PROTECT
A COVID-19 National Core Study

Imperial College London

Omicron breakthrough infections in previously infected or vaccinated hamsters

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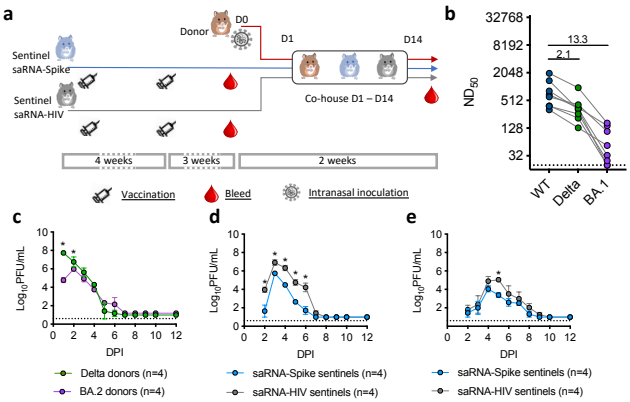
Introduction

The second and third years of the SARS-CoV-2 pandemic have been marked by the repeated emergence and replacement of 'variants' with genetic and phenotypic distance from the ancestral strains, the recent examples being Delta and Omicron. Here we describe a hamster challenge/re-challenge model to assess protection conferred by vaccination or prior infection against re-infection.

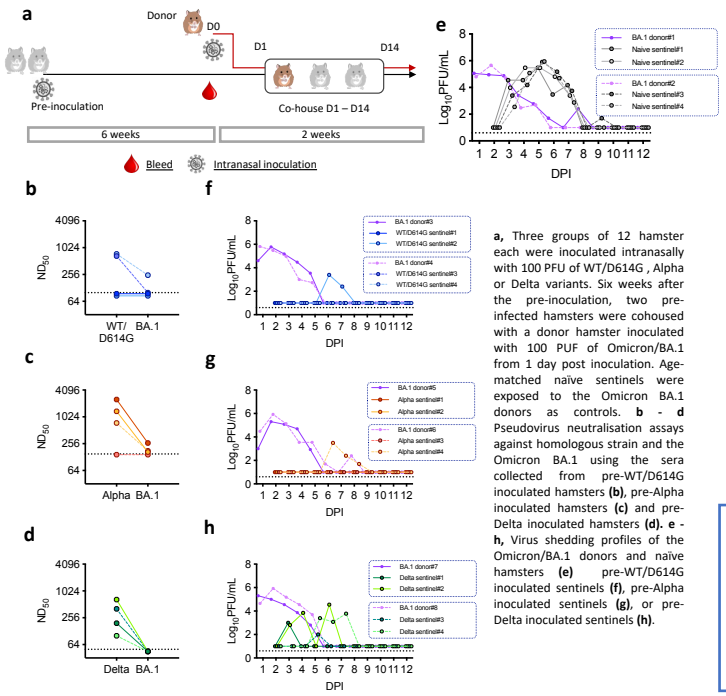
Results

Omicron/BA.1 variant can effectively infect hamsters vaccinated with a Wuhan-hu-1 Spike saRNA vaccine



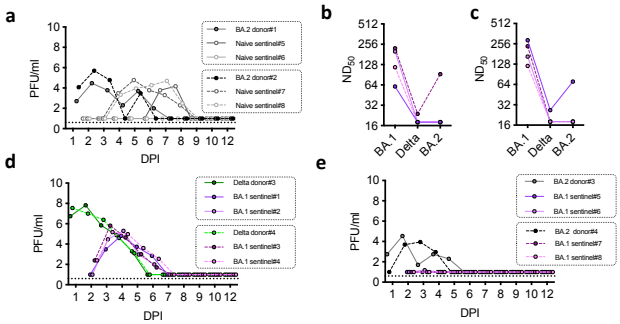
a, Two groups of 16 hamster each were vaccinated with the self-amplified RNA(saRNA) Spike (n=8) or the saRNA-HIV vaccine (n=8). Three weeks after the second dose vaccine, these sentinels were co-housed with the donor hamsters which were inoculated intranasally with 100 PFU Delta or the Omicron BA.1 variant from 1 day post inoculation. **b,** Pseudovirus neutralisation assays using sentinel hamster sera collected two weeks after the second vaccinations. Geometric means are shown above the symbols. **c-e**, Virus shedding in nasal wash samples of the donor hamsters (**c**), the saRNA sentinels exposed to Delta donors (**d**), and the saRNA sentinels exposed to the BA.1 donors (**e**).

Reinfection of hamsters infected with earlier VOCs following exposure to Omicron.



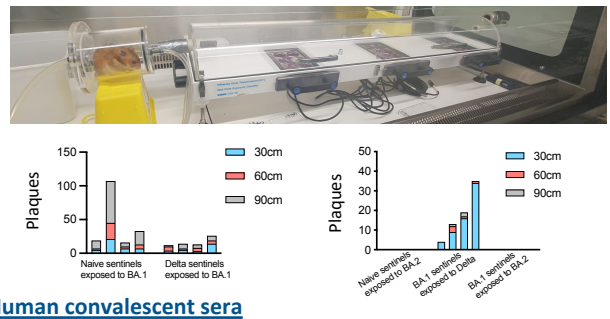
a, Three groups of 12 hamster each were inoculated intranasally with 100 PFU of WT/D614G , Alpha or Delta variants. Six weeks after the pre-inoculation, two pre-infected hamsters were cohoused with a donor hamster inoculated with 100 PUF of Omicron/BA.1 from 1 day post inoculation. Age-matched naïve sentinels were exposed to the Omicron BA.1 donors as controls. **b - d** Pseudovirus neutralisation assays against homologous strain and the Omicron BA.1 using the sera collected from pre-WT/D614G inoculated hamsters **(b),** pre-Alpha inoculated hamsters **(c)** and pre-Delta inoculated hamsters **(d). e - h,** Virus shedding profiles of the Omicron/BA.1 donors and naïve hamsters **(e)** pre-WT/D614G inoculated sentinels **(f),** pre-Alpha inoculated sentinels **(g),** or pre-Delta inoculated sentinels **(h).**

Reinfection of hamsters previously infected by Omicron/BA.1 with Delta variant but not BA.2

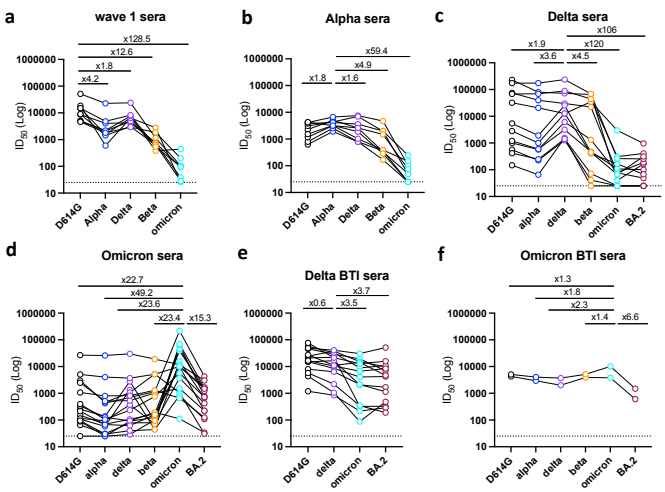


Eight hamster were inoculated intranasally with 100 PFU of the BA.1 variant. Six weeks after the pre-inoculation, two pre-inoculated hamsters were cohoused with a donor hamster inoculated with 100 PUF of the Delta or BA.2 variant from 1 day post inoculation. Age-matched naïve sentinels were exposed to BA.2 donors as controls. **a,** virus shedding in nasal wash samples of the naïve sentinels and the BA.2 donors. **b, c,** Pseudovirus neutralisation assays against homologous strain Omicron/BA.1, Delta and BA.2 using the sera collected from pre-Omicron/BA.1 infected hamsters. **d,** Virus shedding profile of the Delta donors and pre-Omicron/BA.1 inoculated sentinels. **e,** virus shedding profile of the Omicron/BA.2 donors and pre-Omicron/BA.1 inoculated sentinels.

Assessing infectious virus exhaled from infected/re-infected hamsters.



Human convalescent sera



Differences in cross neutralising activity against the Omicron variant from the convalescent sera of the individual previously infected with WT (a), Alpha (b), Delta (c) or Omicron/BA.1 (d) variants, or vaccinated individuals infected with Delta (e) or Omicron/BA.1 (f).

Conclusion

populations whose only immune experience of COVID is Omicron infection may be particularly vulnerable to future circulation of Delta (or Delta-like derivatives). In contrast, repeated exposure to antigenically distinct Spikes, via infection and or vaccination appears to drive a more cross-reactive immune response, both in hamsters and people.