXCL5 + CXCL7 + CXCL8	0	34	P=0.0172
	2-4	29	
	5-6	14.5	

RCT001 was synthesized by adapting the already described procedure (Grytsai et al, in revision) on a 250 mmol scale. Under these conditions, 81.45 g (85% yield) of product could be obtained, with a >99.9% HPLC purity.

¹H NMR (400 MHz, DMSO-*d*₆): δ 11.76 (s, 1H, H-10), 9.62 (s, 1H, H-12), 8.97 (s, 1H, H-6), 8.26 (dd, *J* = 8.9, 2.4 Hz, 1H, H-2), 7.77 (d, *J* = 8.8 Hz, 1H, H-3), 7.65 (s, 2H, H-15, H-19), 7.28 (t, *J* = 1.9 Hz, 1H, H-17).

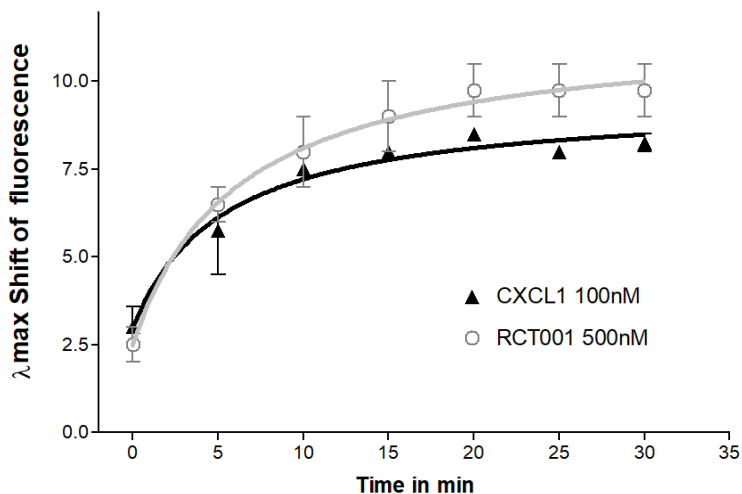


HPLC (λ_{254}): HPLC analysis on a JASCO PU-2089/AS4050 apparatus with a Supelco analytical column Ascentis Express C18, 10 cm × 4.6 mm, 5 μm, employing the flowing method: 50% B for 3 min, 50% B to 95% B over 2 min, 95% B for 10 min then from 95% B to 50% B over 2 min, 50% B for 3 min (total time: 20 min). Flow: 1 mL/min. Solvent A: water with 0.1% formic acid. Solvent B: acetonitrile with 0.1% formic acid.

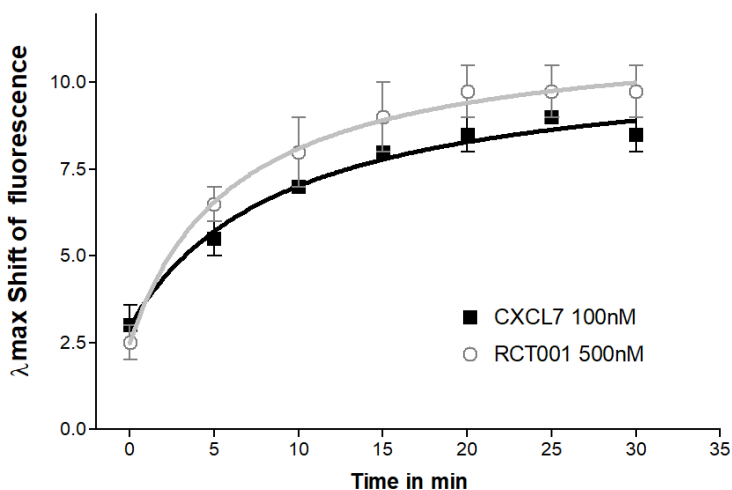


#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	2	5.433	3293089	862920	100.000	100.000	N/A	49035	N/A	1.055	

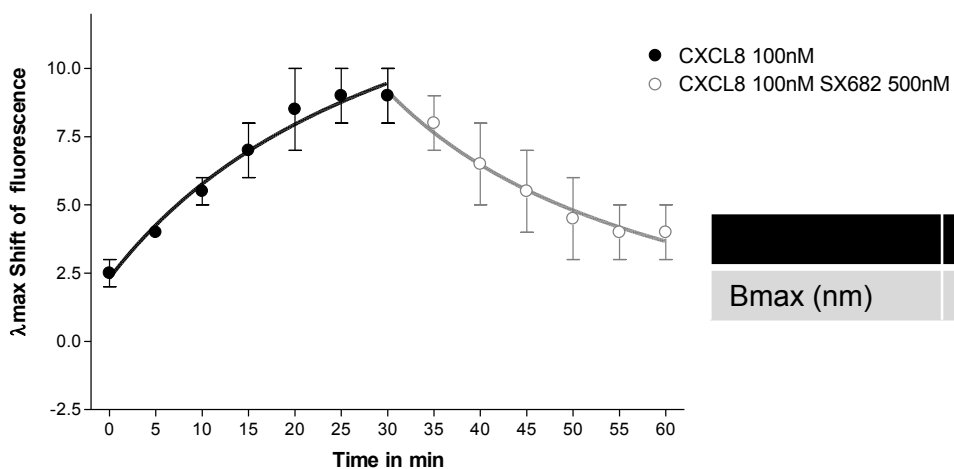
Supplementary Figure S2

a CXCR2 activity kinetics with CXCL1 and RCT001

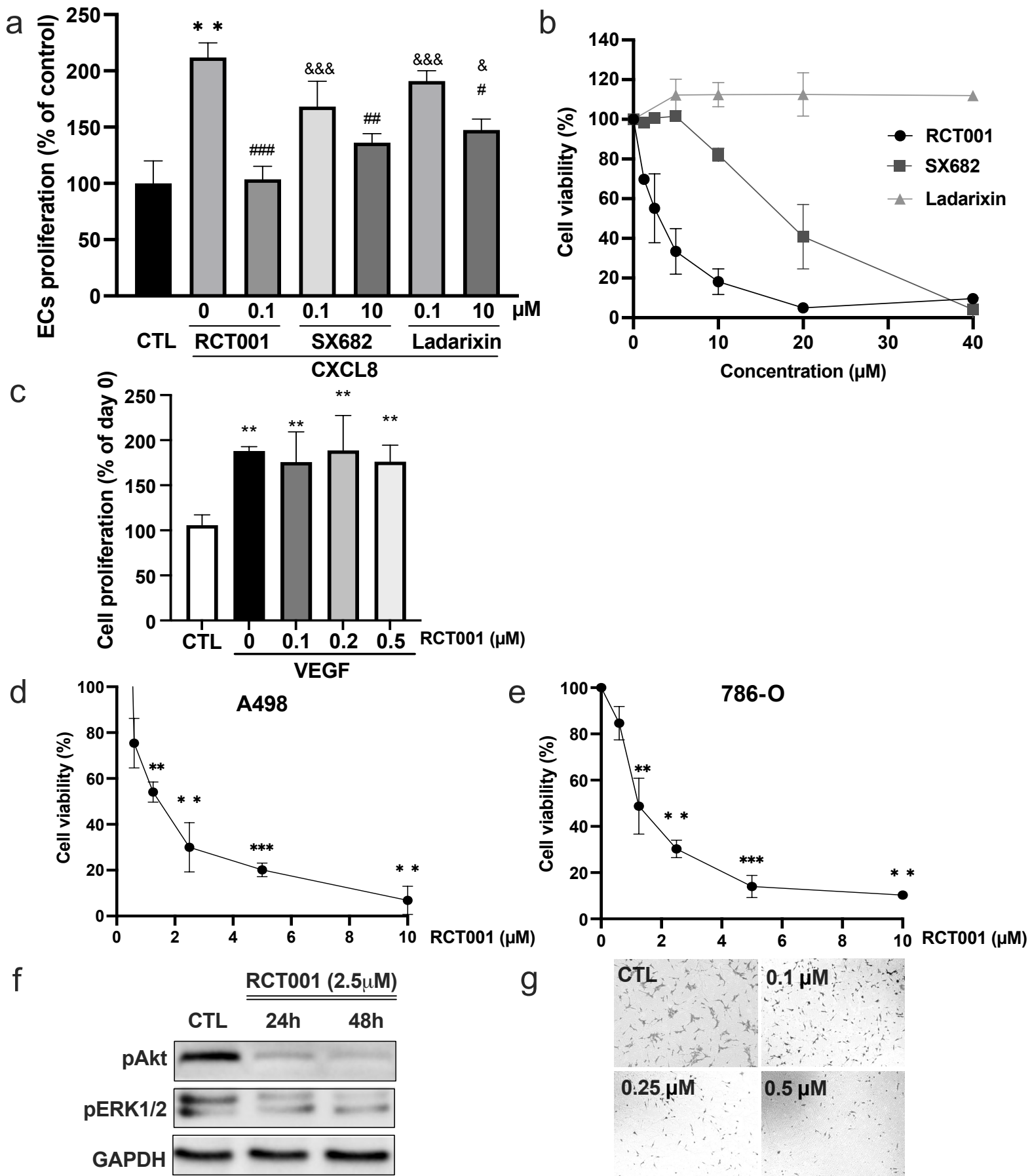
	CXCL1	RCT001
λ_{max} (nm)	6.50	8.38
KD (min)	5.29	7.51

b CXCR2 activity kinetics with CXCL7 and RCT001

	CXCL7	RCT001
λ_{max} (nm)	7.74	8.38
KD (min)	9.06	7.51

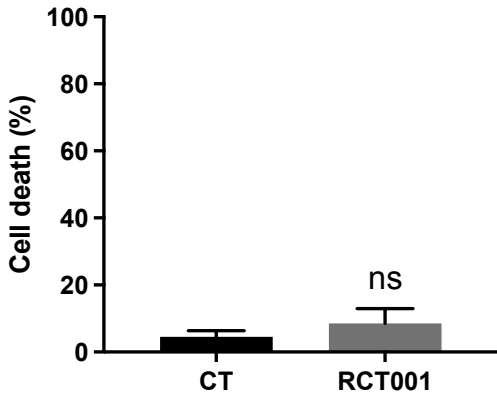
c CXCR2 activity kinetics with CXCL8 and SX682

	CXCL8	SX682
Bmax (nm)	15.38	-11.49

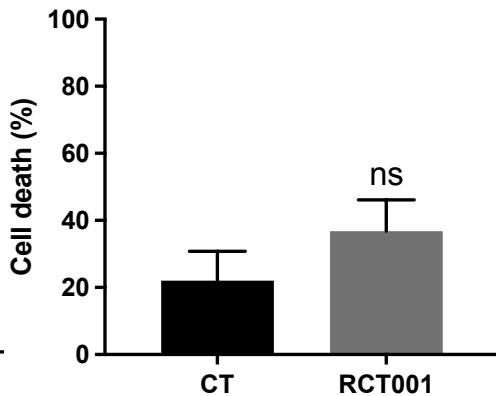


Supplementary Figure S4

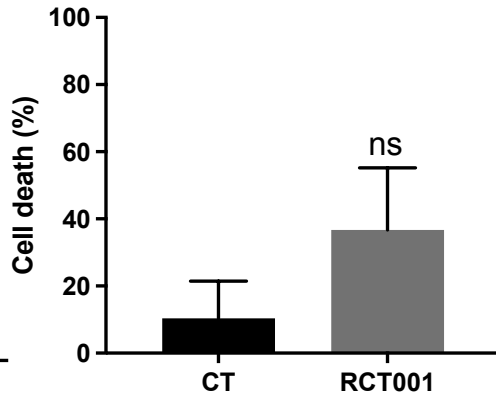
M0-like Macrophages



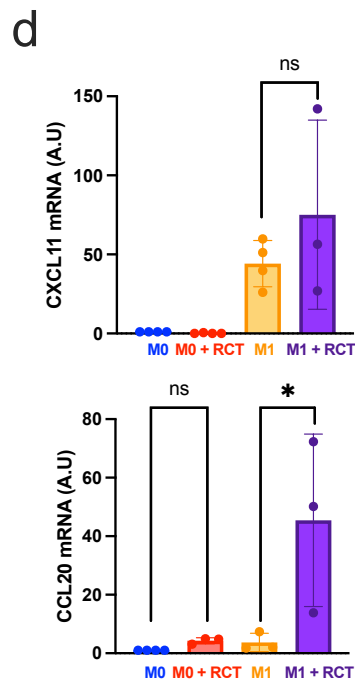
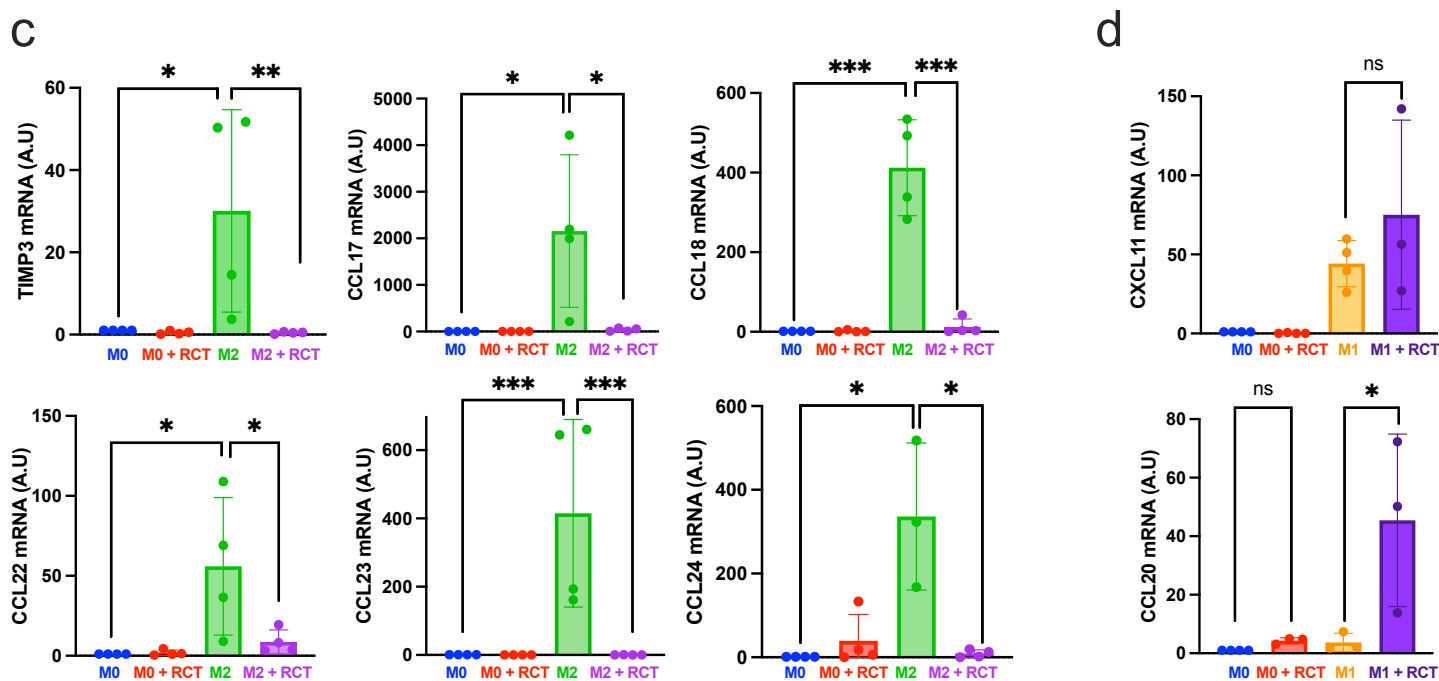
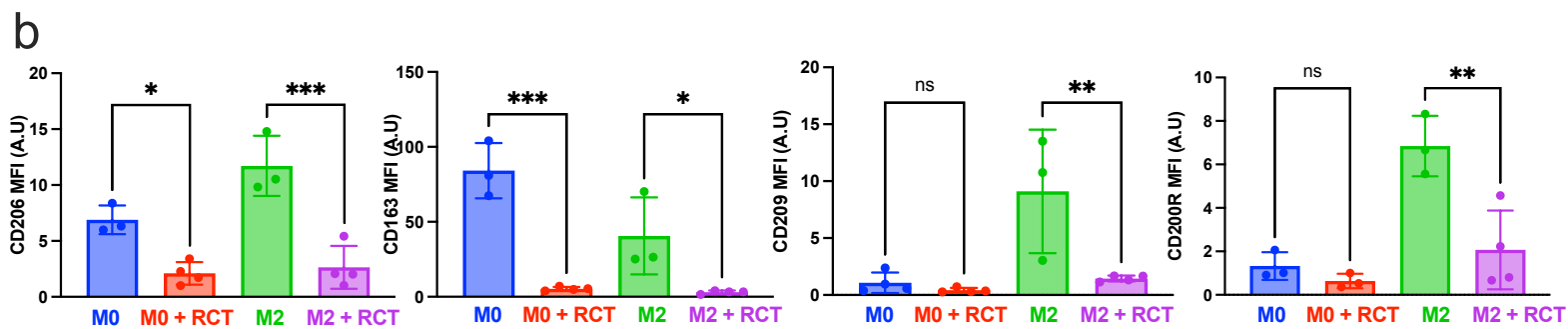
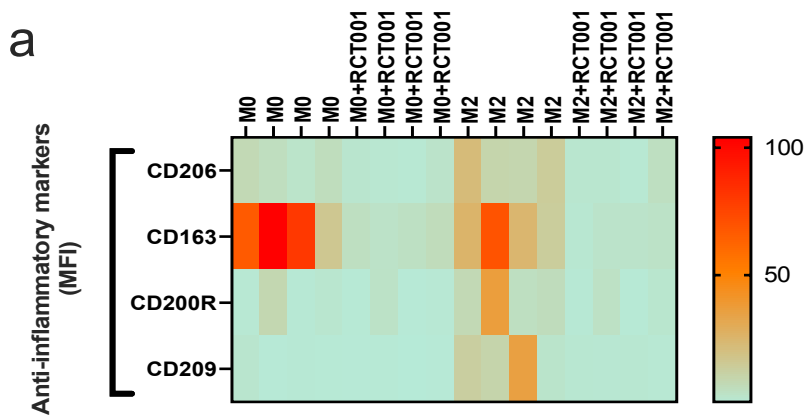
M1-like Macrophages



M2-like Macrophages

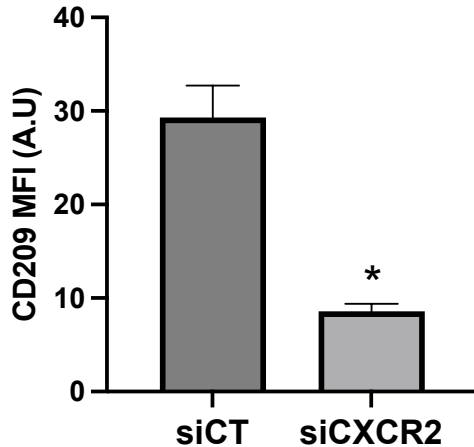
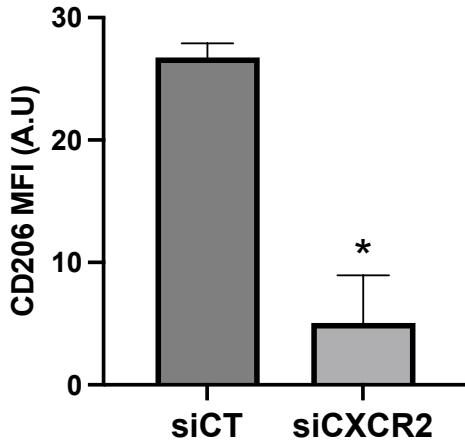
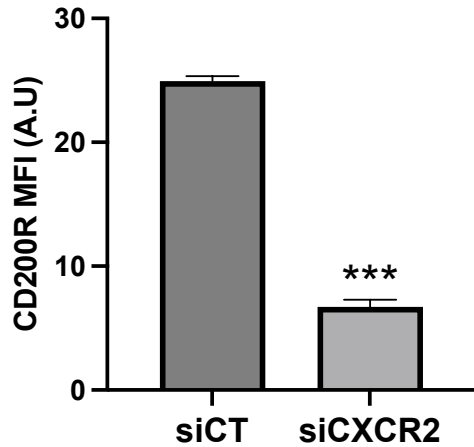
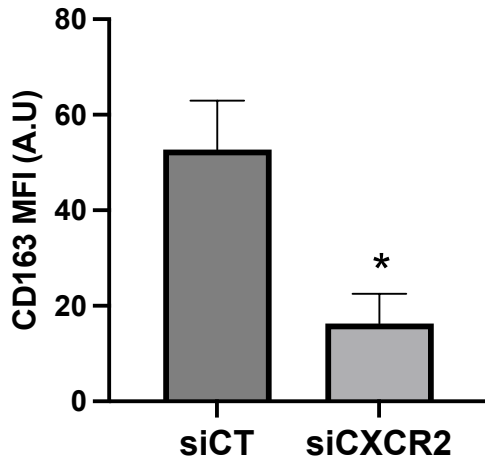


Supplementary Figure S5



Supplementary Figure S6

M2 Macrophages



Supplementary Figure S7

