CCR8-humanized Mouse Models for Drug Discovery

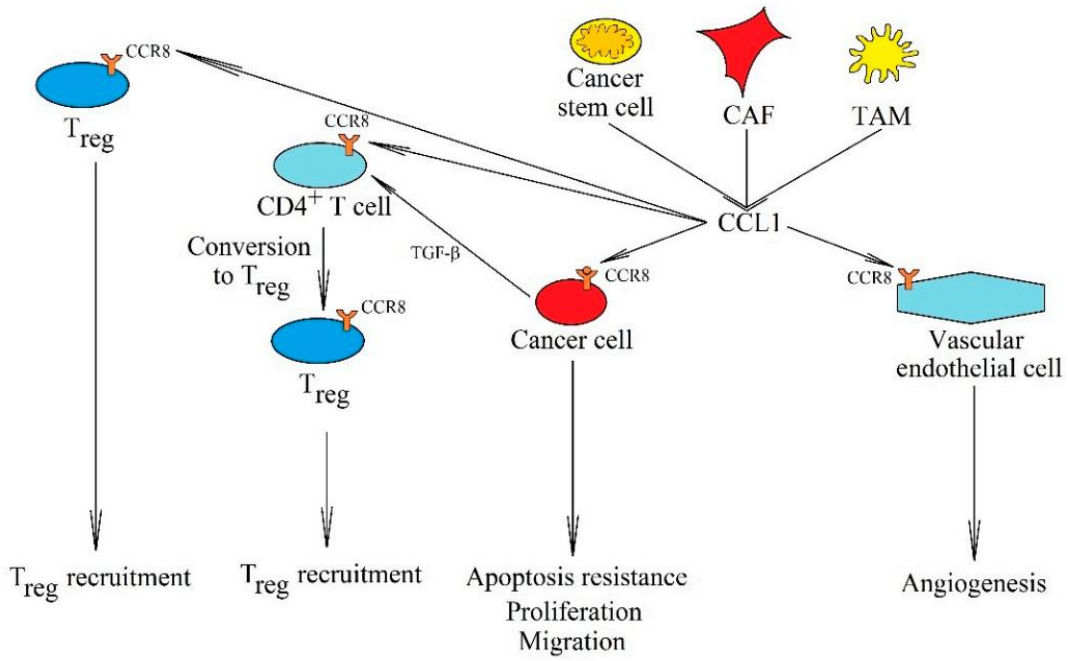
CCL1-CCR8 Signaling in Cancer Progression

CCR8, as a novel immune checkpoint in tumor microenvironment, was hotly discussed during 2022 AACR conference. Since then, numerous prestigious pharmaceutical corporations have shifted their attention to CCR8, previously almost unknown. You may wonder why CCR8 gave rise to so strong interest of pharmaceutical industry. Just follow us to have a quick review of CCR8, a new star in immunotherapy.

CCR8 facilitates recruitment of Treg cells and Th2 cells, and its overexpression is closely associated with multiple cancers including colorectal cancer, breast cancer, metastatic brain cancer, metastatic liver cancer. CCR8 is considered to be potential biomarker of Treg cells in tumor microenvironment, and promising target for immunotherapy.

CCL1 is the major ligand of CCR8, and CCR8 is the only known receptor of CCR8. The interaction between CCR8 and its ligand plays a key role in progression of multiple type-specific tumors and mediation of immune evasion of tumors.

In tumor microenvironment, CCL1, secreted by carcinoma-associated fibroblasts and tumor-associated macrophages, plays a crucial role in angiogenesis and other viral tumoral processes including metastasis, proliferation and apoptosis, through binding to CCR8 receptor. Besides, CCL1 can promote the recruitment of Treg cells and the differentiation of CD4 + T cells into Treg cells. Based on these facts, blocking CCL1/CCR8 signaling is considered to be another strategy of immunotherapies for cancer.



The Role of CCR8 in Cancer Progression

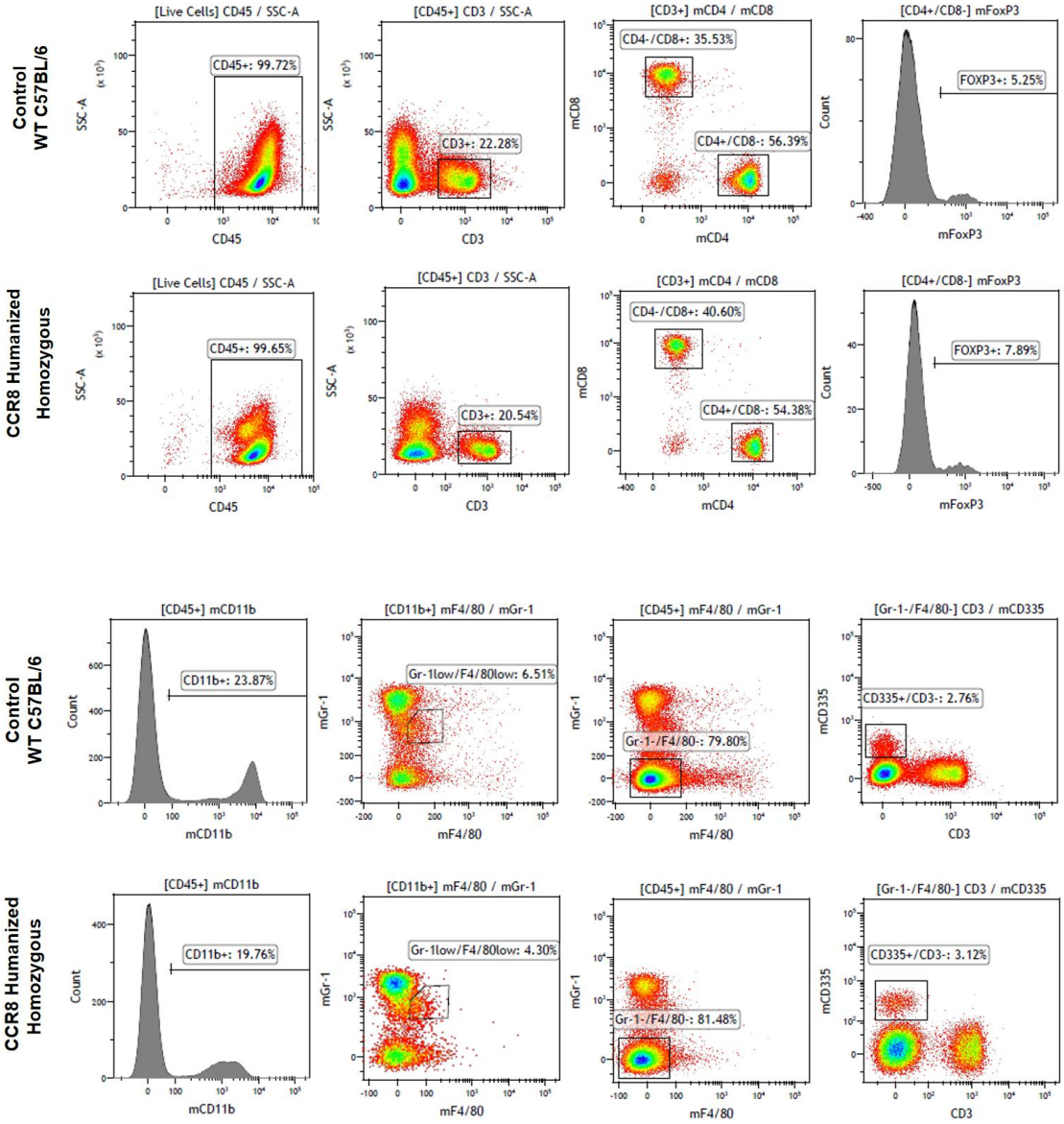
Strain Name: C57BL/6JSmoc-*Ccr8*$^{em1(hCCR8)\ Smoc}$
Catalog No.: NM-HU-190053
Strain State: Repository Live

Model Construction Strategy

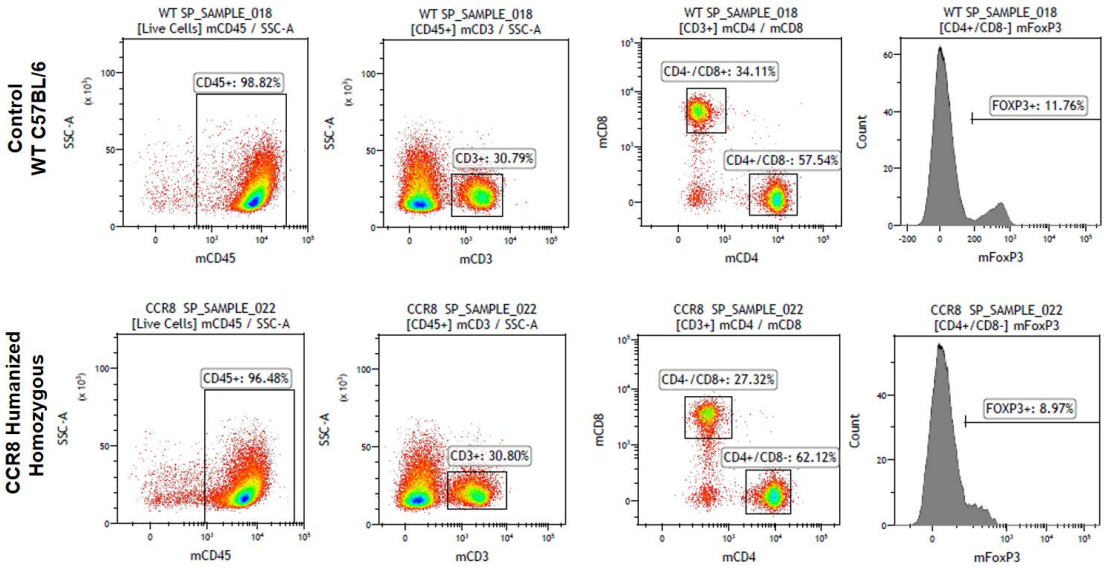
The endogenous mouse CCR8 gene was replaced by human CCR8 gene through specific knock-in.

Validation Data

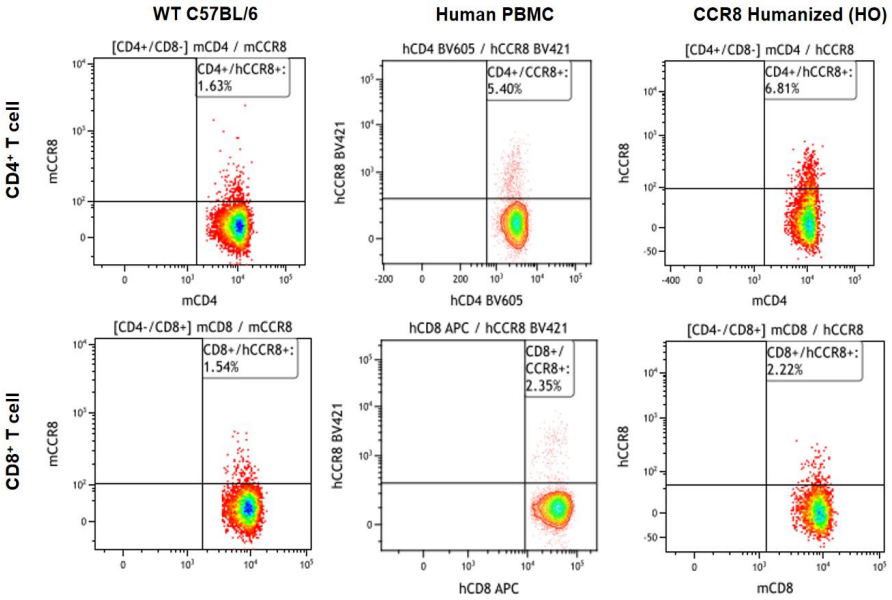
1.FACS analysis of proportion of type-specific immune cells in the peripheral blood derived from wild type C57BL/6 mice and CCR8-humanized mice, respectively.



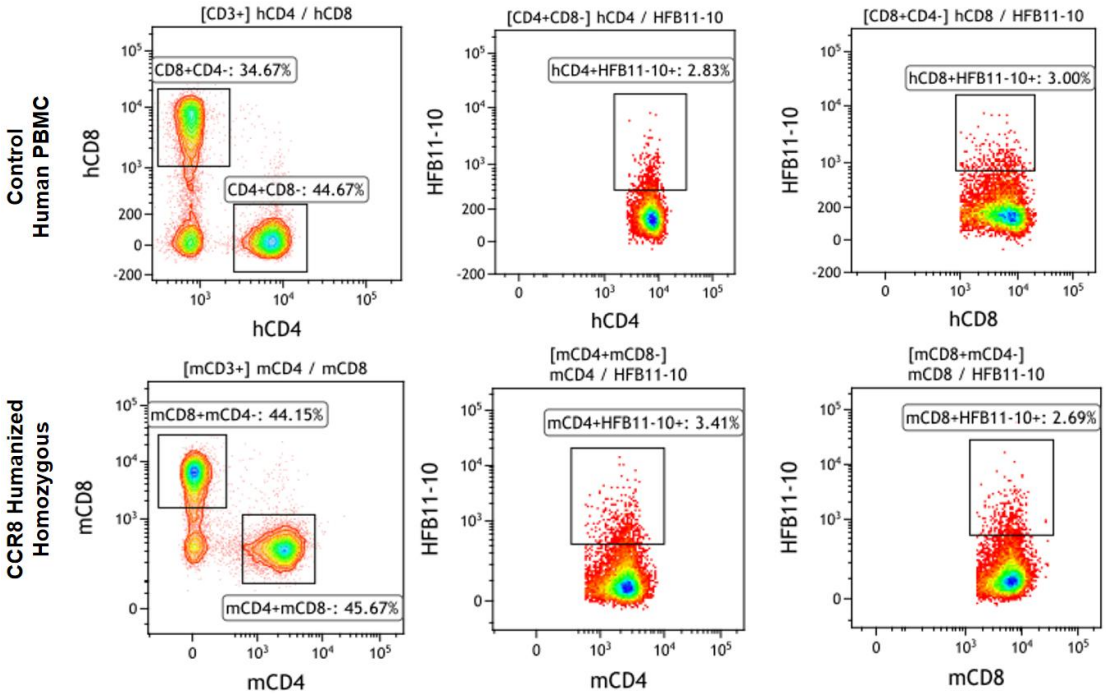
2.FACS analysis of proportion of type-specific immune cells in the spleens derived from wild type C57BL/6 mice and CCR8-humanized mice, respectively.



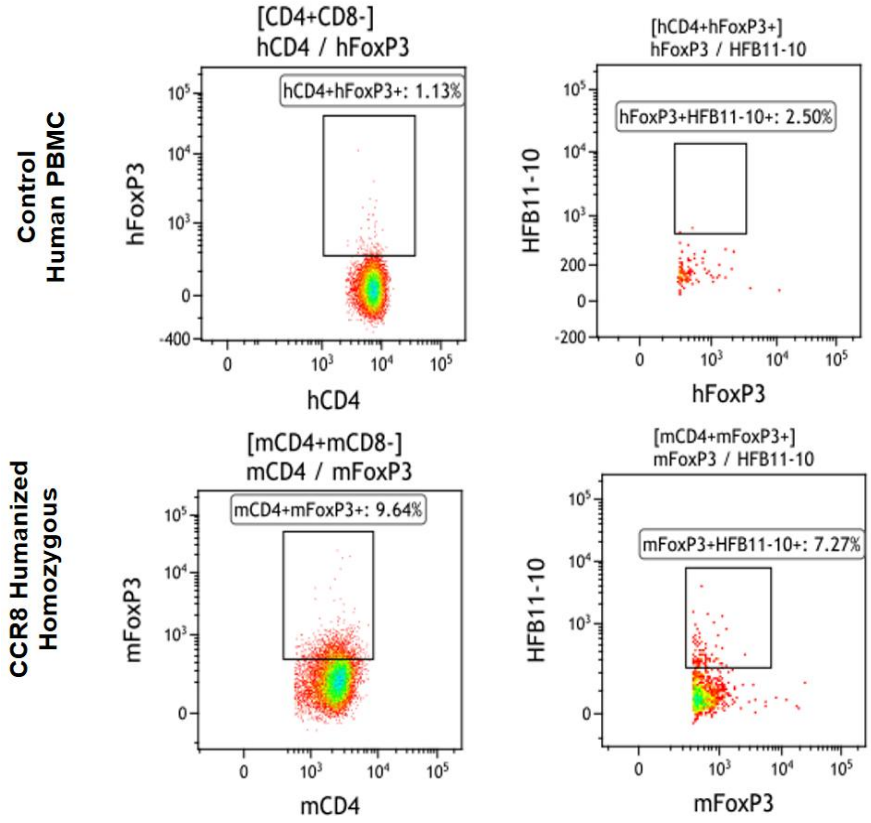
3.FACS analysis of humanized CCR8(hCCR8) expression in CCR8-humanized mice



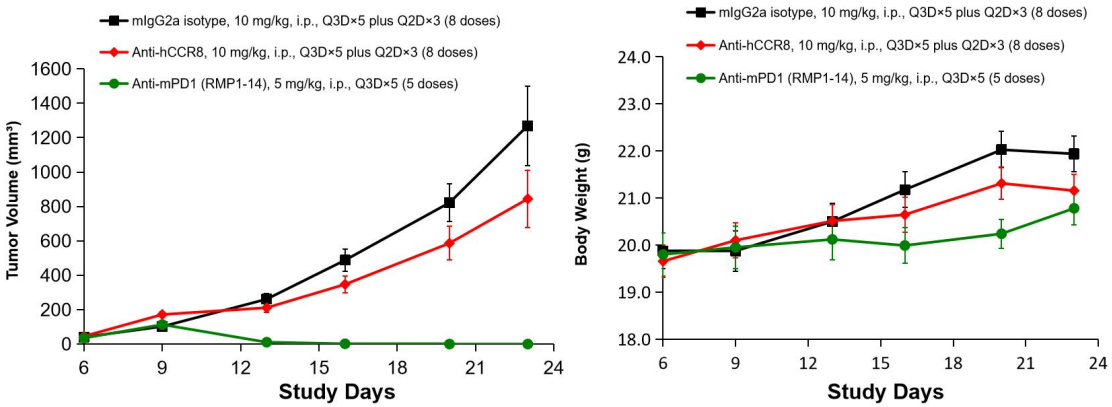
4.FACS analysis of binding of anti-hCCR8 antibody to T cells in peripheral blood of CCR8-humanized mice



5.FACS analysis of binding of anti-hCCR8 antibody to T cells in spleens of CCR8-humanized mice



6.Anti-tumor efficacy validation of anti-CCR8 antibody in CCR8-humanized mice



Humanized Mice for CCR8/CCL1 Signaling-targeted Drug Research

Apart from CCR8-humanized mouse, other strains for CCR8/CCL1signaling-targeted drug research are also available at SMOC.

Genes	Model Names	Catalog No.	Strain state
CCR8	Ccr8-KO	NM-KO-190024	Repository Live
	hCCR8	NM-HU-190053	Repository Live
	hCCR8(2)	NM-HU-200054	Repository Live
	hCCR8(BALB/c)	NM-HU-200048	Repository Live
	hCCR8/hCTLA-4	NM-HU-210435	Repository Live
	hCCR8/hPD-1	NM-HU-210400	Repository Live
	hCCR8/hTIGIT	NM-HU-210426	Embryo Cryopreservation
CCL8	Ccl8-KO	NM-KO-190521	Repository Live
CCL1	Ccl1-KO	NM-KO-190009	Embryo Cryopreservation
	hCCL1	NM-HU-2000074	Embryo Cryopreservation

500+ Therapeutic Target-humanized Mice

We have been updating our repository of humanized mice for drug research. Part of best-selling strains, including immune checkpoint-humanized mice and cytokine receptor-humanized mice, are listed as follows.

Single Target-humanized Models			
PD-1	CD28	TIGIT	CD3e
IL6	TLR7	CD19	OX40
TLR8	IDO1	CXCR2	TLR9
PD-L1	PCSK9	CCR2	CD27
IL6R	TNFR2	TNFSF15	.....
Dual Target-humanized Models			
PD-1/PD-L1	PD-1/TIGIT	PD-1/4-1BB	OX40/CTLA4
PD-1/CTLA4	PD-1/TIM3	PD-L1/CTLA4	PD-1/OX40
PD-1/LAG3	PD-L1/OX40	ALB/FCRN	.....

Multiple Target-humanized Models			
4-1BB/PD-1/PD-L1	PD-1/PD-L1/CTLA4	PD-1/PD-L1/CCR8	PD-1/PD-L1/LAG3
PD-1/PD-L1/TIM3	PD-1/PD-L1/TIGIT	PD-1/PD-L1/PD-L2	SIRPA/CD47/PD-L1
SIRPA/CD47/PD-1/PD-L1	CD3E/CD3D/CD3G	IL3/CSF2/SIRPA/CD47	.....

About Us

Founded in 2000, Shanghai Model Organisms Center, Inc (SMOC), listed on STAR market (Stock code: 688265) and accredited by AAALAC and OLAW, is committed to providing high quality genetically engineered animal models and associated services with more than 20 years of experience in animal modeling and genetics & genomics research.

References

[1] Cinier J, Hubert M, Besson L, et al. Recruitment and Expansion of Tregs Cells in the Tumor Environment-How to Target Them? *Cancers (Basel)*. 2021;13(8):1850. Published 2021 Apr 13.

[2] Korbecki J, Grochans S, Gutowska I, Barczak K, Baranowska-Bosiacka I. CC Chemokines in a Tumor: A Review of Pro-Cancer and Anti-Cancer Properties of Receptors CCR5, CCR6, CCR7, CCR8, CCR9, and CCR10 Ligands. *Int J Mol Sci.* 2020;21(20):7619. Published 2020 Oct 15.

[3] Karin N. Chemokines and cancer: new immune checkpoints for cancer therapy. *Curr Opin Immunol*. 2018;51:140-145.

[4] Campbell JR, McDonald BR, Mesko PB, et al. Fc-Optimized Anti-CCR8 Antibody Depletes Regulatory T Cells in Human Tumor Models. *Cancer Res*. 2021;81(11):2983-2994.