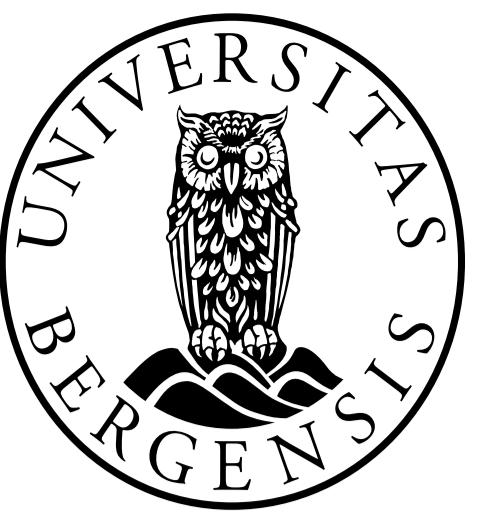


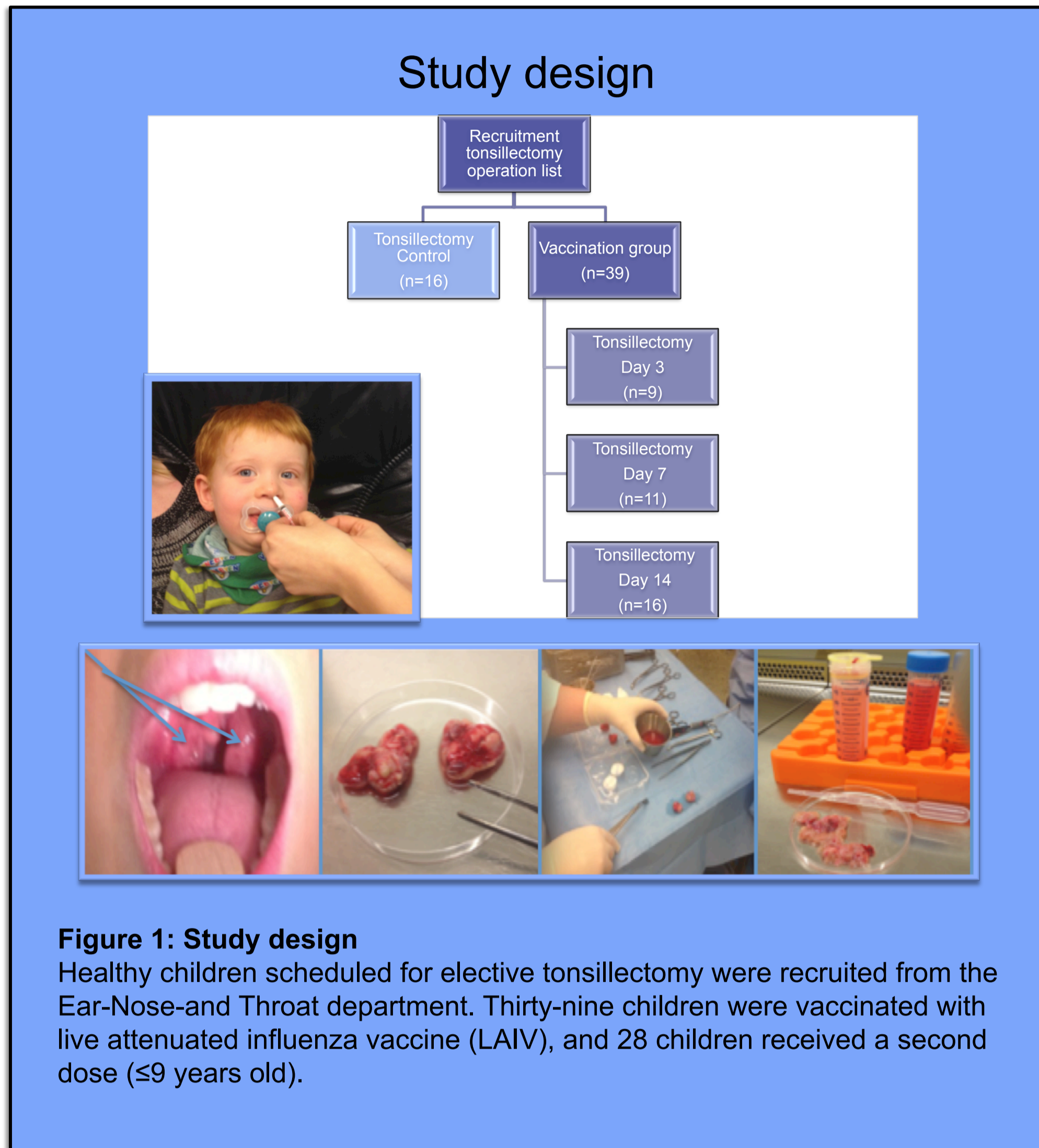
Early T-cell responses in tonsils after LAIV in children



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Results



Background

Young children carry a considerable burden of influenza disease. Recently, an intranasal live attenuated influenza vaccine (LAIV), administered as a nasal spray, has been licensed in Europe for children 2-17 years old. Tonsils are the local draining lymph nodes to the nasal and oral cavities, playing an important role as a reservoir of memory and effector cells in eliciting immune responses against respiratory viruses. Little is known about how the tonsils contribute to the immune response after intranasal vaccination.

Currently there are no agreed correlates of protection after LAIV and increased knowledge is needed to define the protective immune responses. We have recently shown that LAIV elicits long-term (up to one year), systemic CD4+ and CD8+ T-cell responses in children.

Here, we uniquely evaluate the early local tonsillar and systemic T cell responses up to 3-14 days after intranasal live attenuated influenza vaccine (LAIV) in children.

Aims

The aim of this study was to investigate the early mucosal and systemic T-cellular responses after LAIV vaccination in young children.

Methods

In this unique study, we have vaccinated young children with LAIV at specific time points prior to elective tonsillectomy. Fifty-five healthy children (3-17 years old, median 4 years) were recruited from the Ear-nose-throat outpatient clinic at Haukeland University Hospital, Norway (www.clinicaltrials.gov, NCT01866540). Thirty-nine children were immunized with trivalent LAIV (Fluenz™, Astra Zeneca) in 2012-13 at 3, 7 or 14 days prior to elective tonsillectomy. A control group consisted of age-matched unvaccinated children scheduled for tonsillectomy. Blood and saliva samples were collected pre- and post-vaccination, and tonsils were collected at the time of tonsillectomy. Tonsillar and peripheral blood mononuclear cells were stimulated with influenza antigens or peptide libraries for IFN-γ secretion in ELISPOT assays. Plasma samples were tested by the Hemagglutination inhibition (HI) assay. Saliva and serum IgA were determined using ELISA.

Conclusions

This unique study is the first to demonstrate that T-cell (IFN-γ) responses are elicited in the tonsils of young children after LAIV vaccination. Cellular responses play a significant role in anti-influenza which could provide the first line of defense against influenza infection.

Results

Early and durable local saliva and systemic antibody responses after LAIV

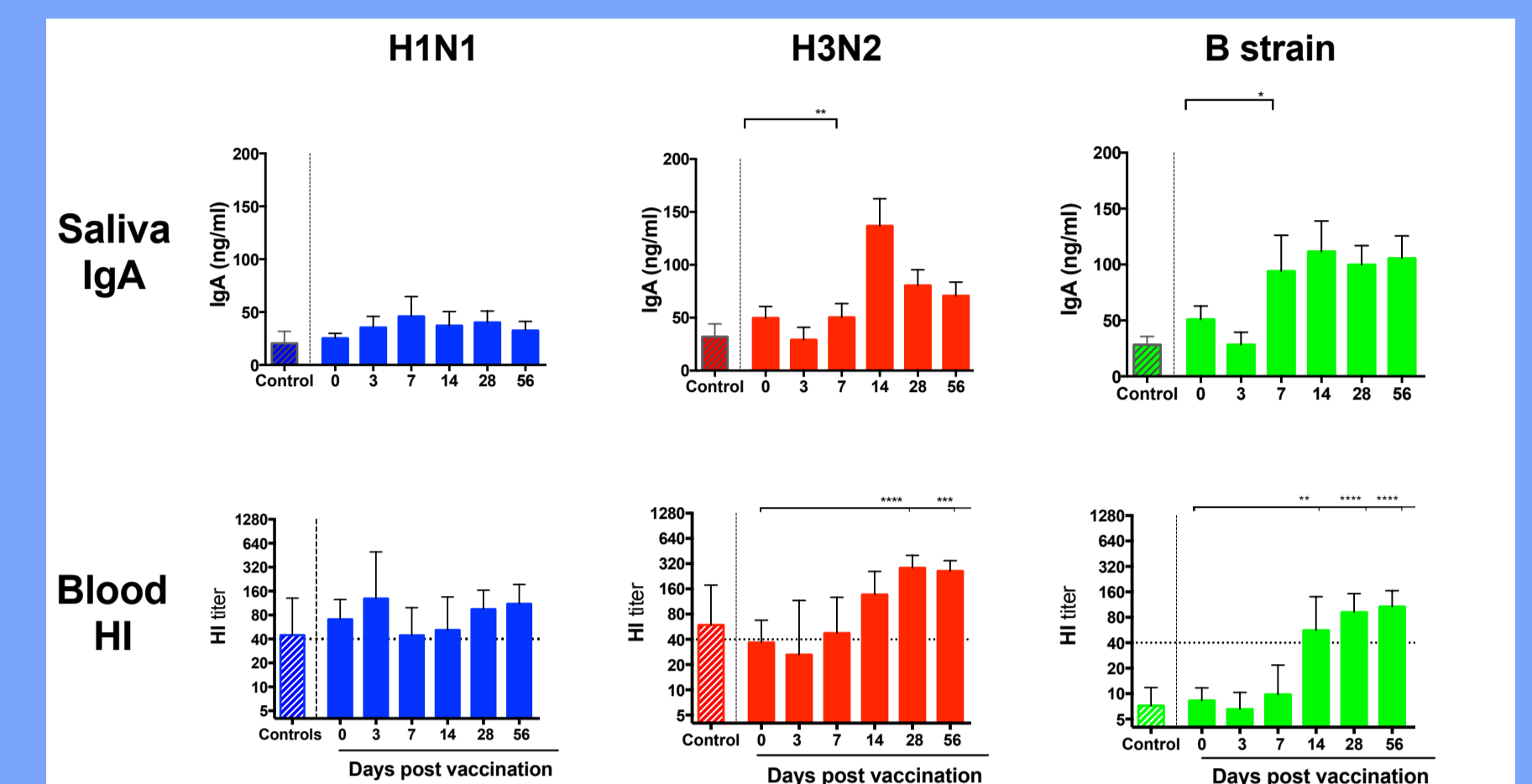


Figure 4: Saliva and Serum IgA antibody response
Influenza specific salivary and serum IgA were measured by ELISA pre-vaccination (day 0), the day of tonsillectomy (day 3, 7 or 14) and days 28 and 56 post-vaccination. A non-vaccinated control group showed similar levels to the day 0 values supporting their use as controls for the tonsillar results.

T-cell INF-γ responses earlier in tonsils than PBMCs after LAIV in children

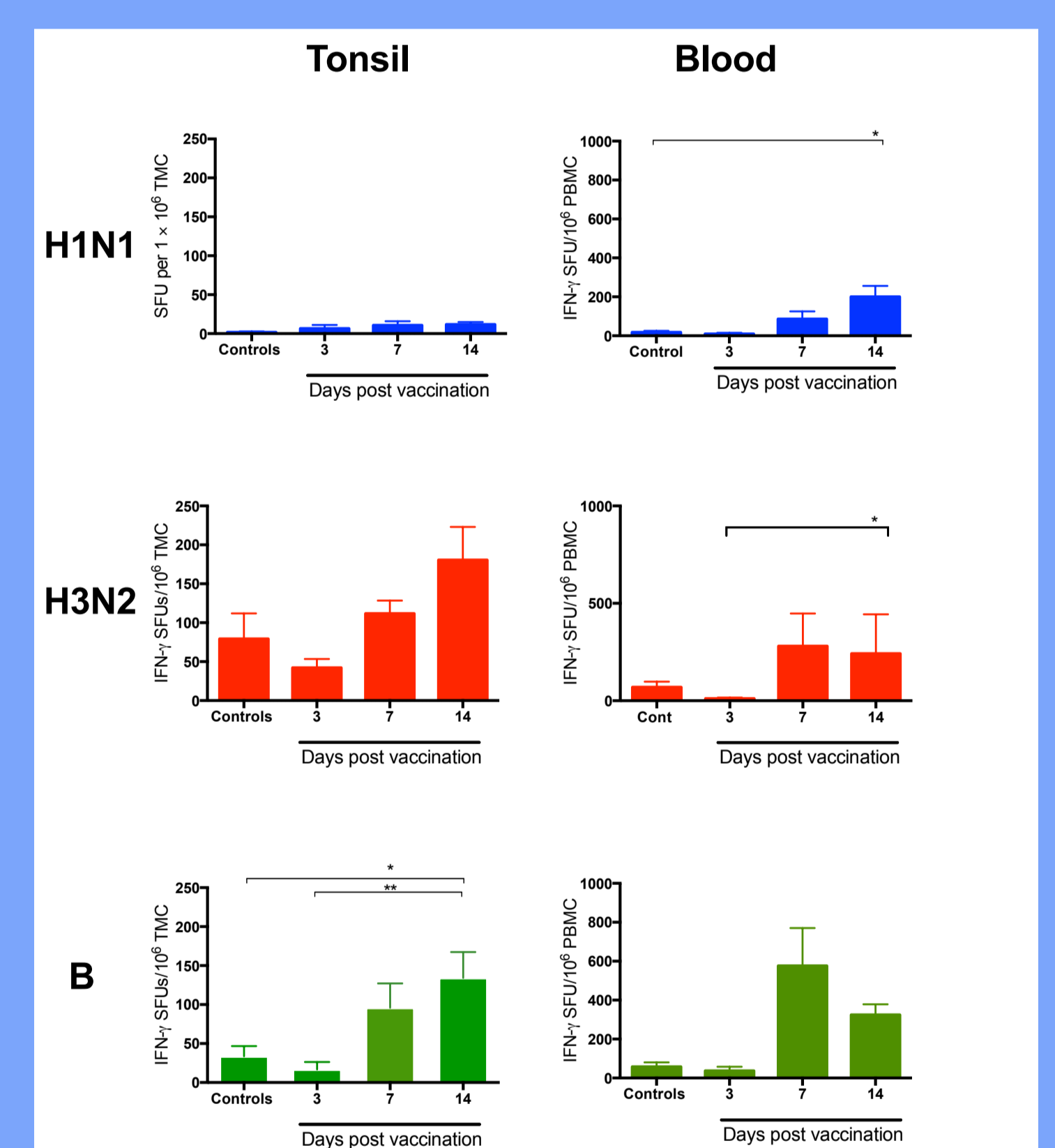


Figure 5: Strain specific T-cell responses in tonsils and PBMC
Influenza specific INF-γ T-cell responses were enumerated in tonsillar and peripheral mononuclear cells after LAIV by ELISPOT.

LAIV induces tonsillar CD8 responses

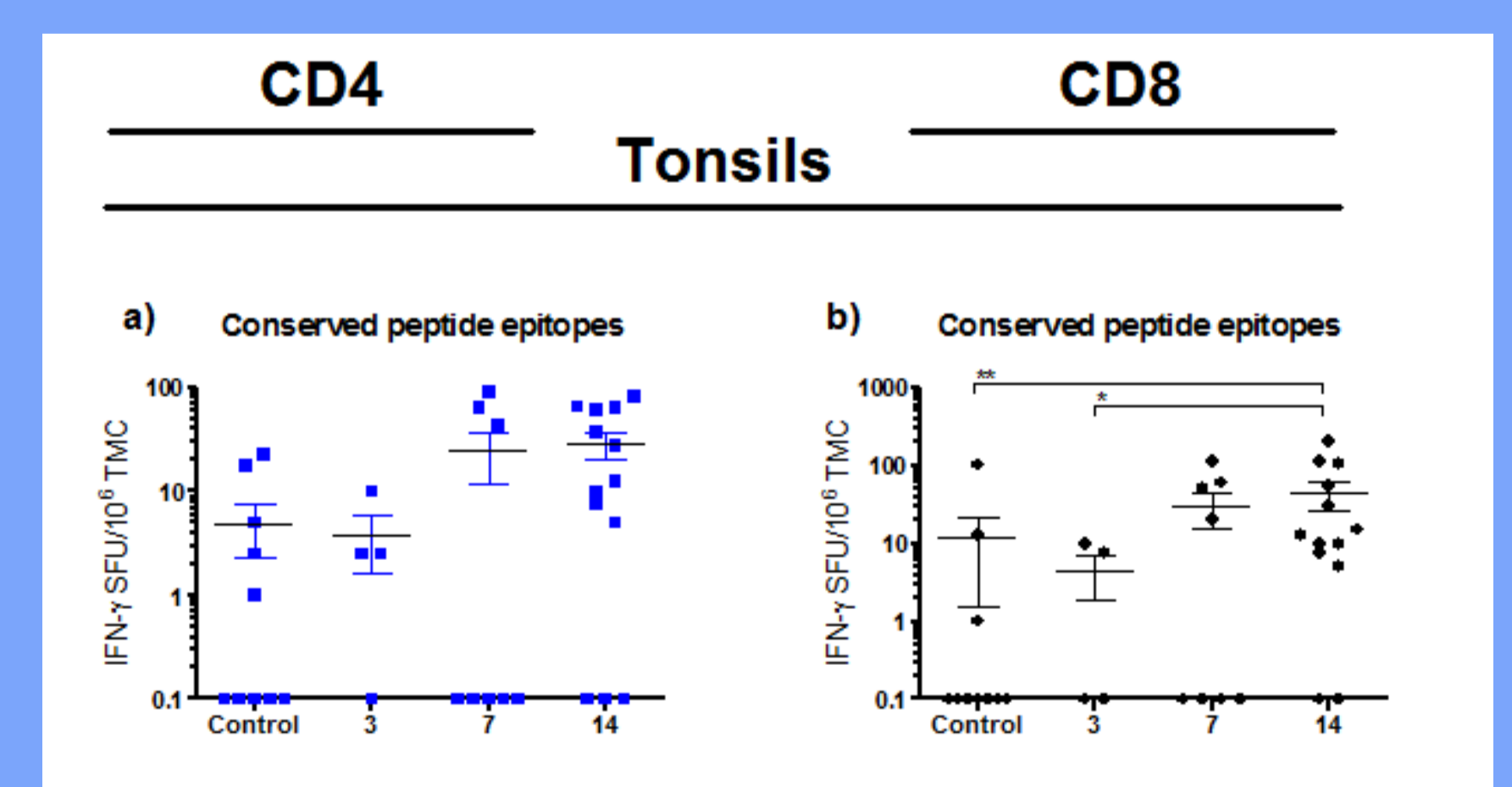
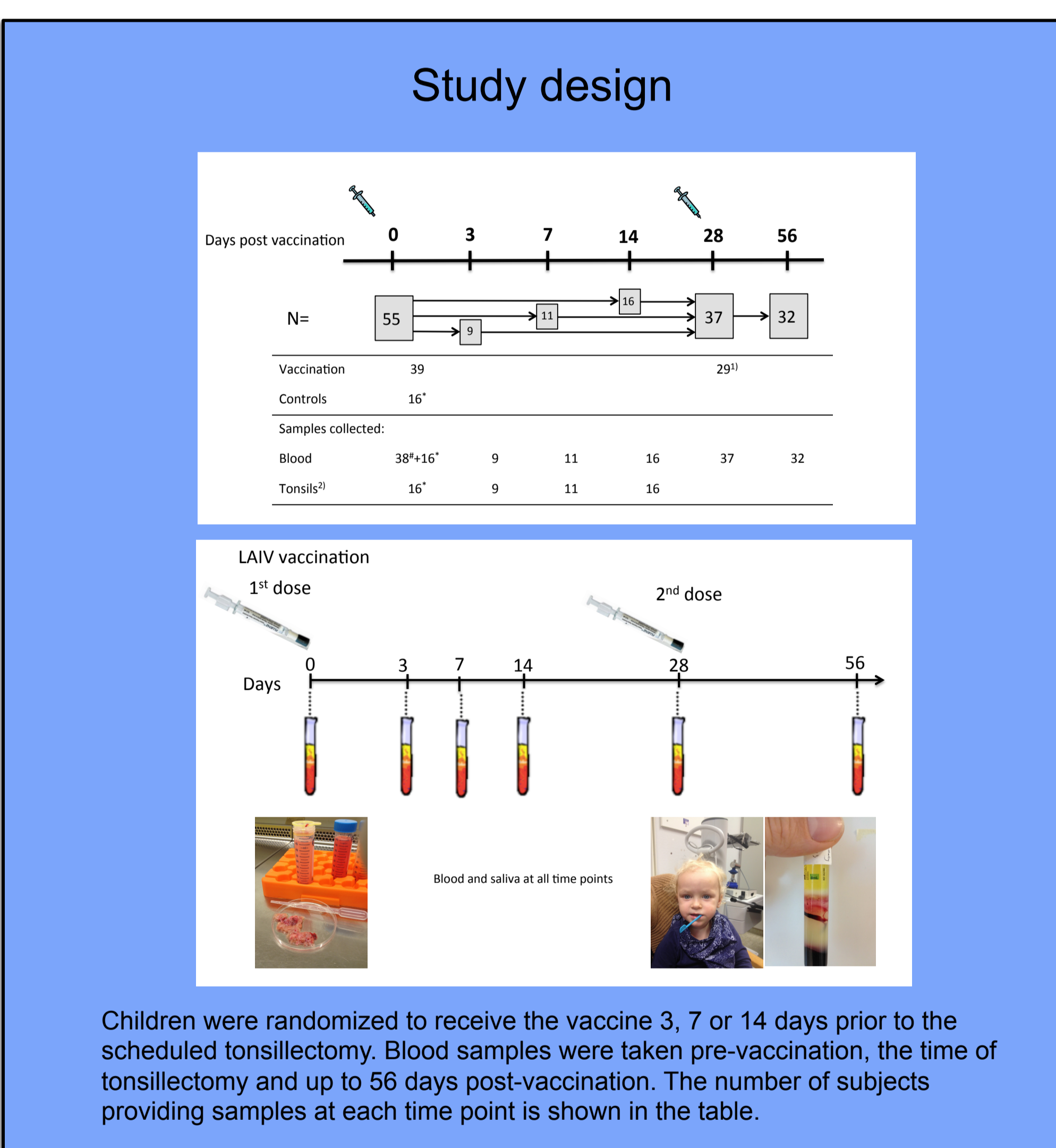
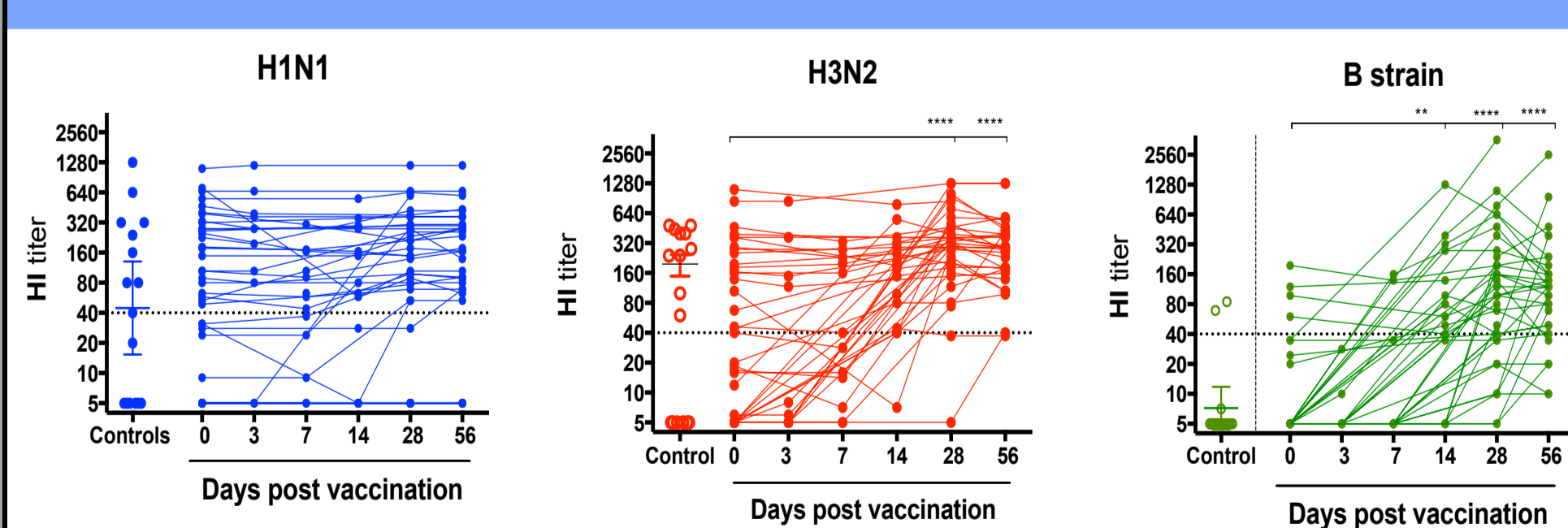


Figure 6: The CD4 and CD8 T-cell after LAIV
The detailed T-cellular immune response after LAIV was evaluated by using CD4 and CD8 specific peptides in vaccinated children, and in a non-vaccinated control group, using the ELISPOT assay. Each symbol represents the influenza specific SFU per million tonsillar mononuclear cells (TMC) for each child with the mean and standard error of the mean (SEM) shown. Statistical differences between vaccinated and non-vaccinated subjects were determined by the nonparametric Kruskal-Wallis multiple comparisons test. *P < .05 and **P < .01.



Early and durable increase in serum HI antibody levels post LAIV-vaccination



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