PLOS BIOLOGY

CORRECTION

Correction: ADAMTS5 Is a Critical Regulator of Virus-Specific T Cell Immunity

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An influenza-specific CD8+ T cell peptide encoded within the nucleoprotein (NP) was incorrectly referred to as NP366-372 throughout the article. The correct designation should be NP366-374. The peptide sequence ASNENMETM stated throughout the 'Methods' section should also be attributed to NP366-374.

The authors have provided corrected versions of Fig 3, Fig 4, Fig 5, Fig 8, S10 Fig and S11 Fig.

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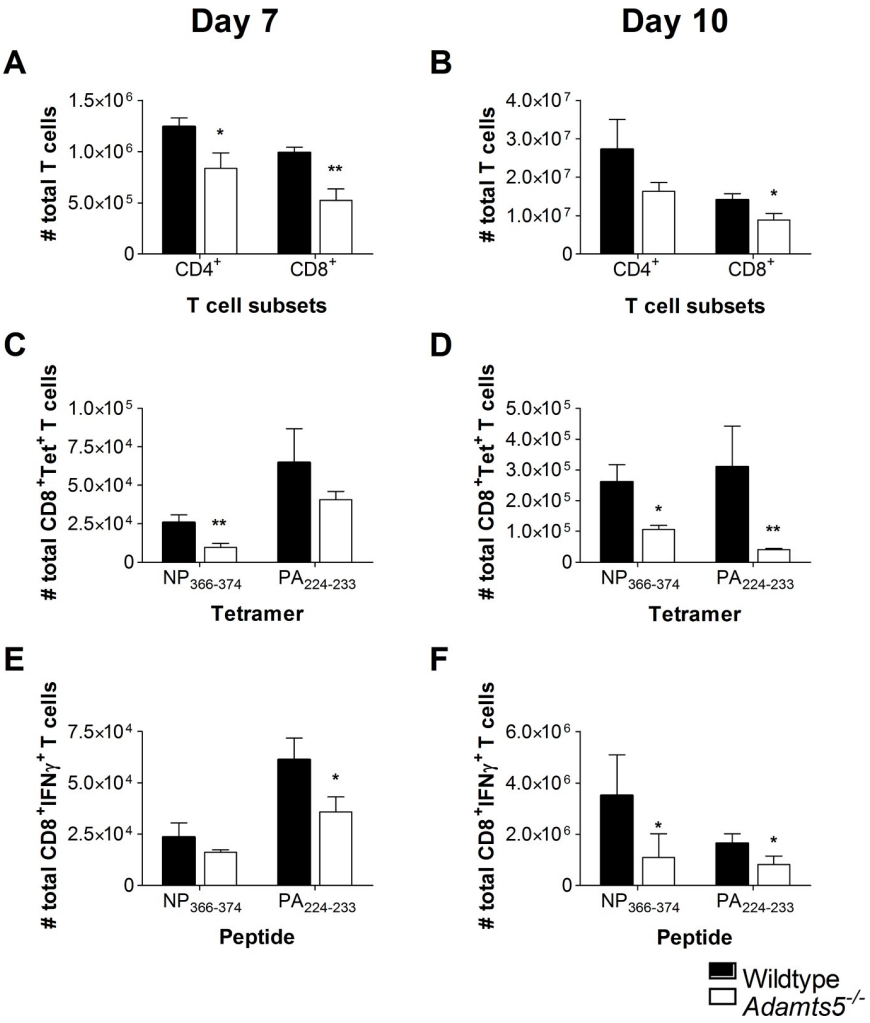

Fig 3. Reduced CD4$^+$ and CD8$^+$ T cell numbers in the spleens of influenza-infected *Adamts5*$^{-/-}$ mice. C57.BL/6 and *Adamts5*$^{-/-}$ mice were intranasally (i.n.) infected (10^4 pfu/mouse) with X31 (H3N2) influenza virus. Spleens were removed at day 7 and day 10 p.i., and CD8$^+$ T cell responses determined. Total CD4$^+$ and CD8$^+$ T cells numbers were calculated at days **(A)** 7 and **(B)** 10 p.i. Influenza-specific $D^bNP_{366\text{-}374}$ CD8$^+$ and $D^bPA_{224\text{-}233}$ CD8$^+$ tetramer-positive T cell numbers were measured at days **(C)** 7 and **(D)** 10 p.i. Functional influenza-specific $D^bNP_{366\text{-}374}{}^+IFN\gamma^+CD8^+$ and $D^bPA_{224\text{-}233}{}^+IFN\gamma^+CD8^+$ T cell activity was determined by ICS, and total IFNγ^+ T cells enumerated at days **(E)** 7 and **(F)** 10 after infection. WT denotes C57.BL/6. The results are expressed as means ± SD, and statistical significance (relative to C57.BL/6) was determined by Student's *t* test ($^*p \leq 0.05$, $^{**}p \leq 0.01$, $n = 5$ representing three experiments). Underlying data are provided in S1 Data.

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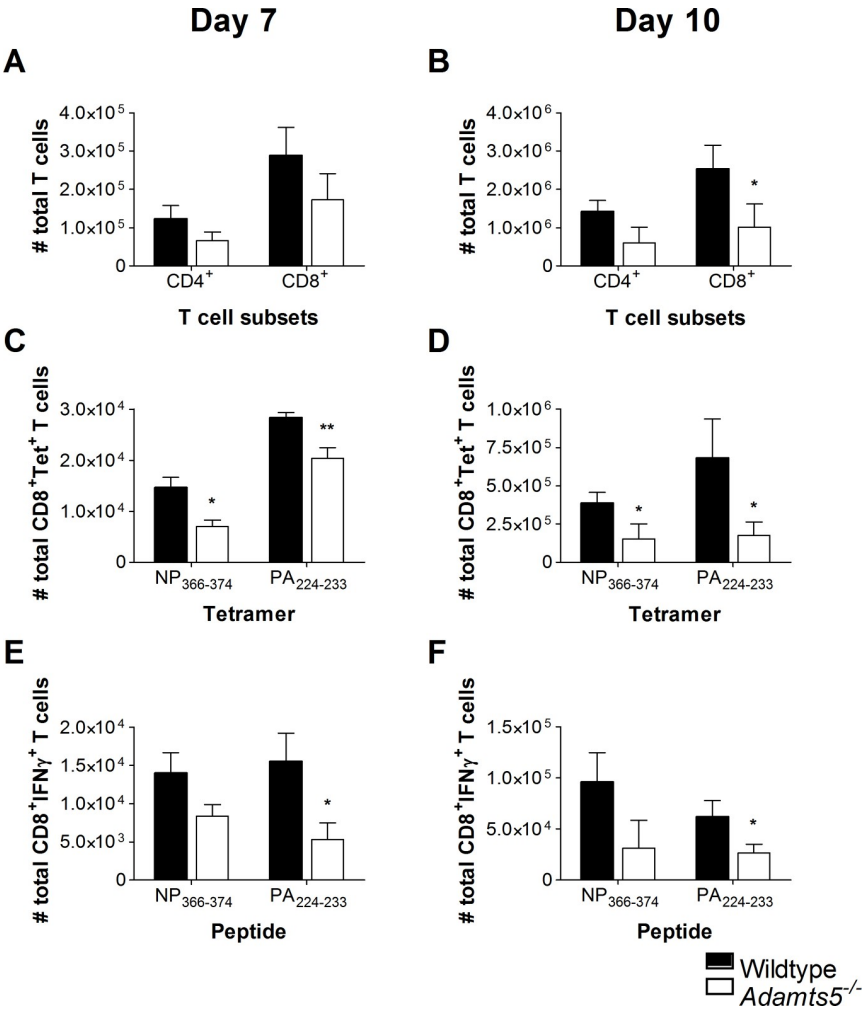

Fig 4. CD4$^+$ and CD8$^+$ T cell responses in the lungs of influenza-infected *Adamts5*$^{-/-}$ mice. C57.BL/6 and *Adamts5*$^{-/-}$ mice were infected i.n. with 10^4pfu X31 (H3N2) influenza virus. Lungs were removed at days 7 and 10 p.i., and CD8$^+$ T cell immunity characterised. Total CD4$^+$ and CD8$^+$ T cell numbers are shown at days **(A)** 7 and **(B)** 10 p.i. Influenza-specific tetramer$^+$ D^{b}NP$_{366\text{-}374}{}^+$ CD8$^+$ and D^{b}PA$_{224\text{-}233}{}^+$ CD8$^+$ T cell responses were enumerated at days **(C)** 7 and **(D)** 10 p.i. CD8$^+$ T cell functionality was assessed by ICS and D^{b}NP$_{366\text{-}374}{}^+$IFNγ$^+$CD8$^+$ and D^{b}PA$_{224\text{-}233}{}^+$IFNγ$^+$CD8$^+$ T cell responses enumerated at days **(E)** 7 and **(F)** 10 p.i. Wildtype denotes C57.BL/6 mice. The results are expressed as means ± SD, and statistical significance (relative to C57.BL/6) was determined by Student's *t* test (* = $p \leq 0.05$, ** = $p \leq 0.01$, $n = 5$ representing three experiments). Underlying data are provided in S1 Data.

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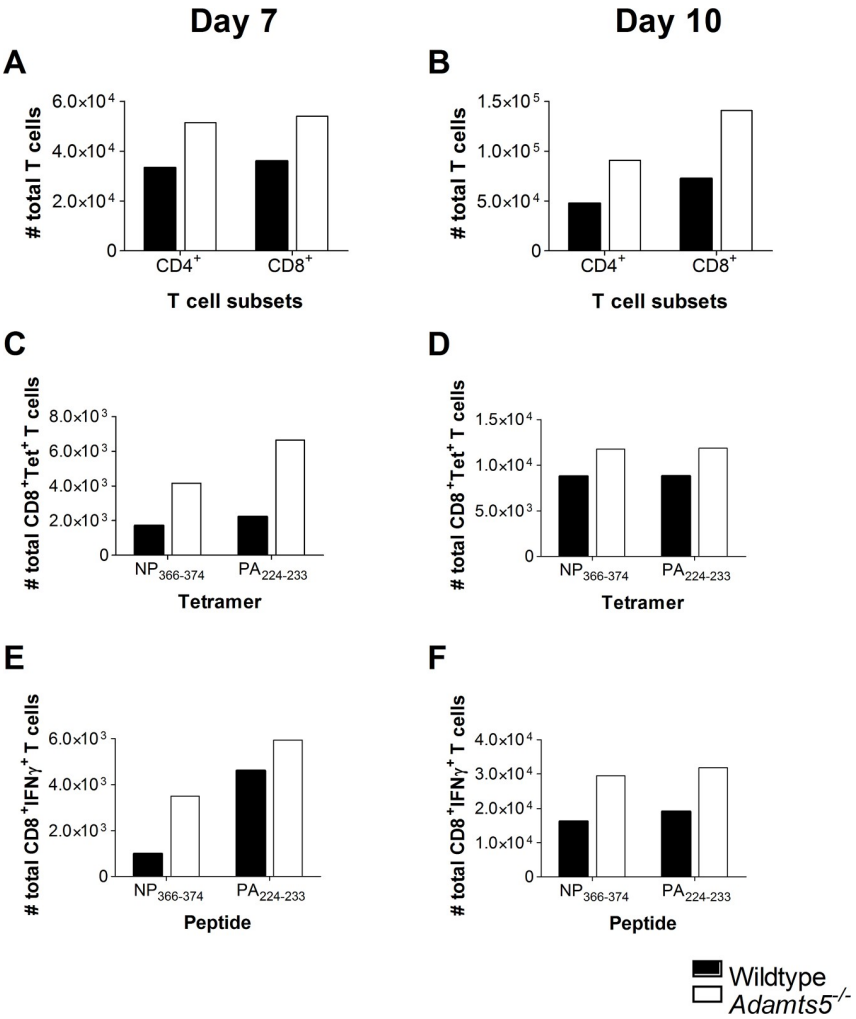

Fig 5. T cell immunity in the pooled MLN. C57.BL/6 and *Adamts5*$^{-/-}$ mice were infected i.n. with 10^4 pfu/mouse X31 (H3N2) influenza virus. MLNs were removed, pooled, and processed at days 7 and 10 p.i., and single-cell suspensions analysed for influenza-specific immunity. Total $CD4^+$ and $CD8^+$ T cell numbers were determined at days **(A)** 7 and **(B)** 10 p.i. Influenza-specific $D^bNP_{366\text{-}374}{}^+$ $CD8^+$ and $D^bPA_{224\text{-}233}{}^+$ $CD8^+$ tetramer positive T cells were enumerated at days **(C)** 7 and **(D)** 10 p.i. $CD8^+$ T cell functionality was measured using ICS. Influenza-specific $D^bNP_{366\text{-}374}{}^+IFN\gamma^+CD8^+$ and $D^bPA_{224\text{-}233}{}^+IFN\gamma^+CD8^+$ T cell responses were characterised at days **(E)** 7 and **(F)** 10 p.i. Results are expressed as total pooled means from five mice repeated three times. Wildtype denotes C57.BL/6 mice. Underlying data are provided in S1 Data.

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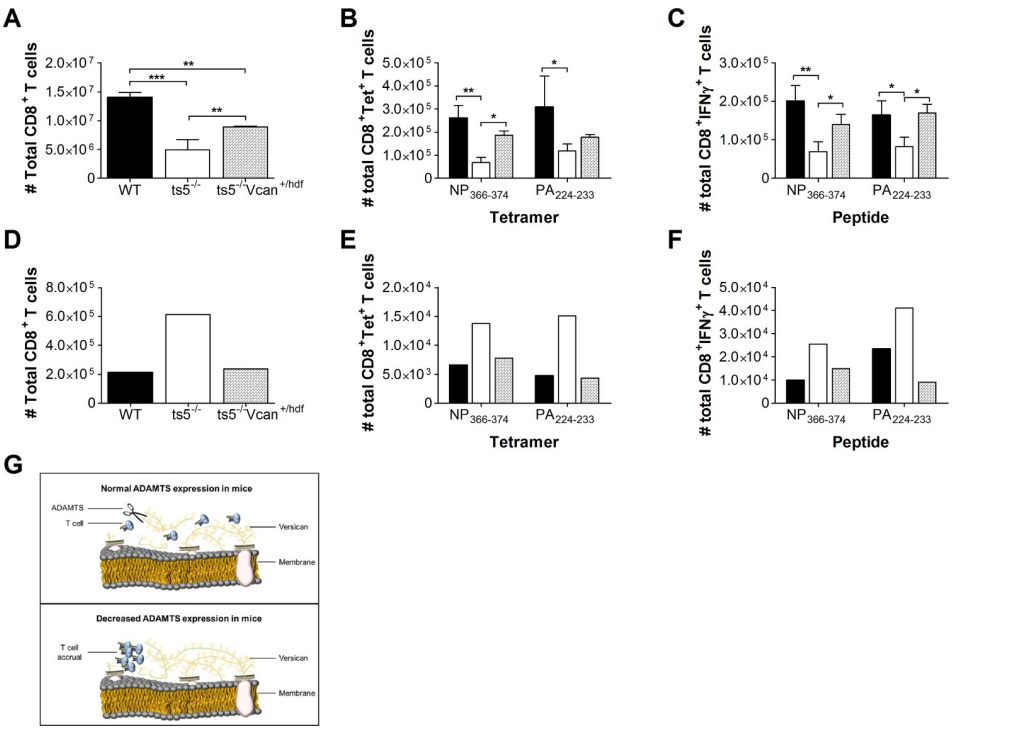

Fig 8. Versican reduction in *Adamts5*$^{-/-}$*Vcan*$^{+/hdf}$ mice restores normal T cell function. Spleen and MLNs were removed from C57.BL/6, *Adamts5*$^{-/-}$*Vcan*$^{+/+}$, and *Adamts5*$^{-/-}$*Vcan*$^{+/hdf}$ mice and processed at day 10 p.i., and single cell suspensions were analysed for influenza-specific immunity. **(A)** Total CD8$^+$ T cell numbers were determined at day 10 p.i. in the spleen. **(B)** Influenza-specific $D^bNP_{366\text{-}374}{}^+$ CD8$^+$ and $D^bPA_{224\text{-}233}{}^+$ CD8$^+$ tetramer positive T cells in the spleen were enumerated at day 10 p.i. CD8$^+$ T cell functionality was measured using ICS. **(C)** Influenza specific $D^bNP_{366\text{-}374}{}^+IFN\gamma^+CD8^+$ and $D^bPA_{224\text{-}233}{}^+IFN\gamma^+CD8^+$ T cell responses were characterised in the spleen at days 10 p.i. **(D)** Total CD8$^+$ T cell numbers were assessed at day 10 p.i. in the pooled MLN. **(E)** Influenza-specific $D^bNP_{366\text{-}374}{}^+$ CD8$^+$ and $D^bPA_{224\text{-}233}{}^+$ CD8$^+$ tetramer positive T cells in the pooled MLN were enumerated at day 10 p.i. CD8$^+$ T cell functionality was measured using ICS. **(F)** Influenza-specific $D^bNP_{366\text{-}374}{}^+IFN\gamma^+CD8^+$ and $D^bPA_{224\text{-}233}{}^+IFN\gamma^+CD8^+$ T cell responses were characterised in the pooled MLN at day 10 p.i. The results are expressed as means ± SD (spleen data) or as pooled means (MLN data), and statistical significance (relative to C57.BL/6 mice) was determined by one-way ANOVA ($^*p \leq 0.05$, $^{***}p \leq 0.005$ relative to C57.BL/6, $n = 5$ representing three individual experiments). WT denotes C57.BL/6 mice and *ts5*$^{-/-}$ denotes *Adamts5*$^{-/-}$. **(G)** Our model for ADAMTS5 enzyme activity and T cell migration proposes that versican can inhibit T cell effector function by acting as a physical block. Cleavage of versican by ADAMTS5 removes the ECM blockade, allowing migration (top panel). Moreover, versican accumulation in the absence of ADAMTS enzyme activity results in T cell clustering (bottom panel). Underlying data are provided in S1 Data.

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The relevant figure legends have been amended to reflect this change and are presented below.

Supporting information

S10 Fig. Influenza virus infection of *Vcan*$^{+/hdf}$ mice. Lung tissue and MLNs were removed from influenza virus infection C57.BL/6 and *Vcan*$^{+/hdf}$ mice and processed to generate single cell suspensions at day 10 p.i. for analysis of influenza-specific immunity. **(A)** Total CD8$^+$ T cell numbers were determined at day 10 p.i. in the lung. **(B)** Influenza-specific $D^bNP_{366\text{-}374}{}^+$ CD8$^+$ and $D^bPA_{224\text{-}233}{}^+$ CD8$^+$ tetramer positive T cells in the lung were enumerated at day 10 p.i. CD8$^+$ T cell functionality was measured using ICS. **(C)** Influenza specific $D^bNP_{366\text{-}374}{}^+IFN\gamma^+CD8^+$ and $D^bPA_{224\text{-}233}{}^+IFN\gamma^+CD8^+$ T cell responses were characterised in the lung at day 10 p.i. **(D)** Total CD8$^+$ T cell numbers were determined at day 10 p.i. from pooled MLN samples. **(E)** Influenza-

specific $D^bNP_{366-374}{}^+$ $CD8^+$ and $D^bPA_{224-233}{}^+$ $CD8^+$ tetramer positive T cells in pooled MLN were enumerated at day 10 p.i. **(F)** $CD8^+$ T cell functionality was measured using ICS to assess influenza-specific $D^bNP_{366-374}{}^+IFN\gamma^+CD8^+$ and $D^bPA_{224-233}{}^+IFN\gamma^+CD8^+$ T cell responses at day 10 p.i. The results are expressed as means ± SD or as pooled means (MLN data) and statistical significance (relative to C57.BL/6 mice) determined by a Student's *t* test ($^*p \leq 0.05$, $^{***}p \leq 0.005$ relative to C57.BL/6, $n = 5$ representing three individual experiments). WT denotes C57.BL/6 mice. Underlying data are provided in S2 Data.
(TIF)

S11 Fig. Influenza infection of *Adamts5*$^{-/-}$ and WT littermate controls. *Adamts5*$^{-/-}$ and WT mice were infected i.n with X31 (H3N2) influenza virus and spleens, lungs, and MLNs removed from C57.BL/6 and *Adamts5*$^{-/-}$ mice days 7 p.i. Single cell suspensions were then analysed for influenza-specific immunity. **(A)** Weight loss was calculated over the time course of infection. Total $CD4^+$ and $CD8^+$ T cells were enumerated in the **(B)** spleen, **(C)** lung, and **(D)** MLN. Influenza-specific $D^bNP_{366-374}{}^+$ $CD8^+$ and $D^bPA_{224-233}{}^+$ $CD8^+$ tetramer positive T cell numbers were also characterised in the **(B)** spleen, **(C)** lung, and **(D)** MLN. Lung and spleen results are expressed as means ± SD or as pooled means (MLN data), and statistical significance (relative to C57.BL/6 mice) was determined by a Student's *t* test ($^*p \leq 0.05$, $^{**}p \leq 0.01$ relative to C57.BL/6 mice, $n = 5$ representing three individual experiments). WT denotes C57.BL/6 mice. Underlying data are provided in S2 Data.
(TIF)

Reference

1. McMahon M, Ye S, Izzard L, Dlugolenski D, Tripp RA, Bean AGD, et al. (2016) ADAMTS5 Is a Critical Regulator of Virus-Specific T Cell Immunity. PLoS Biol 14(11): e1002580. https://doi.org/10.1371/journal.pbio.1002580 PMID: 27855162