

**Table S1.** Sequence alignment of influenza-LEAPS conjugated peptides.

| Influenza A Protein: HA                              |                                       | HA1 |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
|------------------------------------------------------|---------------------------------------|-----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| LEAPS Sequence HA1: DLLKNGERIEKVEGGGLKSTQNAIDEITNKVN |                                       | L   | K  | S  | T  | Q  | N  | A  | I  | D  | E  | I  | T  | N  | K  | V  | N  |
| Sequence used in LEAPS Conjugate                     |                                       | L   | K  | S  | T  | Q  | N  | A  | I  | D  | E  | I  | T  | N  | K  | V  | N  |
| Position                                             |                                       | 38  | 39 | 40 | 41 | 42 | 43 | 44 | 45 | 46 | 47 | 48 | 49 | 50 | 51 | 52 | 53 |
| AAM75158                                             | A/Puerto Rico/8/34/Mount Sinai (H1N1) | Q   | -  | -  | -  | -  | -  | -  | -  | N  | G  | -  | -  | -  | -  | -  | -  |
| ACP44189                                             | A/California/07/2009(H1N1)            | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |
| ACQ55359                                             | A/California/07/2009(H1N1)            | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |
| ABW90127                                             | A/Viet Nam/1203/2004(H5N1)            | K   | E  | -  | -  | -  | K  | -  | -  | -  | G  | V  | -  | -  | -  | -  | -  |
| AAW80717                                             | A/Viet Nam/1203/2004(H5N1)            | K   | E  | -  | -  | -  | K  | -  | -  | -  | G  | V  | -  | -  | -  | -  | -  |

| Influenza A Protein: HA                         |                                       | HA2 |   |   |   |   |   |   |   |   |    |    |    |
|-------------------------------------------------|---------------------------------------|-----|---|---|---|---|---|---|---|---|----|----|----|
| LEAPS Sequence HA2: DLLKNGERIEKVEGGGLFGAIGFIEGG |                                       | G   | L | F | G | A | I | A | G | F | I  | E  | G  |
| Sequence used in LEAPS Conjugate                |                                       | G   | L | F | G | A | I | A | G | F | I  | E  | G  |
| Position                                        |                                       | 1   | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| AAM75158                                        | A/Puerto Rico/8/34/Mount Sinai (H1N1) | -   | - | - | - | - | - | - | - | - | -  | -  | -  |
| ACP44189                                        | A/California/07/2009(H1N1)            | -   | - | - | - | - | - | - | - | - | -  | -  | -  |
| ACQ55359                                        | A/California/07/2009(H1N1)            | -   | - | - | - | - | - | - | - | - | -  | -  | -  |
| ABW90127                                        | A/Viet Nam/1203/2004(H5N1)            | -   | - | - | - | - | - | - | - | - | -  | -  | -  |
| AAW80717                                        | A/Viet Nam/1203/2004(H5N1)            | -   | - | - | - | - | - | - | - | - | -  | -  | -  |

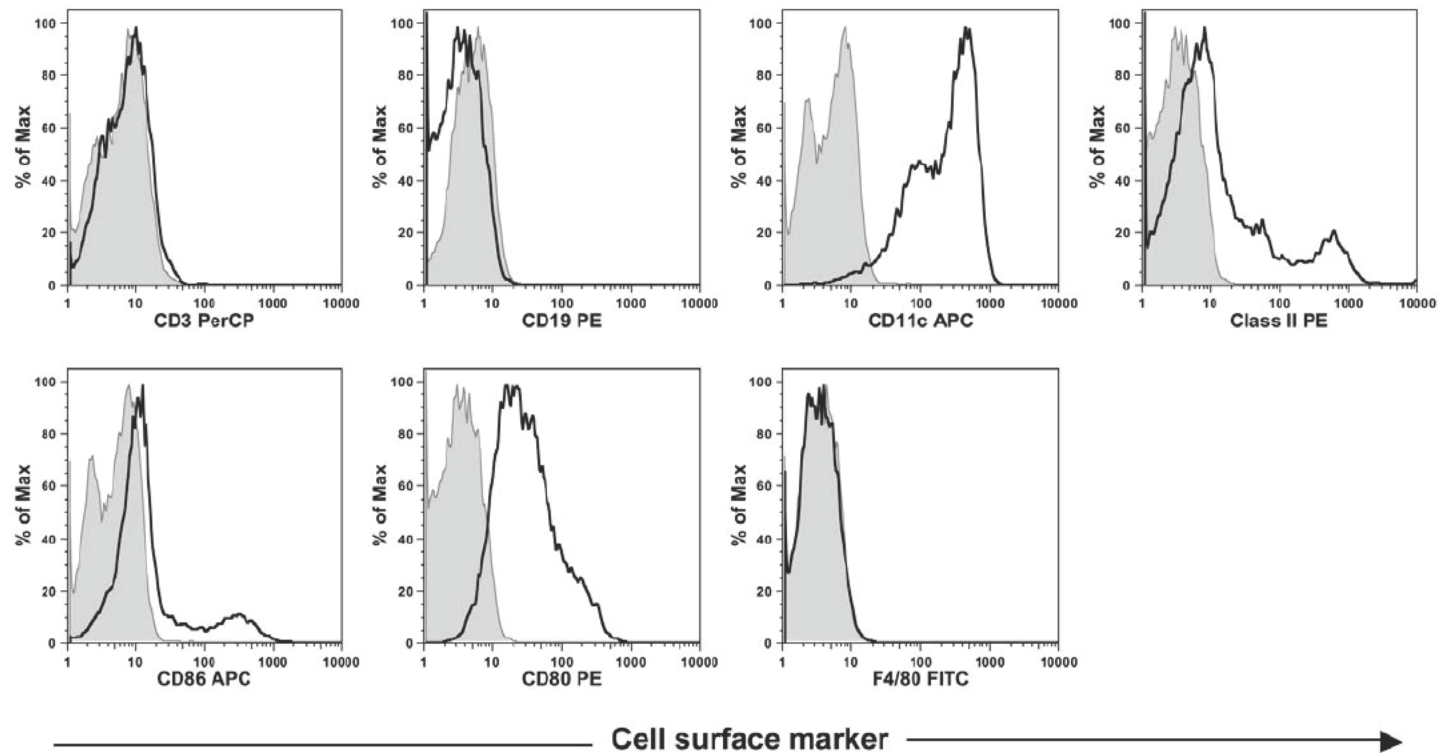
| Influenza A Protein: NP                           |                                       | NP  |     |     |     |     |     |     |     |     |     |     |     |     |     |
|---------------------------------------------------|---------------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| LEAPS Sequence NP: DLLKNGERIEKVEGGGNDATYQRTALVRTG |                                       | N   | D   | A   | T   | Y   | Q   | R   | T   | R   | A   | L   | V   | R   | T   |
| Sequence used in LEAPS Conjugate:                 |                                       | N   | D   | A   | T   | Y   | Q   | R   | T   | R   | A   | L   | V   | R   | T   |
| Position                                          |                                       | 144 | 145 | 146 | 147 | 148 | 149 | 150 | 151 | 152 | 153 | 154 | 155 | 156 | 157 |
| AAM75159                                          | A/Puerto Rico/8/34/Mount Sinai (H1N1) | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   |
| AAM94596                                          | A/Puerto Rico/8/34/Mount Sinai (H1N1) | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   |
| ACP44183                                          | A/California/07/2009(H1N1)            | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   |
| ACS94534                                          | A/California/07/2009(H1N1)            | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   |
| AAT70630                                          | A/Viet Nam/1203/2004(H5N1)            | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   |
| AAW80720                                          | A/Viet Nam/1203/2004(H5N1)            | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   |
| ADN78224                                          | A/Bethesda/NIH107-D31/2009 #          | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   |
| KC885957                                          | A/Zhejiang/DTID-ZJU01/2013(H7N9)      | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   |

# Note: Oseltamivir resistant pH1N1

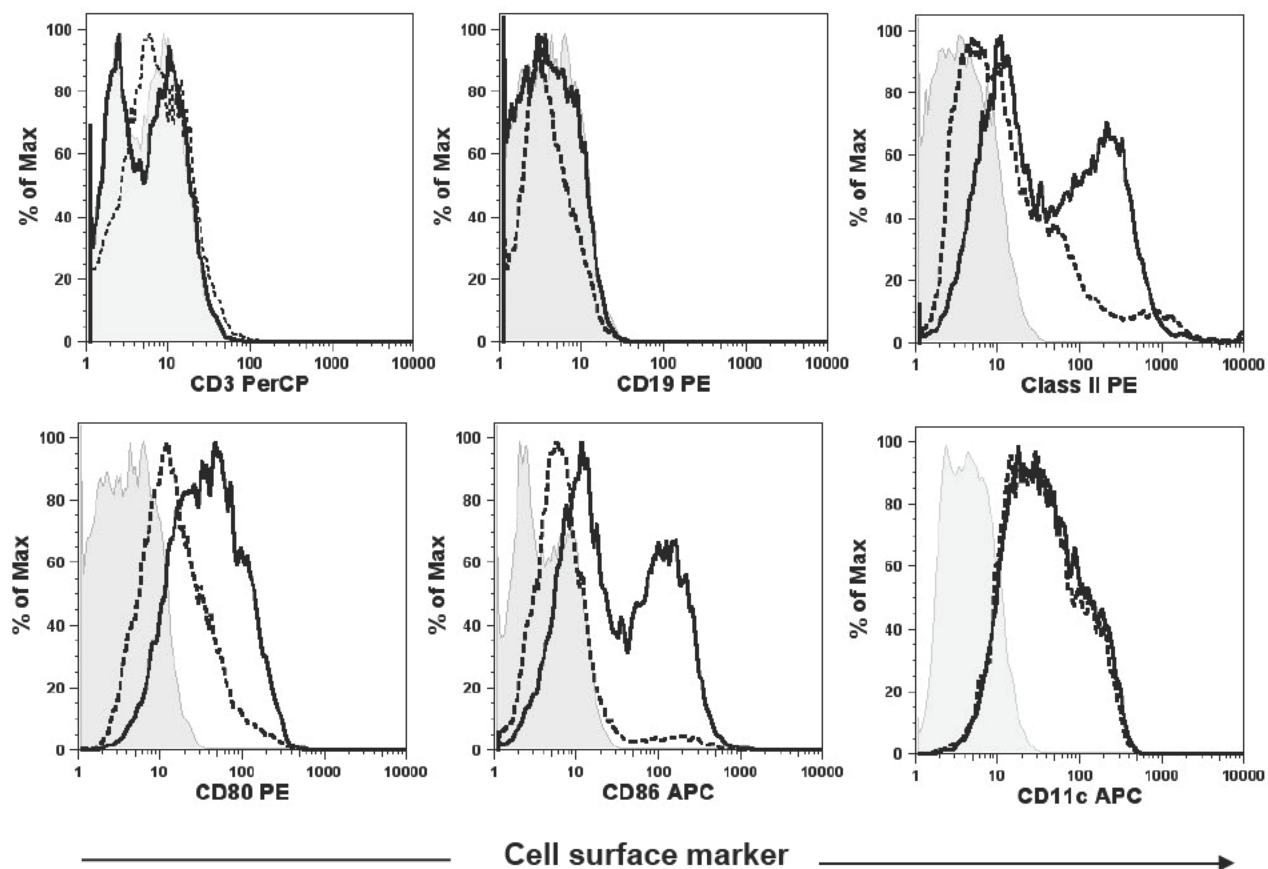
| Influenza A Protein: M2e                                  |                                  | M2e |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
|-----------------------------------------------------------|----------------------------------|-----|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| LEAPS Sequence M2e: DLLKNGERIEKVEGGGSLTEVETPIRNEWGSRSDSSD |                                  | S   | L | L | T | E | V | E | T | P  | I  | R  | N  | E  | W  | G  | S* | R  | S* | N  | D  | S  | S  | D  |
| Sequence used in LEAPS Conjugate:                         |                                  | S   | L | L | T | E | V | E | T | P  | I  | R  | N  | E  | W  | G  | C  | R  | C  | N  | D  | S  | S  | D  |
| Position                                                  |                                  | 2   | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 |
| ACP41955                                                  | A/California/07/2009(H1N1)       | -   | - | - | - | - | - | - | - | -  | T  | -  | S  | -  | -  | E  | -  | -  | -  | S  | -  | -  | -  | -  |
| ACP44185                                                  | A/California/07/2009(H1N1)       | -   | - | - | - | - | - | - | - | -  | T  | -  | S  | -  | -  | E  | -  | -  | -  | S  | -  | -  | -  | -  |
| ACP44171                                                  | A/California/07/2009(H1N1)       | -   | - | - | - | - | - | - | - | -  | T  | -  | S  | -  | -  | E  | -  | -  | -  | S  | -  | -  | -  | -  |
| ABP35634                                                  | A/Viet Nam/1203/2004(H5N1)       | -   | - | - | - | - | - | - | - | -  | T  | -  | -  | -  | -  | E  | -  | -  | -  | S  | -  | -  | -  | -  |
| AAT70528                                                  | A/Viet Nam/1203/2004(H5N1)       | -   | - | - | - | - | - | - | - | -  | T  | -  | -  | -  | -  | E  | -  | -  | -  | S  | -  | -  | -  | -  |
| ADN78223                                                  | A/Bethesda/NIH107-D31/2009 #     | -   | - | - | - | - | - | - | - | -  | T  | -  | S  | -  | -  | E  | -  | -  | -  | S  | -  | -  | -  | -  |
| KC853764                                                  | A/Hangzhou/1/2013(H7N9)          | -   | - | - | - | - | - | - | - | -  | T  | -  | T  | G  | -  | E  | -  | N  | -  | S  | G  | -  | -  | E  |
| KC885959                                                  | A/Zhejiang/DTID-ZJU01/2013(H7N9) | -   | - | - | - | - | - | - | - | -  | T  | -  | T  | G  | -  | E  | -  | N  | -  | S  | G  | -  | -  | E  |

# Note: Oseltamivir resistant pH1N1

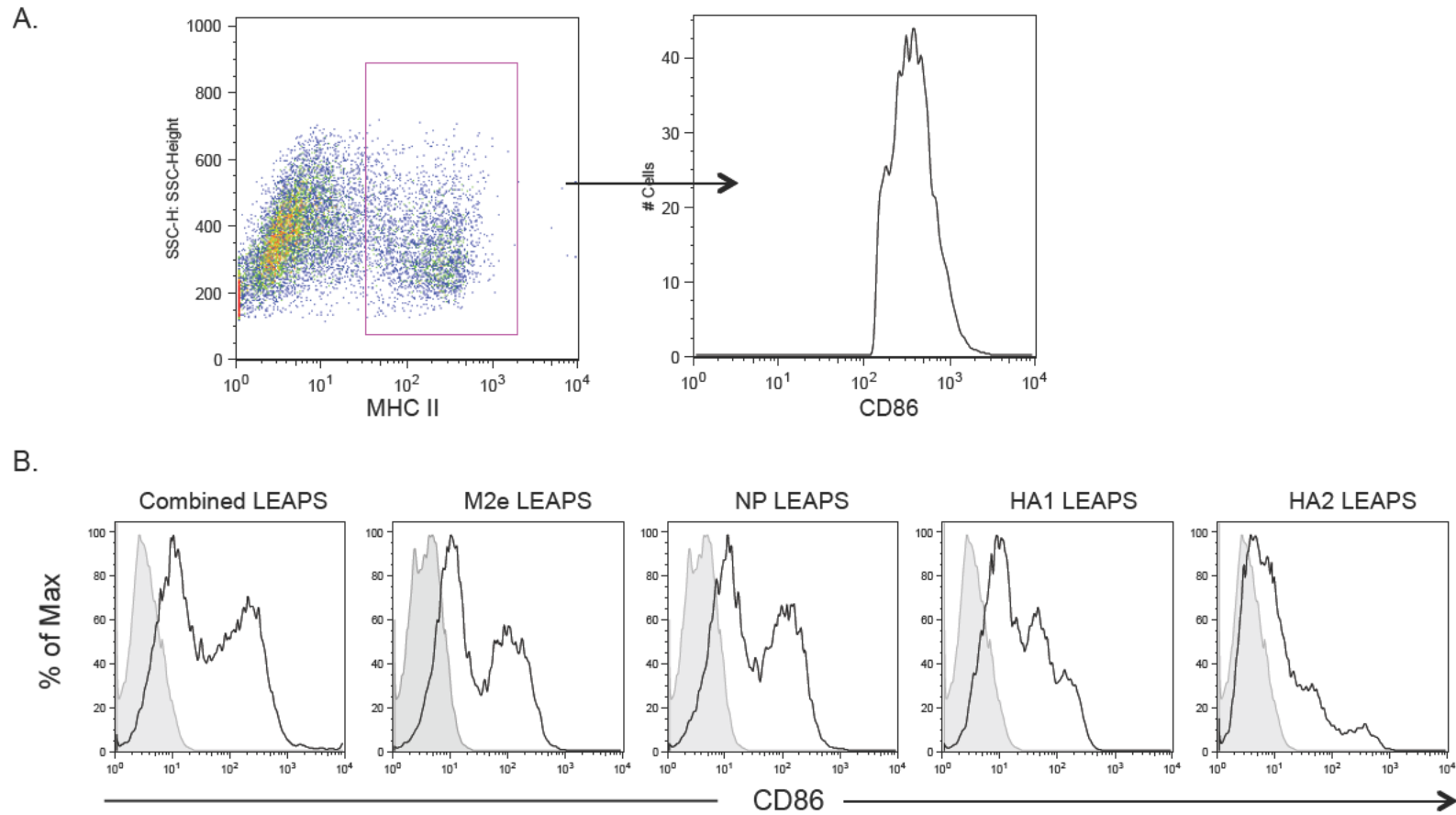
\* Changed to S for increased peptid stability and to avoid formation of inter an intra disulfide bonds.



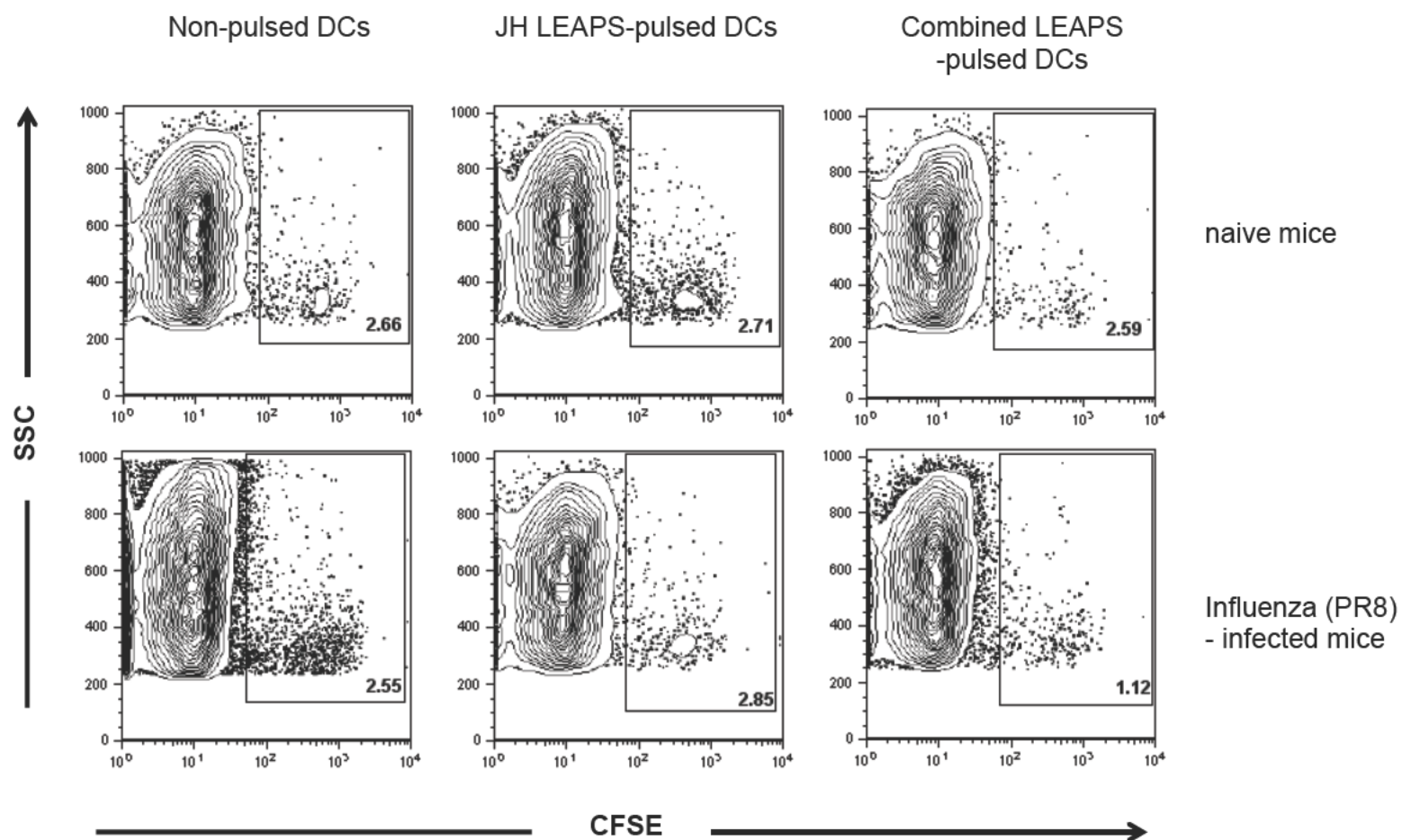
**Fig. S1.** Phenotypic characterization of murine bone marrow derived DCs (BMDCs). A representative phenotype of BMDCs from at least 3 independent experiments; isotype control(  ) and specific cell surface markers ( — ).



**Fig. S2.** Cell surface markers on the surface of BMDCs upon stimulation with influenza-conjugated LEAPS. Representative BMDCs phenotype upon influenza-LEAPS stimulation from at least 3 independent experiments; isotype control (  ) and non-pulsed DCs, immature DCs ( ..... ) and pulsed DCs ( — )

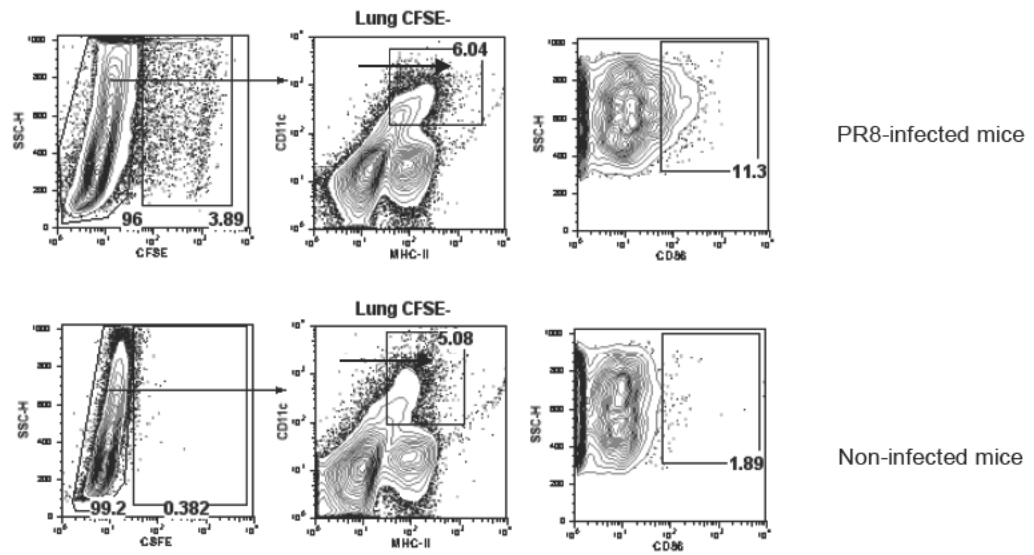


**Fig. S3** Cell surface markers on the surface of BMDCs A) High levels of CD86 expression on MHC II<sup>+</sup> DCs B) CD86 expression on BMDCs upon stimulation with combined, M2e, NP, HA1 and HA2 conjugated LEAPS; isotype control (■) and pulsed DCs (—)

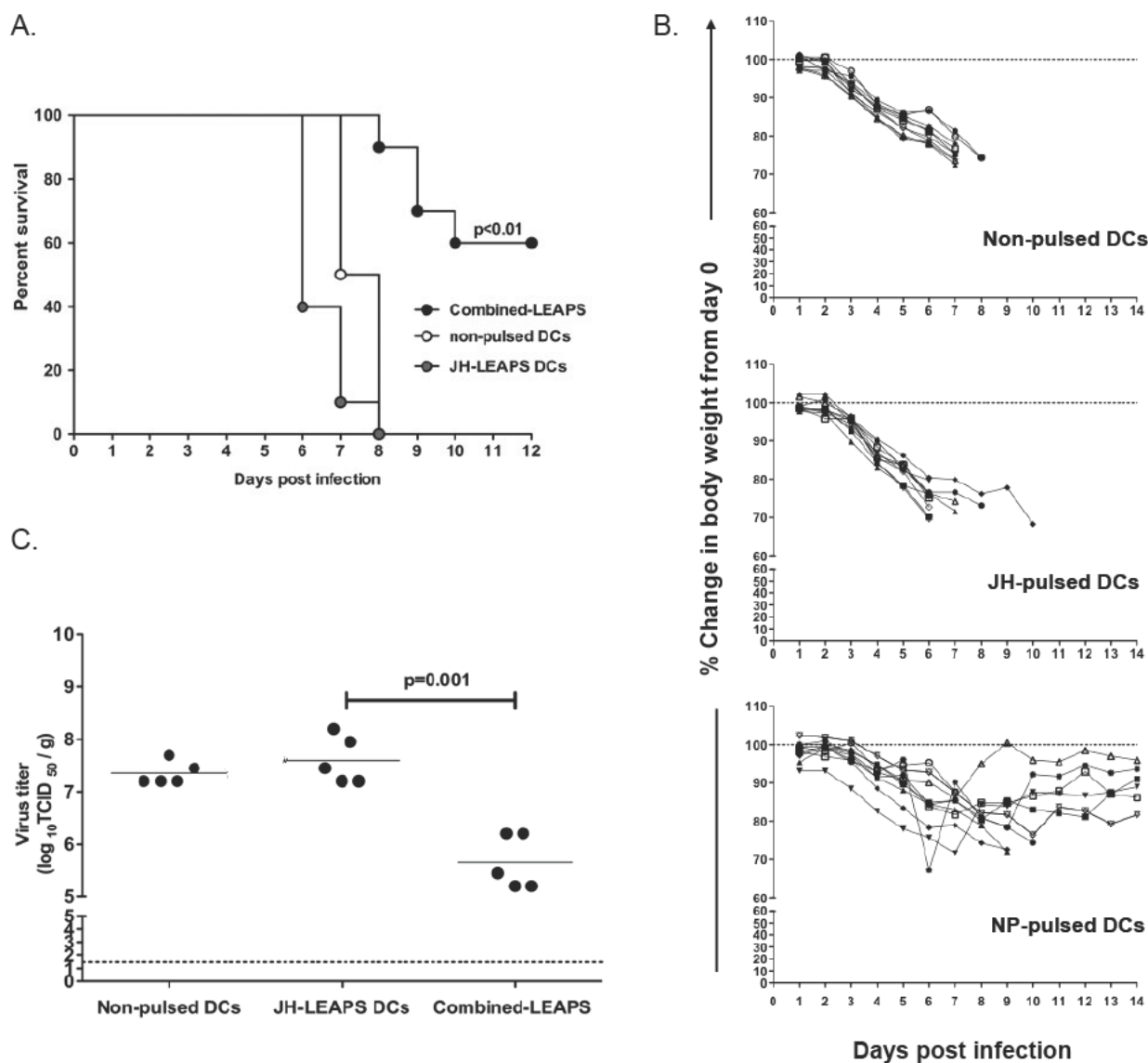


**Fig. S4** LEAPS-loaded DCs in whole blood.  $10^7$  CFSE labeled combined LEAPS stimulated DCs were injected I.V. into naïve (A) or influenza (PR8) virus infected mice ( $10\text{LD}_{50}$ , PR8 virus, I.N.)(B). The number of CFSE positive cells was measured in whole blood 24 h post-administration of CFSE- combined LEAPS stimulated DCs. The data are representative FACS plots from each group (n=5 mice/group).

A.



**Fig. S5** Activation of endogenous DCs following LEAPS treatment. Representative FACS plots from naïve (A) or 10LD<sub>50</sub> influenza virus (PR8) infected (B) mice received CFSE labeled combined LEAPS pulsed DCs. At 24 h post-administration, the mice were sacrificed and their lungs analyzed by flow cytometry for CFSE<sup>-</sup> CD11c<sup>+</sup>MHC II<sup>+</sup>CD86<sup>+</sup> DCs.



**Fig. S6.** DCs loaded with influenza-LEAPS reduce morbidity and mortality in pH1N1 virus infected mice. Mice were infected intranasally with  $10^7$  TCID<sub>50</sub> of A/California/07/2009. Twenty-four hours later, mice were treated with combined-LEAPS conjugated or non-specific peptide conjugated-LEAPS pulsed DCS. Percent survival,  $p < 0.01$  log-rank (Mantel-Cox) test (A), % change in body weight (B) and virus titer in the lungs of infected mice harvested 4 days post-infection are presented;  $p = 0.001$  Student's  $t$  test (C).