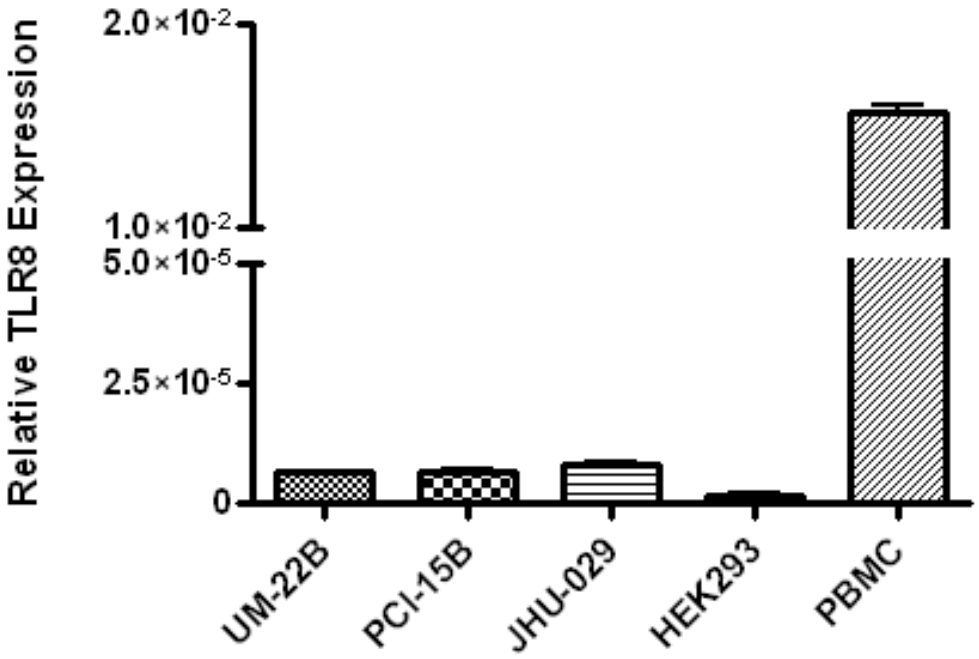
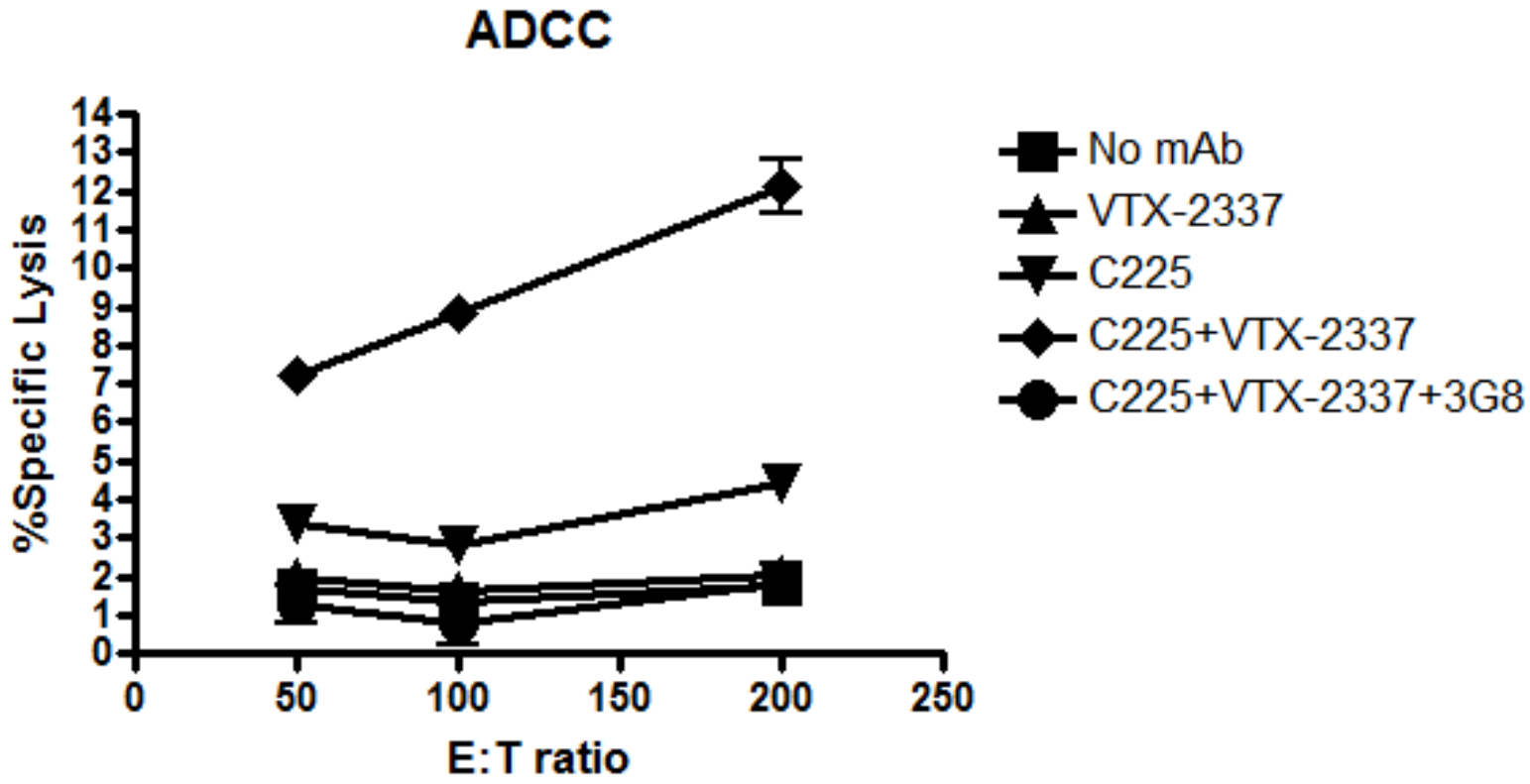
Supplementary Figure 1



Supplementary Figure 1 Caption

TLR8 expression. HNC cell lines express a negligible amount of TLR8 mRNA. RNA was isolated from HNC tumor cells lines, HEK293 and PBMC, and thereafter used to generate cDNA. qRT-PCR for TLR8 expression relative to GUS was performed. PBMC relative TLR8 expression is 1000Xs higher than HNC tumor cell lines assayed, and HNC tumor cells show similar relative TLR8 expression as TLR8-negative HEK293.

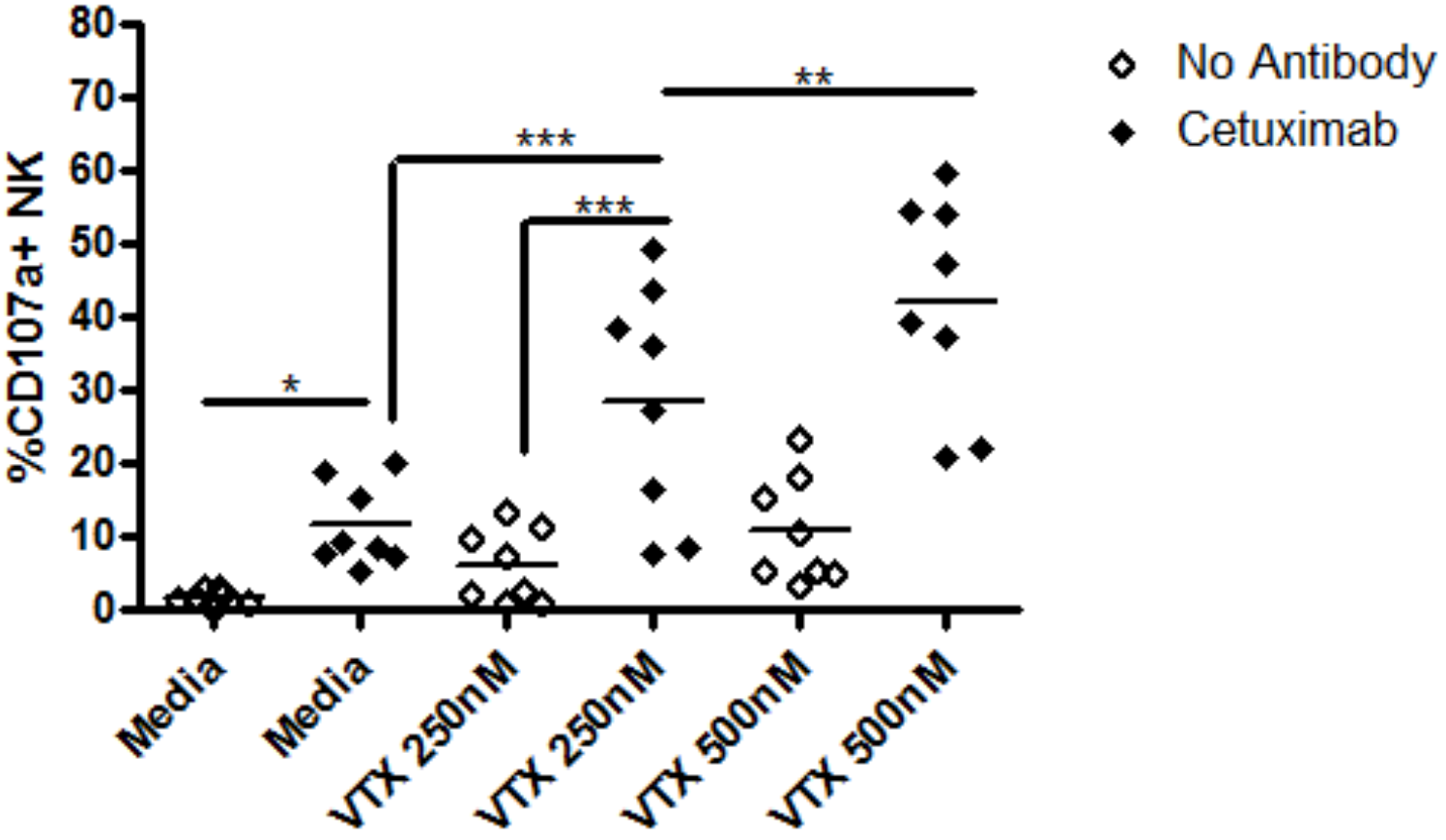
Supplementary Figure 2



Supplementary Figure 2 Caption

CD16 blockade abrogates TLR8-stimulated cetuximab-mediated ADCC. PBMC were treated 18 h with media or VTX-2337 (250nM). They were then incubated with 10μg/mL of IgG1 isotype mAb or anti-CD16 (3G8) for 30 min. A 51-Cr release assay was then performed at the indicated E:T ratios.

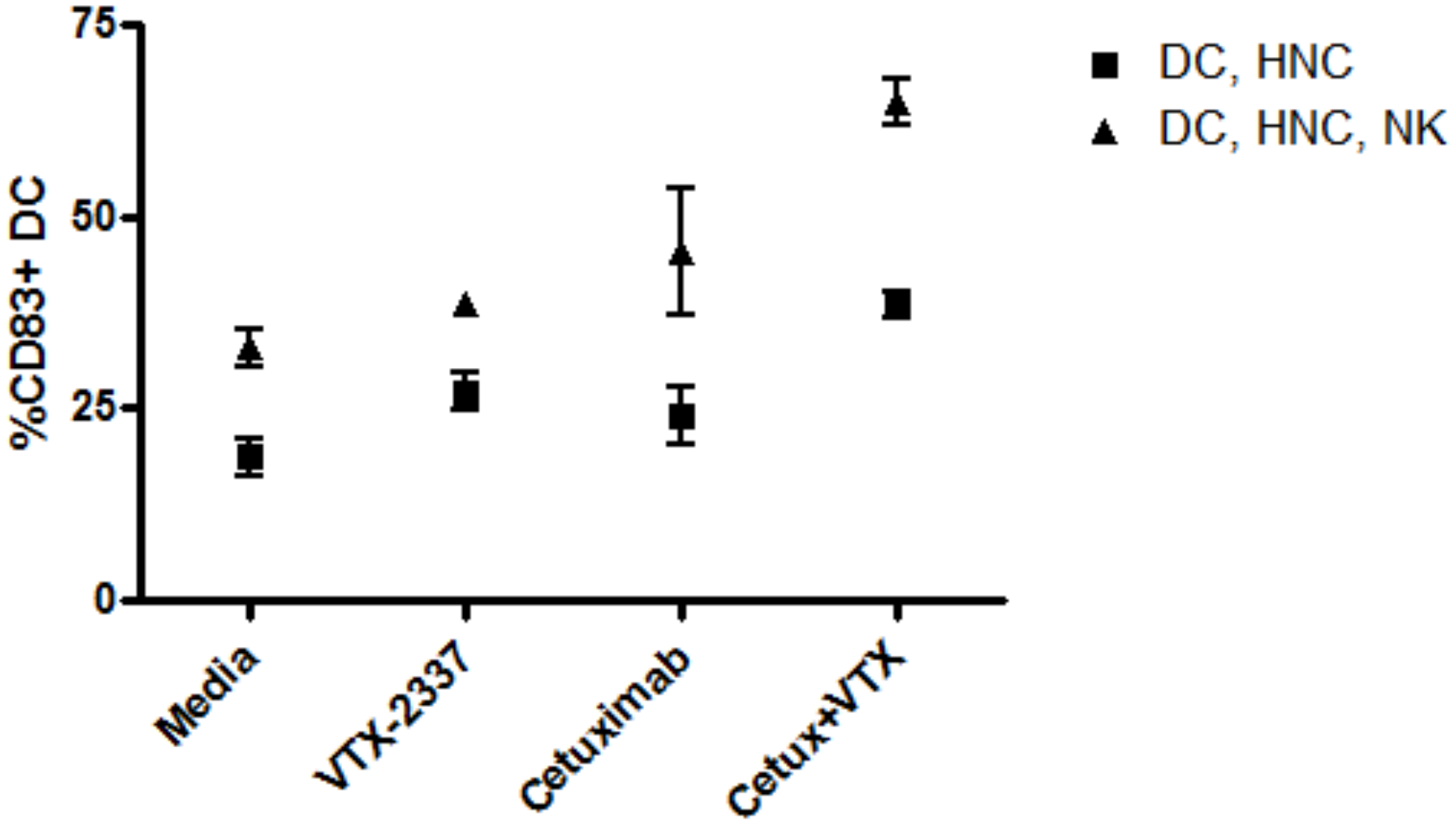
Supplementary Figure 3



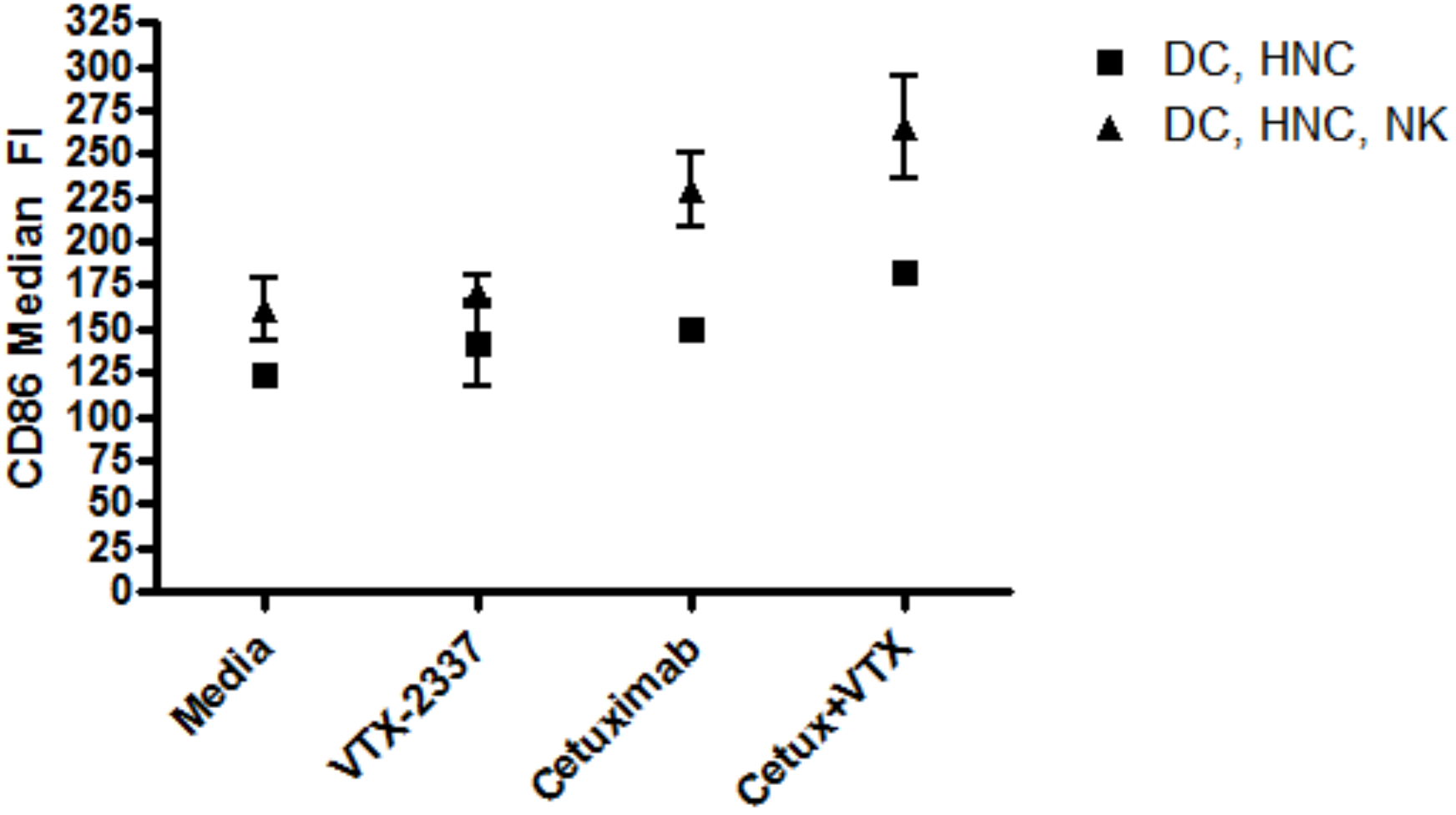
Supplementary Figure 3 Caption

TLR8 stimulation and cetuximab coating of HNC cells enhance NK cell degranulation more than TLR8 stimulation alone. PBMC were incubated with TLR8 selective agonist VTX-2337 (250nM) or with media for 18 h, then co-cultured with PCI-15B HNC cells (E:T=1:1) with or without cetuximab.

Supplementary Figure 4a



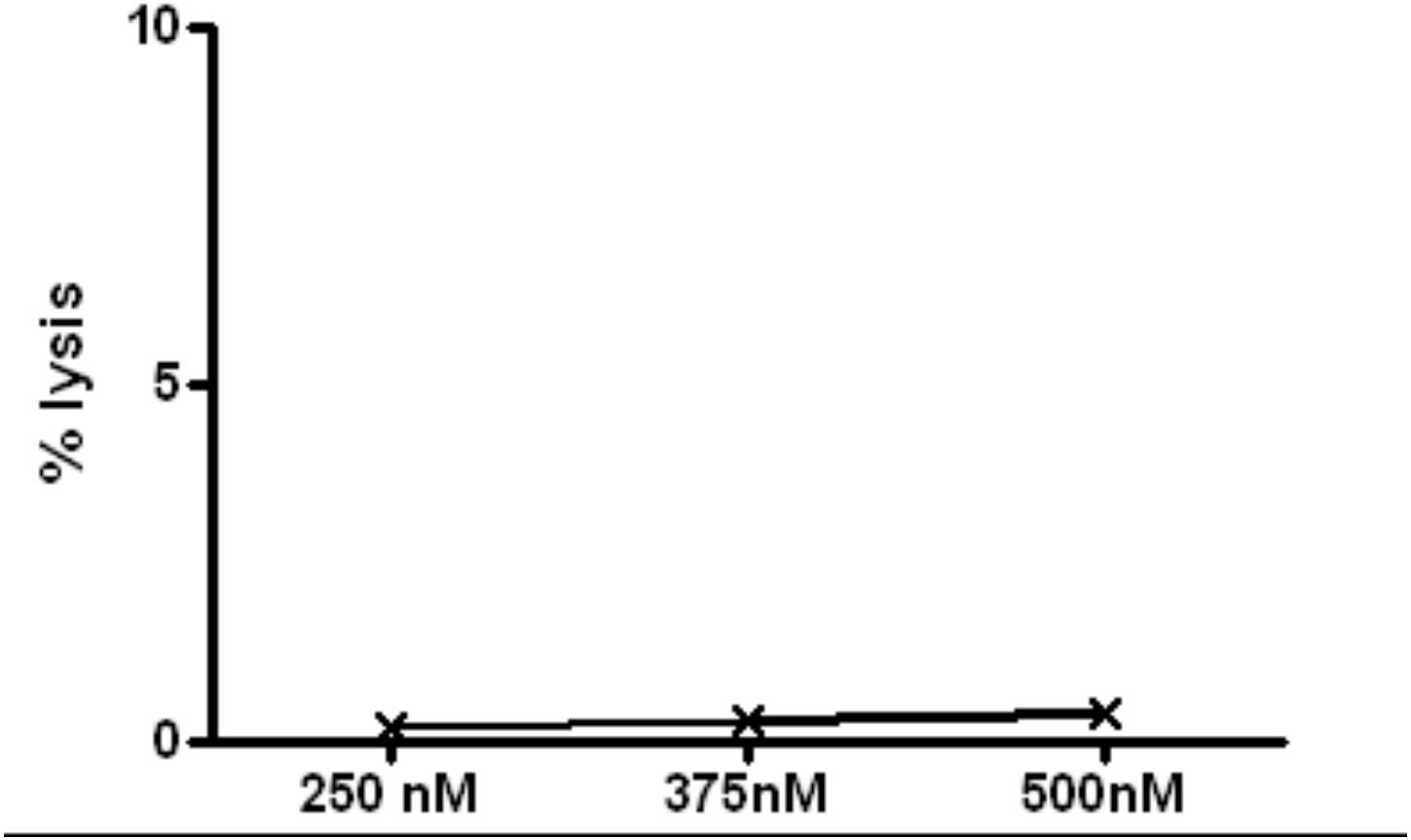
Supplementary figure 4b



Supplementary Figure 4 Caption

NK cells mediate VTX-2337- and cetuximab-enhanced DC maturation **(A,B)** DC were co-cultured with NK cells and PCI-15B HNC cells at 1:1:1 ratio for 48 h. DC were then isolated and stained for $CD11c^{+}EpCAM^{neg}$ DC and analyzed for %CD83 positive, and CD86 median FI. DC in the presence of TLR8-stimulation, cetuximab-coated HNC and NK demonstrated the greatest maturity.

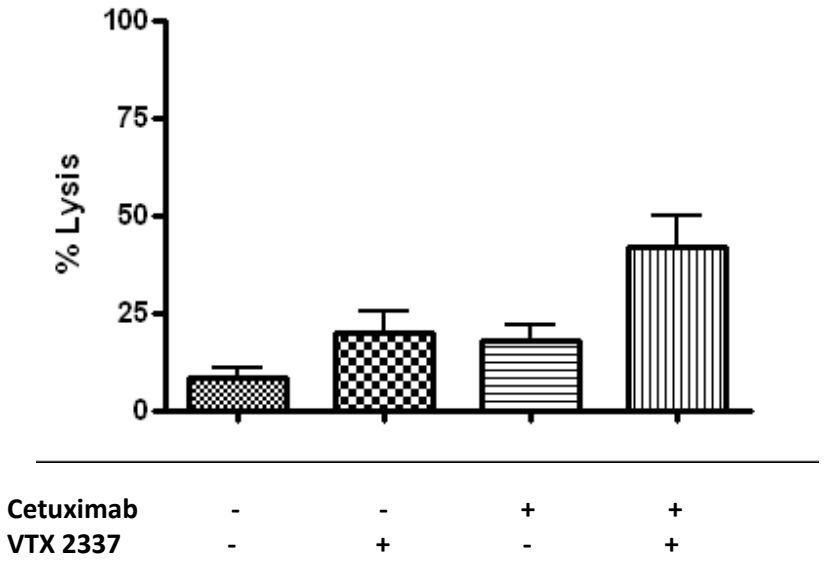
Supplementary Figure 5



Supplementary Figure 5 Caption

VTX-2337 lacks direct cytotoxic effect on HNC. UM-22B HNC cells were tagged with ^{51}Cr and treated 4 h with VTX-2337 at indicated doses. VTX-2337 does not directly induce appreciable lysis of UM-22B.

Supplementary Figure 6



Supplementary Figure 6 Caption

TLR8 stimulation enhances cetuximab-mediated ADCC and direct cell killing by NK cells. PBMC were treated 18 h with media, or VTX-2337 (250nM). They were then utilized in a ^{51}Cr release assay without mAb or with cetuximab. VTX-2337 enhances lysis in absence of antibody, and enhances cytolytic activity further in the presence of antibody.