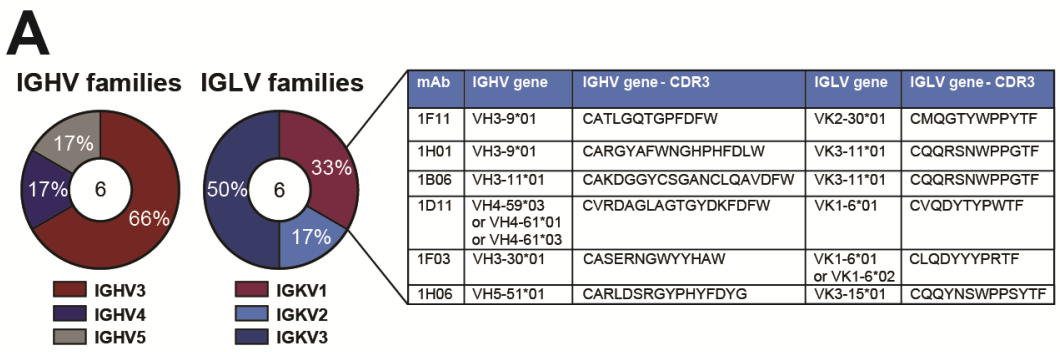
Fig S1. Genetic landscape of isolated mAbs from a H3N2 infected individual. **A**) IGHV and IGLV gene usage, distribution and amino acid sequence of the heavy and light chain CDR3 for each human mAb. Distribution of IGHV (**B**) and IGLV (**C**) gene CDR3 lengths for the mAbs.



mAb	IGHV gene	IGHV gene - CDR3	IGLV gene	IGLV gene - CDR3
1F11	VH3-9*01	CATLGQTGPFDFW	VK2-30*01	CMQGTYWPPYTF
1H01	VH3-9*01	CARGYAFWNGHPHFDLW	VK3-11*01	CQQRSNWPPGTF
1B06	VH3-11*01	CAKDGGYCSGANCLQAVDFW	VK3-11*01	CQQRSNWPPGTF
1D11	VH4-59*03 or VH4-61*01 or VH4-61*03	CVRDAGLAGTGYDKFDFW	VK1-6*01	CVQDYTYPWTF
1F03	VH3-30*01	CASERNGWYYHAW	VK1-6*01 or VK1-6*02	CLQDYYYPRTF
1H06	VH5-51*01	CARLDSRGYPHYFDYG	VK3-15*01	CQQYNSWPPSYTF

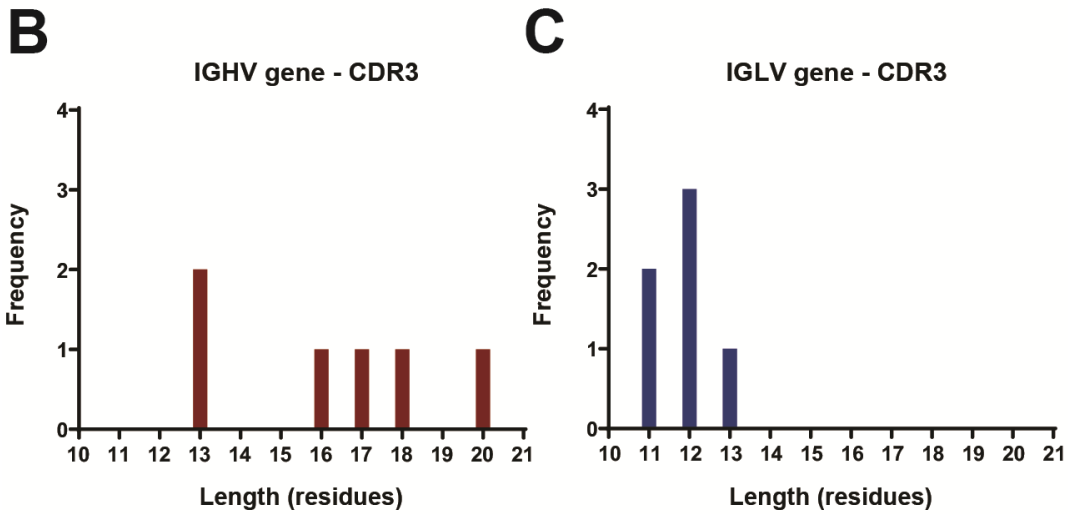


Fig S2. Confirmation of passive transfer of anti-M1 and anti-NP mAbs in mice. mAb titers of the groups used in the prophylactic H3N2 (**A**) and H1N1 (**B**) mouse challenge model measured by cell-based ELISA with A/Hong Kong/4801/2014 (H3N2) used as substrate. Blood was collected from mice 3 hours after intraperitoneal immunization. mAbs 1G01, a pan NA mAb, and 1C11, a SARS-CoV-2 mAb, were used as a positive and negative control, respectively. Each symbol represents one animal, in which five animals were used per mAb. AUCs with a cutoff value of the average background plus three SDs is shown.

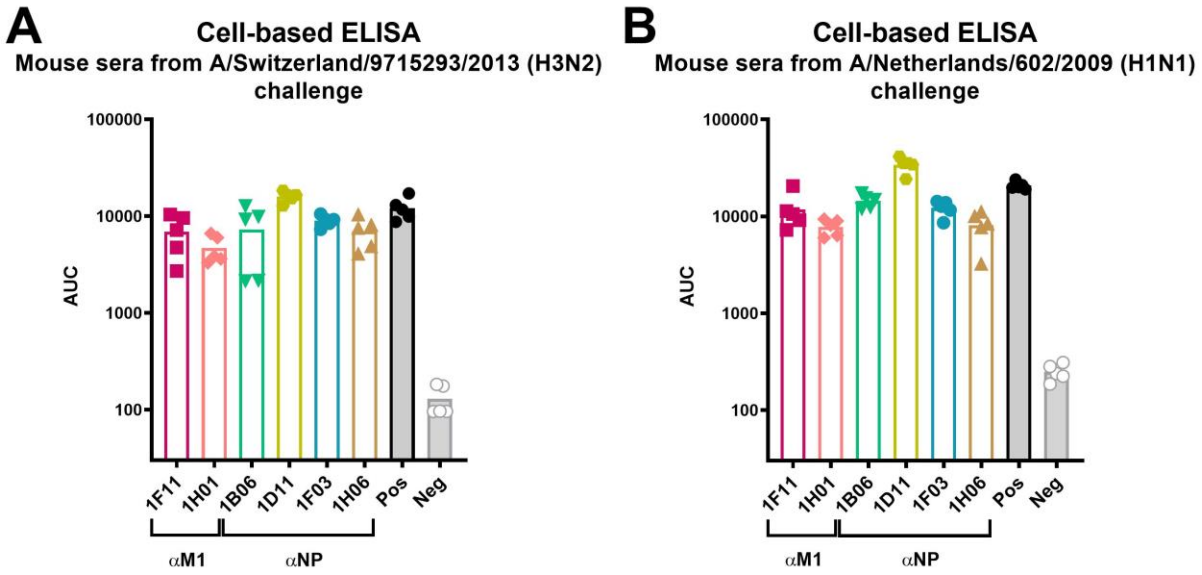


Fig S3. Repetition of *in vitro* characterization of ADCC Fc-effector mechanisms mediated by anti-M1 and anti-NP mAbs. *In vitro* ADCC activity of anti-M1 and anti-NP mAbs against A/Netherlands/602/2009 (H1N1) **(A)**, A/Hong Kong/4801/2014 (H3N2) **(B)** and B/Colorado/06/2017 **(C)**. CR9114 functioned as a positive control, whereas the anti-CHIKV E1 mAb (1D04) served as a negative control. Data are presented as AUCs calculated with a lower detection limit of the average background plus three SDs. Every symbol represents the AUC of a single mAb and bars denote mean ± SD of one experiment conducted with two technical replicates. For statistical significance calculations, values were first log(y) transformed and subsequently a one-way ANOVA corrected for multiple comparison test was performed. Only *p* values lower than 0.05 are shown.

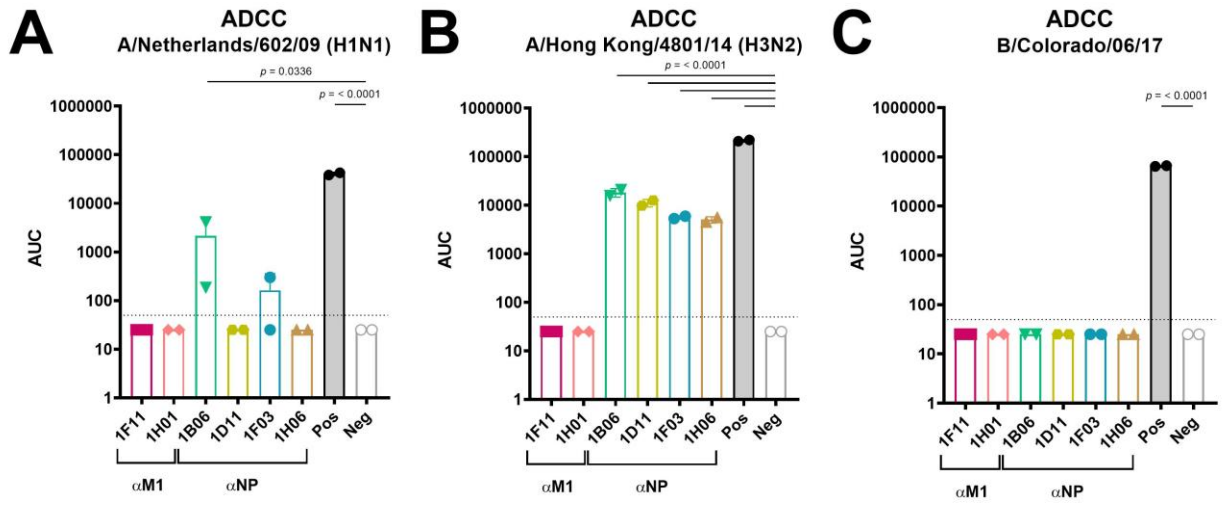


Fig S4. Assessment of anti-M1 and anti-NP mAb protection in a lethal mouse challenge model. Morbidity and mortality in A/Switzerland/9715293/2013 (H3N2) **(A)** and A/Netherlands/602/2009 (H1N1) **(B)** infected female DBA2/j (for H3N2 study) or BALB/c (for H1N1 study) mice following intraperitoneal administration of two anti-M1 (1F11 and 1H01) and four anti-NP (1B06, 1D11, 1F03 and 1H06) mAbs (*n*=5 mice/mAb tested). The H6 mAb, 8H9, served as a negative control. Weight loss and survival were monitored daily for 12-14 days post challenge. Weight loss curves and survival graphs are shown in percentage (%). Error bars indicate the standard error of the mean (SEM). The dashed vertical grey line represents 75% of initial body weight, which was defined as the humane endpoint. *P* values indicate the statistical significance of the difference between the groups and the irrelevant antibody control assessed by one-way ANOVA followed by a multiple comparison test for weight loss or a Log-rank (Mantel-Cox) test for survival. For weight loss comparisons, the maximum weight loss in percentage for each mouse was used. Mice that reached the human endpoint were assigned 75%. Only *p* values lower than 0.05 are shown