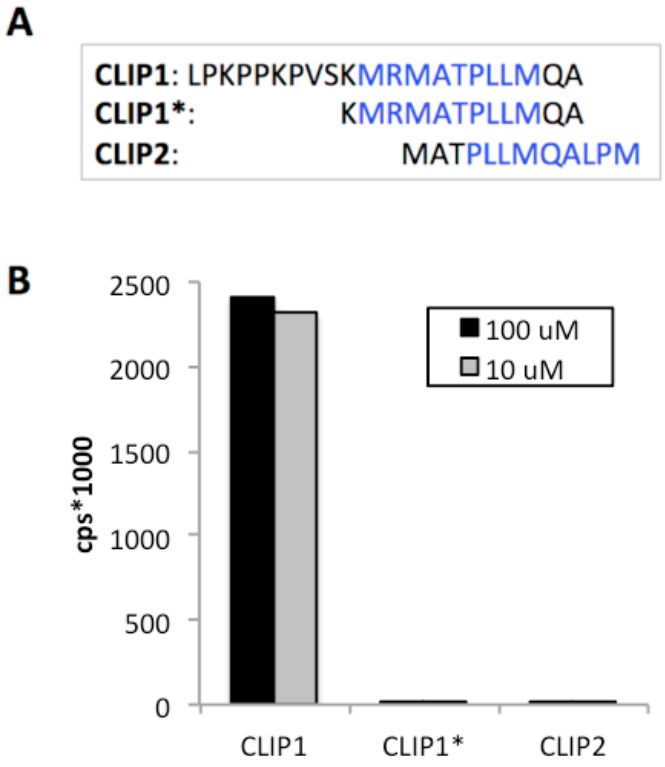
Supporting Information

Supplemental Table I: T1D-associated auto-antigen derived peptides eluted from 293T transductants with or without DM expression [a].

DQ Molecules	Start AA	Sequence	AutoAg (-DM)	AutoAg (+DM)	Accession #
DQ2	126	KPPSKRLTFGWHRAEILGAL	ZnT8		Q8IWU4
	321	GGAVFGEEGLTLNLEDV	HSP60		P10809
	323	AVFGEEGLTLNLEDV	HSP60		P10809
DQ8	876	PAEGTPASTRPLLDFRRKVNKCYR	IA-2		Q16849
	989	VQTKEQFEFALTAVAEEVNAILKALP	IA-2beta		Q92932
	126	KPPSKRLTFGWHRAEILGALLS	ZnT8	ZnT8	Q8IWU4
	126	KPPSKRLTFGWHRAEILGAL	ZnT8	ZnT8	Q8IWU4
	448	IPALDSLTPANEDQK		HSP60	P10809
DQ2-8	424	VPSPVSSEPPKAARPPVTPVLLE	IA-2		Q16849
	622	GDTTFEYQDLCRQ		IA-2	Q16849
	330	DGMAELMAGLMQGVDHG		IA-2beta	Q92932
	126	KPPSKRLTFGWHRAEILGALLS		ZnT8	Q8IWU4
	448	IPALDSLTPANEDQK		HSP60	P10809
	523	KVVRTALLD		HSP60	P10809
DQ8-2	541	LEAQTGLQILQTGVGQREEAAAVLP		IA-2	Q16849
	956	KDQFEFALTAVAEEVNAILKALP	IA-2		Q16849
	126	KPPSKRLTFGWHRAEILGALLS	ZnT8	ZnT8	Q8IWU4
	126	KPPSKRLTFGWHRAEILGAL		ZnT8	Q8IWU4
	455	TPANEDQKIGIEIIK		HSP60	P10809

[a] *Nested peptides derived from ZnT8 and identified from different DQ molecules is highlighted in light gray. Nested peptides derived from HSP60 and identified from different DQ molecules is highlighted in dark gray. The "-DM" represents autoantigen-derived peptides detected in DQ+Ii samples, while the "+DM" represents autoantigen-derived peptides detected in DQ+Ii+DM samples.*

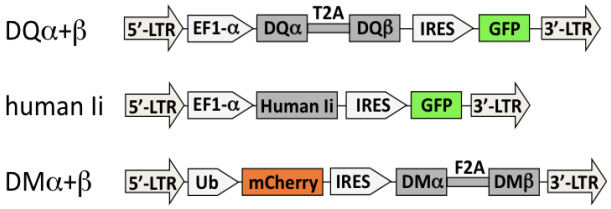


Supplemental Figure 1: N-terminus sequence of CLIP peptides and the specificity of CerCLIP.1 mAb. (A) Sequence alignment of Ii-derived CLIP1, CLIP1* and CLIP2 peptides for the identification of CerCLIP.1 mAb specificity. (B) The CerCLIP.1 mAb specificity. ELISA plate was coated with 100 µM or 10 µM of CLIP peptides (in 50 µL) listed in (A); then detected with 2 µg/ml of purified CerCLIP.1 mAb (Santa Cruz Biotech), followed by 2 µg/ml of biotinylated goat-anti-mouse IgG mAb (SouthernBiotech), and developed with Eu-ELISA, n=2.

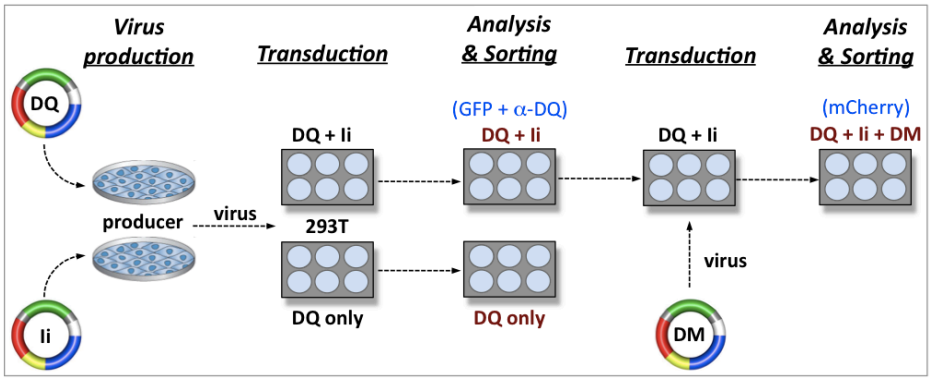
A

MHC	α chain	β chain	T1D association
DQ1	DQA1*0101	DQB1*0501	Neutral
DQ6	DQA1*0102	DQB1*0602	Protective
DQ2	DQA1*0501	DQB1*0201	Susceptible
DQ8	DQA1*0301	DQB1*0302	
DQ2-8	DQA1*0501	DQB1*0302	
DQ8-2	DQA1*0301	DQB1*0201	

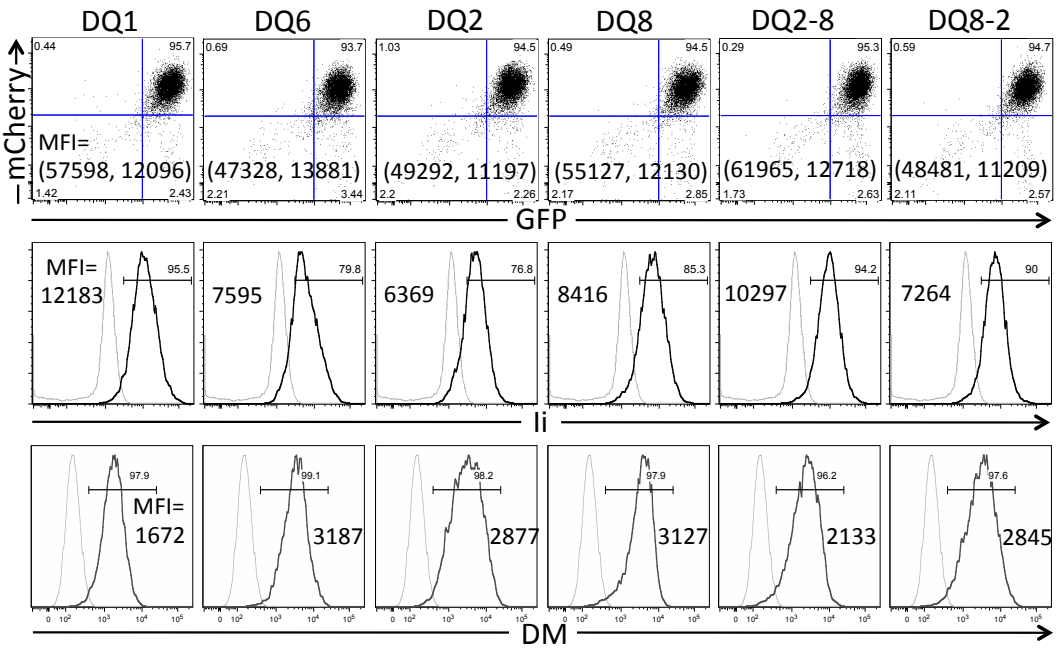
B



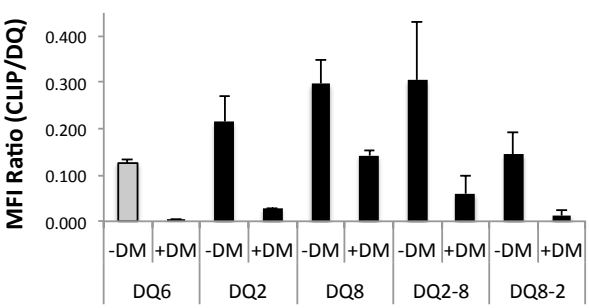
C



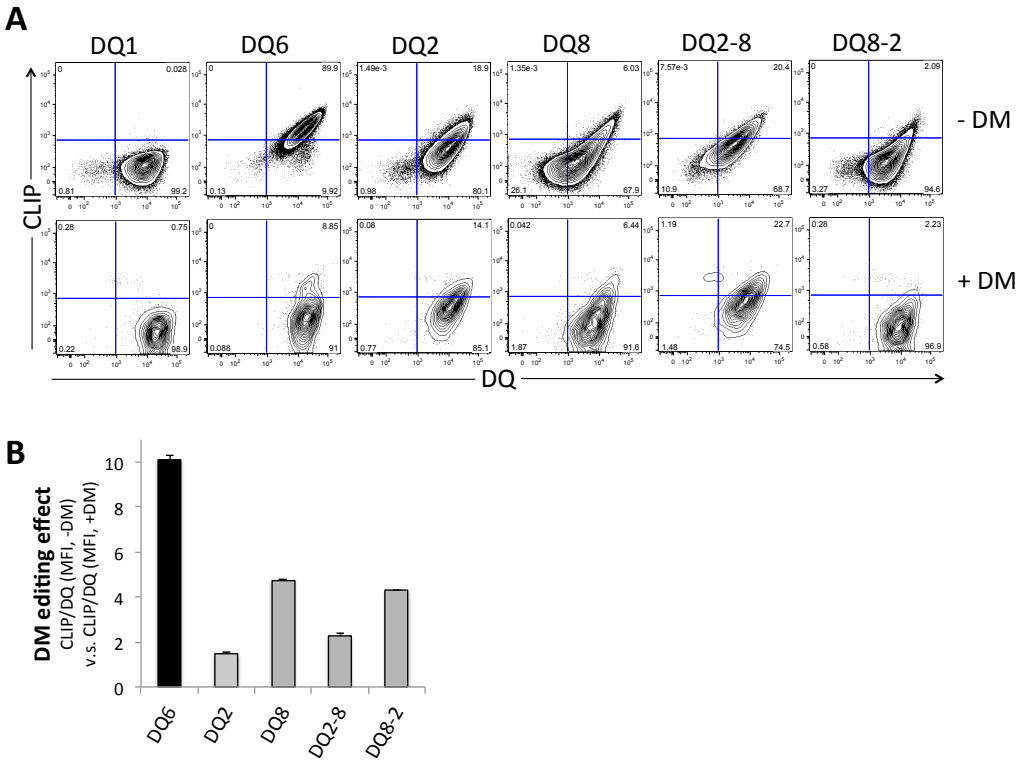
D



E



Supplemental Figure 2: The expression of Ii, DQ and DM in 293T cells. (A) The α and β chain gene allele information of T1D neutral, protective and susceptible DQ molecules. (B) Diagrams of the constructs and the markers for the expression of Ii, DQ or DM in 293T cells. (C) Strategies of lentiviral mediated gene transduction and the markers used for the cell sorting. 293T cells were firstly transduced by high titer of fresh lentivirus generated in producer cells transfected with DQ or Ii construct. Then, the transductants were sorted by GFP and DQ (SPVL3) expression. To generate the DQ+Ii+DM cells, DQ+Ii cells were further transduced by lentivirus with DM, and sorted by GFP, mCherry and cell surface DQ expression. (D) Comparison of the relative expression level of GFP and mCherry (top panel), intracellular Ii (PIN-1, middle panel) and intracellular DM (Map.DM1, bottom panel) in DQ+Ii+DM cells with the negative control. The MFI showed in the top panel with (x, y) represents the MFI of GFP and mCherry expression level, respectively. The MFI showed in the middle or the bottom panel represents the MFI of Ii or DM expression level, respectively. (E) The MFI ratio of cell surface CLIP and DQ levels in the absence or presence of DM expression. Cells were surface stained for CLIP (CerCLIP.1) and DQ (SPVL3) and gated on the same level of GFP and/or mCherry expression. n=3.



Supporting Figure 3. DM editing effects of T1D associated DQ molecules on Ii-derived CLIP peptides in T2 transductants. (A) Cell surface presentation of Ii-derived CLIP peptides and DQ molecules in T2 transductants in the absence or presence of DM expression. T2 cells were transduced with DQ and DM, using GFP and mCherry as the marker of DQ and DM expression, respectively. Cells were gated on GFP+mCherry- (top panel) or GFP+mCherry+ (bottom panel). (B) Difference of DM editing effects between T1D associated and non-associated DQ molecules. The DM editing effects are indicated by the ratio of surface CLIP/DQ MFI (mean fluorescence index) between the cells in the absence or presence of DM expression, as shown in (A), n=3.