Exploring the effect of host factors on the relationship between pre-existing immunity and influenza vaccine response

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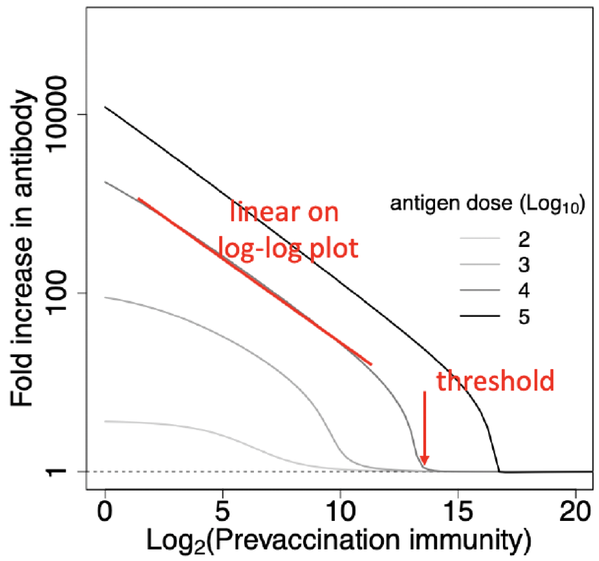
Introduction

- In general, individuals with higher preexisting immunity have weaker responses to vaccination.
- Our collaborators used a mechanistic host vaccine response model to make quantitative predictions about this relationship. (Zarnitsyna et al., 2016)



- We expect to see a negative linear response on a log-log scale, with a threshold at a high enough baseline titer value, and the relationship will be modified by the dose of the vaccine.
- We used data from a prospective, open, human cohort vaccine study which is described in Ross et al., 2014.
- Each data point represents a set of assays (pre and post vaccination HAI titers) for a subject during a given flu season–some subjects repeated multiple years, and this repetition was not taken into account.

Goals with cohort data

1. Validate the model predictions, and determine in what cases the predictions do not match the data.
2. Examine effect modification by host demographic factors, such as age, BMI, gender, and race.
3. Examine cross-protective vaccine responses rather than homologous responses alone.

Results

- All of these figures are for Influenza A(H1N1) strains, but we have similar plots for A(H3N2) and B.
- For the plots that do not stratify by age, only standard dose patients are shown.

We observed a negative trend on the log-log plot for all responses, but some trends were very close to zero.

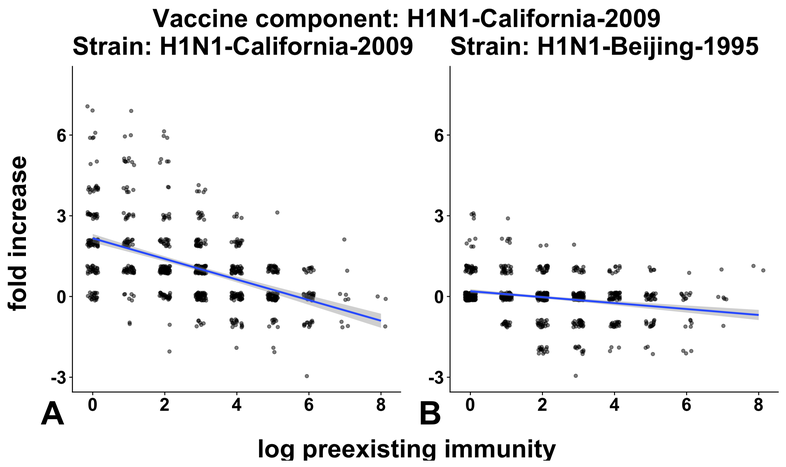


Figure 1: All of the plots showed either a strong downward trend (A) or a very slight negative trend which was not always significant (B).

Some responses showed the expected modification when stratified by dose, but in others the trend lines crossed.

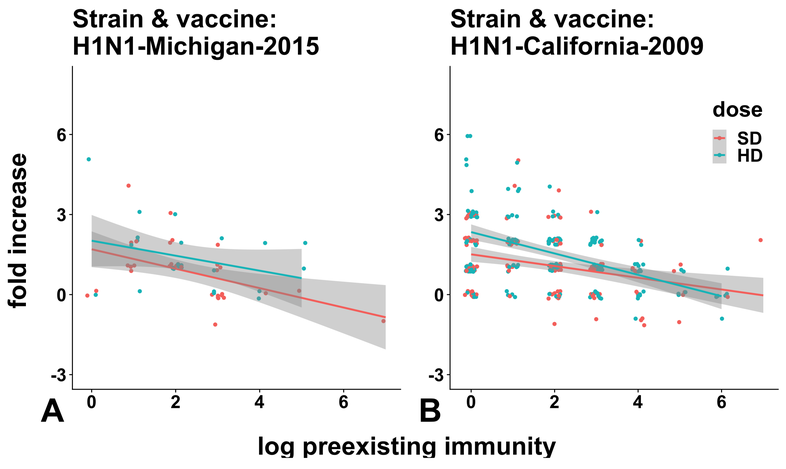


Figure 2: We observed either the expected effect modification (A) or a crossover effect between the two trendlines (B). This may be an actual effect or an artifact of the data. Only subjects at least 65 years or older are shown here (the group eligible for high dose vaccines).

Age appears to be an important covariate. From exploratory plots we can see that both the baseline titer and the fold increase depend on age.

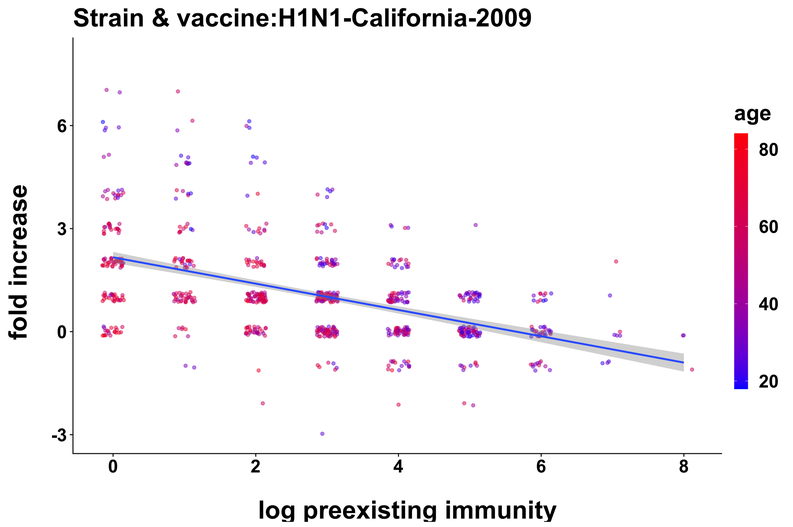


Figure 3: In this plot, older subjects are colored red. We see that most of the red points are clustered in the bottom left, indicating that elderly patients tended to have both lower baseline titers as well as lower responses to the vaccine.

Conclusion

- We did observe the predicted negative linear relationship on a log-log scale! However the observed dose effect was not always as predicted.
- Age is also a potential variable of importance and we need to explore potential interactions with other covariates.
- We have many exploratory results that are not shown–please get in touch if you are interested.

Acknowledgements

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- Yang Ge wrote a lot of code used for this project.

References

1. Zarnitsyna VI, et al. 2016. *PLoS Pathog* 12(6):e1005692.
2. Ross TM, et al. 2014. *Hum Vaccin Immunother* 10(5):1195–1203.