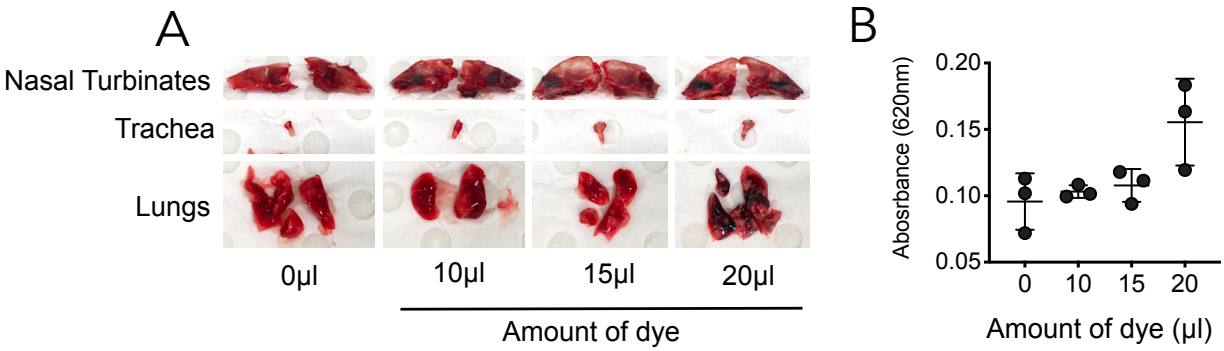
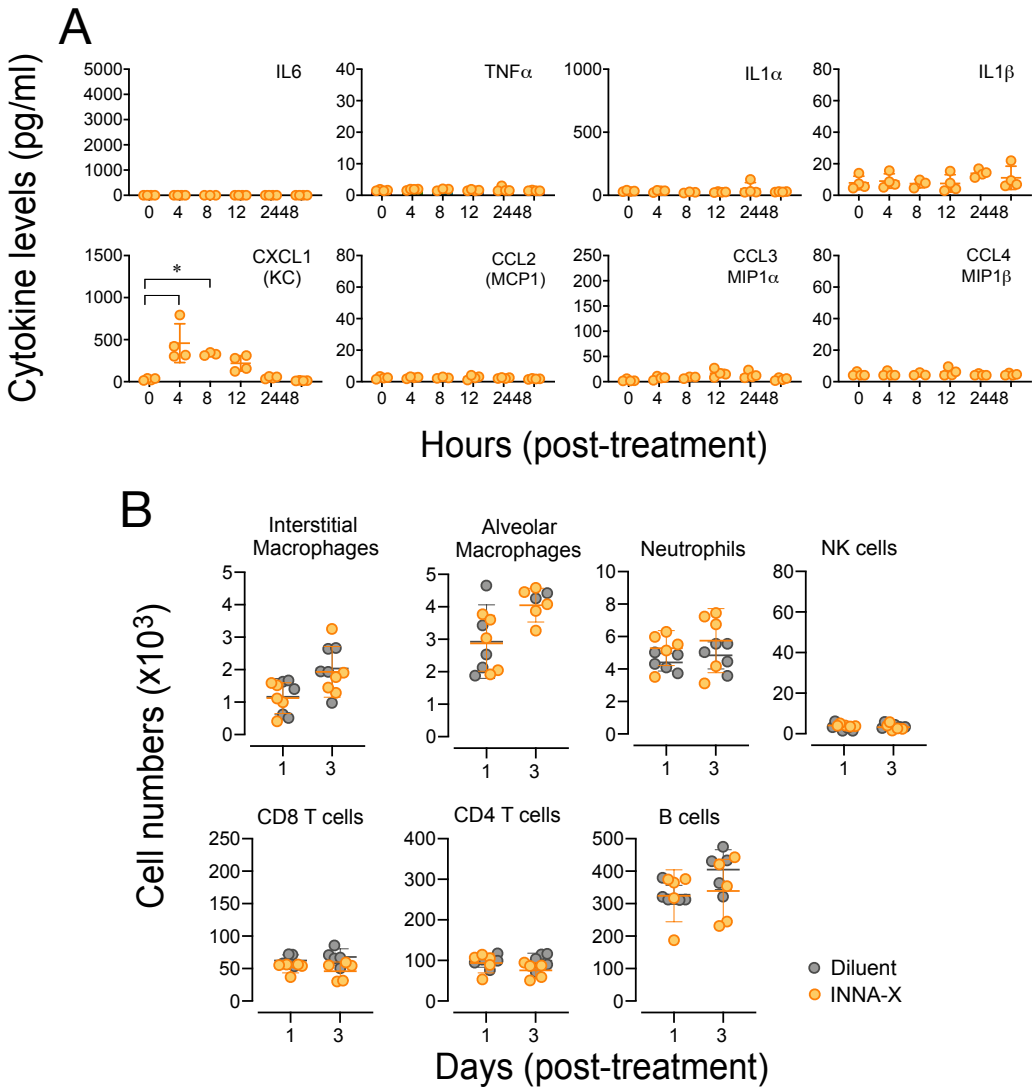
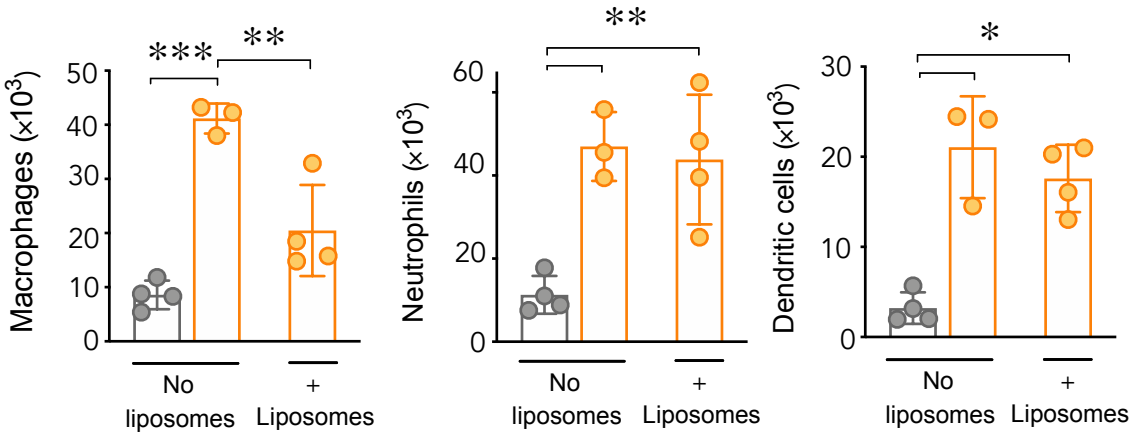


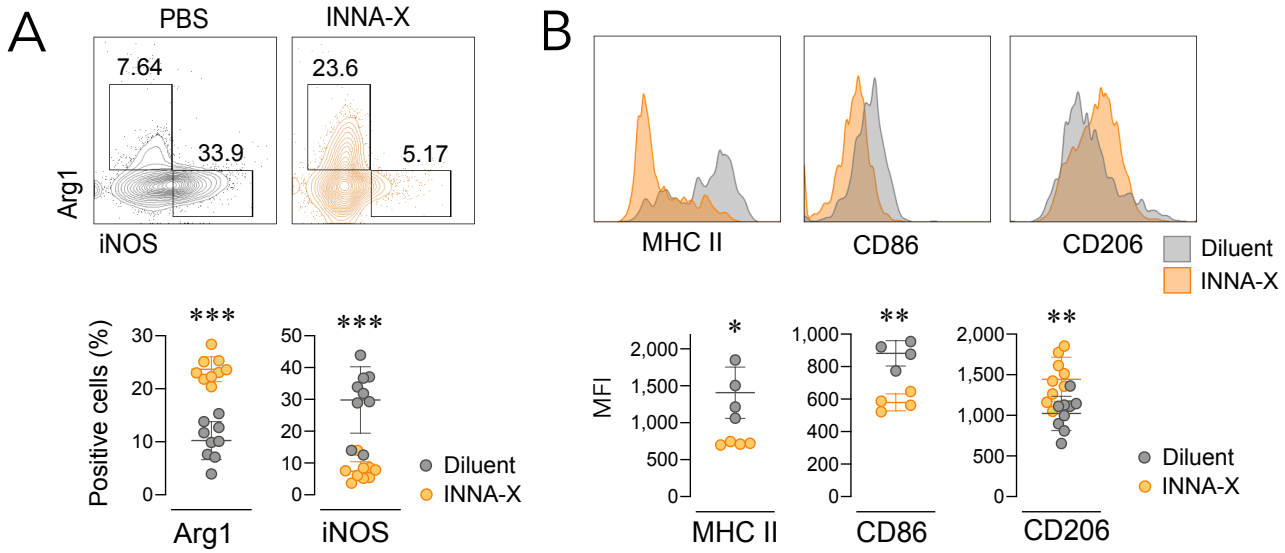

***Supplementary Figure 1. Administration of increasing volumes of Evans blue dye and distribution within the respiratory tract.*** Increasing volumes of PBS containing 0.125% Evans blue dye were administered intranasally to anaesthetised mice (n=3/group). **(A)** Mice were killed by $CO_2$ asphyxiation 5 minutes after Evans blue administration and nasal turbinates, trachea and lungs harvested for visual inspection. **(B)** Evans blue in mouse lungs was quantified by reading the absorbance (at 620nm) of acid precipitated, clarified lung supernatants.



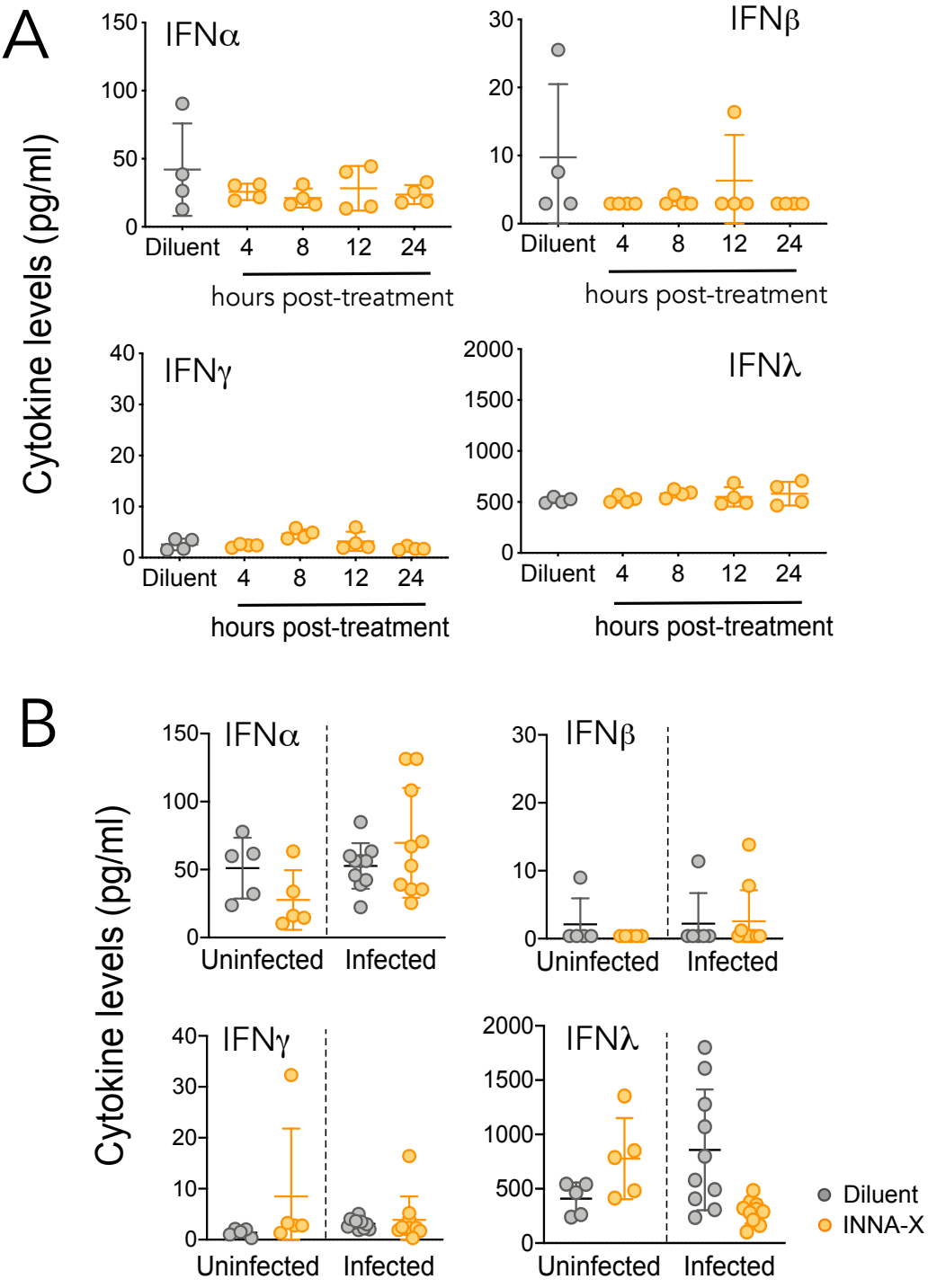

***Supplementary Figure 2. Cytokines and cell populations in the lungs following INNA-X treatment.*** Mice (n=4/group) were inoculated with 1nmole of INNA-X or diluent only and at various time points, (A) cytokine levels in nasal turbinates were analysed in a multiplex bead array assay. (B) Lungs from mice (n=5/group) treated similarly were also harvested 1 and 3 days later and cell populations analysed by flow cytometry. Statistical analysis was performed by (A) one-way ANOVA with a Tukey post-hoc test and (B) two-away ANOVA with a Bonferroni post-hoc test. *$p<0.05$.




***Supplementary Figure 3. Clodronate administration results in selective depletion of macrophages***
Mice (n=3/group) were inoculated with 1nmole of INNA-X or diluent and 1 day later received clodronate liposomes via the intravenous (200µl) and intranasal route (50µl) or were left untreated. Nasal turbinates were harvested 1 day later and cell populations analysed by flow cytometry. Statistical analysis was performed by one-way ANOVA with a Tukey post-hoc test. *$p<0.05$, **$p<0.01$, ***$p<0.001$.




***Supplementary Figure 4. M1 and M2 phenotype of nasal turbinate macrophages following INNA-X treatment***. Mice (n=4-9/group) were inoculated with 1nmole of INNA-X or diluent only. Nasal turbinates were harvested 1 day later and F480$^{+}$ macrophages analysed for expression of (A) intracellular (Arg-1 and iNOS). The results depict (top) a representative dot plot from a single animal and (bottom) percentage of positive cells for each marker within each group. (B) Cells were also analysed for surface expression of MHC II, CD86 and CD206 with (top) a representative histogram from a single animal and (bottom) mean fluorescence intensity (MFI) of each marker within each group. Statistical analysis was performed using a Welch t-test. *$p<0.05$, **$p<0.01$, ***$p<0.001$.




***Supplementary Figure 5. IFN levels in the nasal turbinate following INNA-X treatment and virus challenge.*** **(A)** Mice (n=4/group) were inoculated in the URT with 1nmole of INNA-X and 4, 8, 12 or 24 hours later, IFN levels in the nasal turbinates were measured. Levels of IFN were also determined in mice treated 24-hours prior with diluent. **(B)** IFN levels were measured in the nasal turbinates of mice treated 1 day earlier with diluent or INNA-X but were not challenged with virus. Separate groups of identically treated animals (n=5/group) were challenged with 500pfu of Udorn IAV 1 day after inoculation with INNA-X and IFN-levels present in nasal turbinates measured at 1 day after viral challenge.