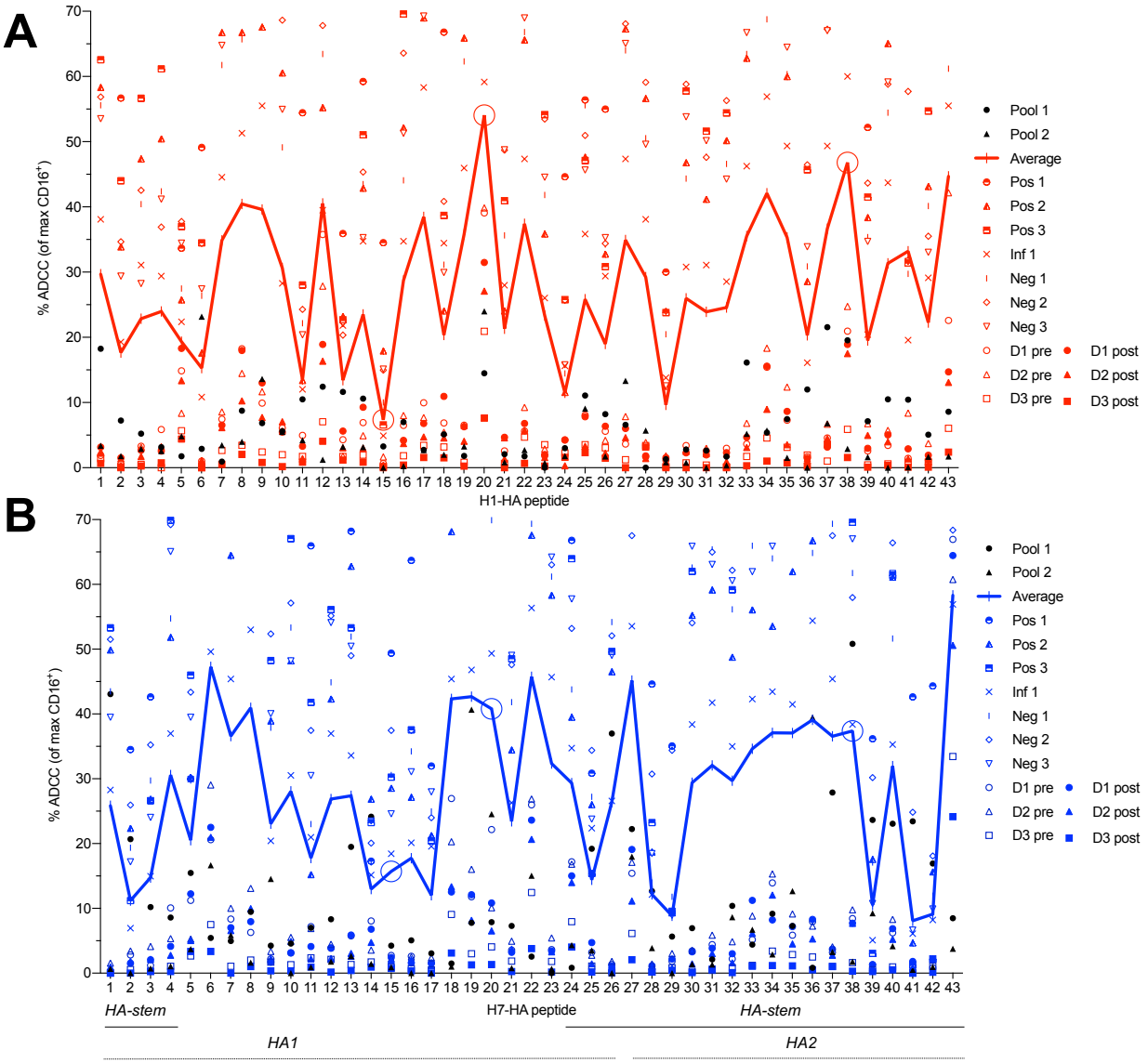
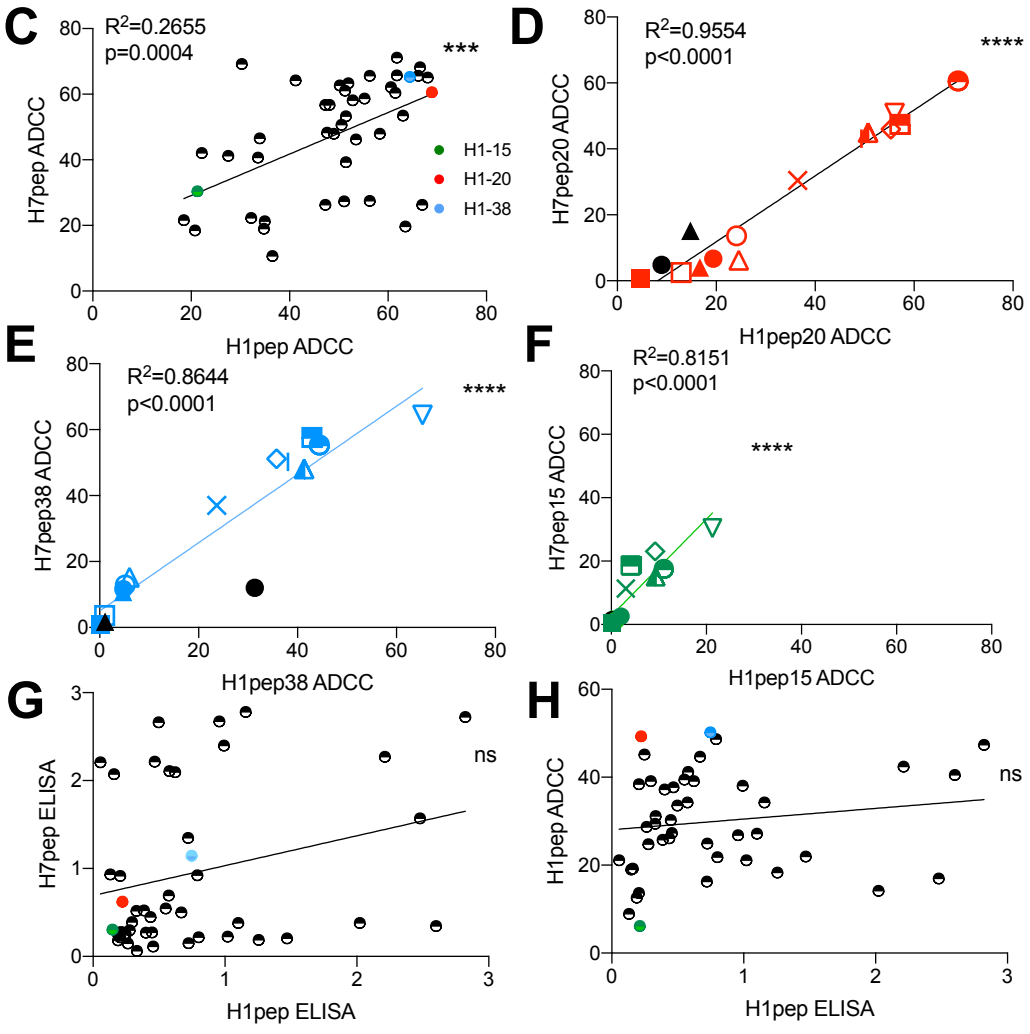
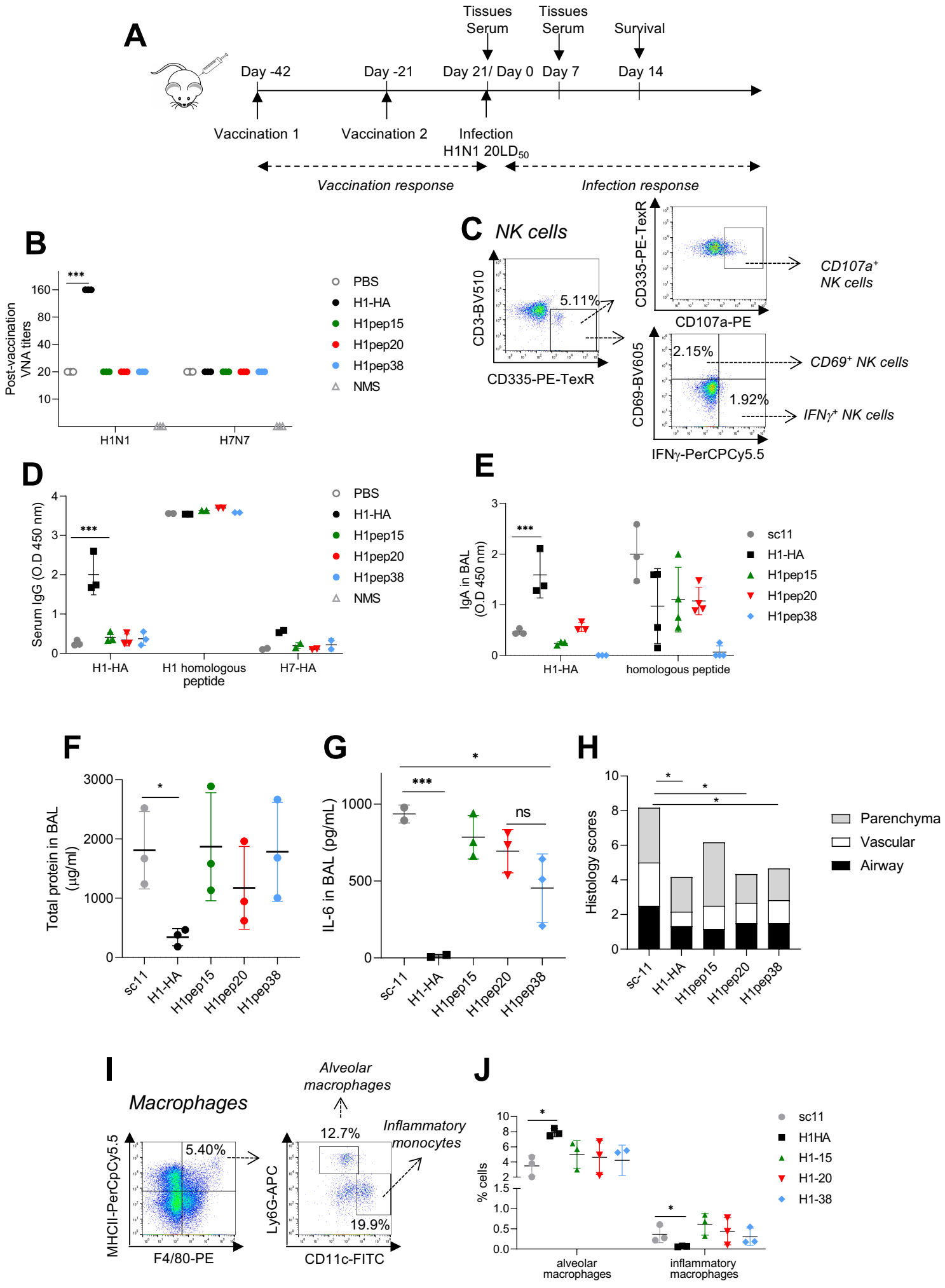

A
% ADCC (of max CD16+)
H1-HA peptide
Pool 1
Pool 2
Average
Pos 1
Pos 2
Pos 3
Inf 1
Neg 1
Neg 2
Neg 3
D1 pre
D1 post
D2 pre
D2 post
D3 pre
D3 post
B
% ADCC (of max CD16+)
H7-HA peptide
HA-stem
HA1
HA2
Pool 1
Pool 2
Average
Pos 1
Pos 2
Pos 3
Inf 1
Neg 1
Neg 2
Neg 3
D1 pre
D1 post
D2 pre
D2 post
D3 pre
D3 post


C
R2=0.2655
p=0.0004
***
H7pep ADCC
H1pep ADCC
H1-15
H1-20
H1-38
D
R2=0.9554
p<0.0001
****
H7pep20 ADCC
H1pep20 ADCC
E
R2=0.8644
p<0.0001
****
H7pep38 ADCC
H1pep38 ADCC
F
R2=0.8151
p<0.0001
****
H7pep15 ADCC
H1pep15 ADCC
G
ns
H7pep ELISA
H1pep ELISA
H
ns
H1pep ADCC
H1pep ELISA

Supplementary figure 1: ADCC antibody responses are more cross-reactive than total IgG. (A) H1-HA and (B) H7-HA ADCC responses from overlapping peptides. Data represents the average (line) and individual (symbols). The average HApep15, 20 and 38 peptide responses are circled. Linear regression analysis for H7-HA and H1-HA peptide ADCC responses for Pos 1 donor (C), and all donors HApep20 (D), HApep38 (E) and HApep15 (F) peptides ADCC responses. H7-HA and H1-HA peptide ELISA responses for Pos 1 donor (G) and H1-HA peptide ELISA and ADCC responses for Pos 1 donor (H).


A
Tissues Serum
Tissues Serum
Survival
Day -42
Day -21
Day 21/ Day 0
Day 7
Day 14
Vaccination 1
Vaccination 2
Infection H1N1 20LD50
Vaccination response
Infection response
B
Post-vaccination VNA titers
H1N1
H7N7
PBS
H1-HA
H1pep15
H1pep20
H1pep38
NMS
C NK cells
CD3-BV510
CD335-PE-TexR
5.11%
CD107a-PE
CD107a+ NK cells
CD69-BV605
2.15%
CD69+ NK cells
1.92%
IFNγ+ NK cells
IFNγ-PerCPCy5.5
D
Serum IgG (O.D 450 nm)
H1-HA
H1 homologous peptide
H7-HA
E
IgA in BAL (O.D 450 nm)
homologous peptide
sc11
F
Total protein in BAL (µg/ml)
G
IL-6 in BAL (pg/mL)
ns
H
Histology scores
Parenchyma
Vascular
Airway
I
Macrophages
Alveolar macrophages
Inflammatory monocytes
MHCII-PerCpCy5.5
F4/80-PE
5.40%
Ly6G-APC
CD11c-FITC
12.7%
19.9%
J
% cells
alveolar macrophages
inflammatory macrophages
H1HA
H1-15
H1-20
H1-38

Supplementary figure 2: Antibody response following ADCC-peptide vaccination and influenza infection. (A) Schematic diagram of mouse vaccination and infection timeline. (B) H1N1 virus neutralizing antibodies (VNA) from day 21 post vaccination serum. (C) Representative FACS plots for NK cell activation at day 7 post infection from the lung (gated prior on FSC/SSC, live/dead). (D) H1-HA and homologous peptide IgG production in the serum by ELISA at day 7 post-infection. (E) H1-HA IgA production in BAL supernatants by ELISA at day 7 post-infection. (F) Total protein in BAL at day 7 post-infection measured by BCA assay. (G) IL-6 levels in BAL at 7 post-infection measured by ELISA. (H) Histopathology scores of airways, parenchyma and vascular murine lung tissues by H&E staining at day 7 post-challenge. (I) Representative FACS plots for Macrophage responses at day 7 post infection from the BAL (gated prior on FSC/SSC, live/dead), and % of cells in the lung. Data represents the mean average and SD. n=3 mice per group. * shows statistical significance by one-way ANOVA with Dunnett's multiple comparison test versus PBS group, *$p<0.05$, **$p<0.01$, ***$p<0.005$, experiments were repeated twice.