Can human challenge studies provide critical information?

Professor Chris Chiu
Department of Infectious Disease
Imperial College London
Key strengths of human infection challenge

- Defined viral strain & dose
- Consistent high infection rate
- Carefully selected participants
- Small number of participants needed
- Beginning, middle & end of infection
- Pre-infection & early assessment

Rapid & flexible controlled studies
Evidence of efficacy early in clinical development for antivirals, vaccines & diagnostics
Identify host protective factors
Risk mitigation

1. Careful participant selection
   - Healthy 18-30yo
   - No significant risk factors
2. High quality virus
   - Low dose inoculation
3. High-containment quarantine unit & strict discharge criteria
4. Close clinical monitoring & access to higher-level care
   - Pre-emptive treatment
   - Early “rescue” treatment
5. Long-term follow-up & specialist referral

SARS-CoV-2 challenge of seronegative volunteers

Infected (2 consecutive PCR+)
n=18

“Uninfected”
n=16

SARS-CoV-2/human/GBR/484861/2020 nasal drops
10 TCID50/55 FFU

Killingley et al. https://doi.org/10.21203/rs.3.rs-1121993/v1
Clinical readouts

No serious adverse events. Fever in 39%. Single individual with measurable smell reduction at 6 months steadily improving.
Next steps for the programme

• Why did 47% of participants resist infection?
  – May provide new targets for prevention

• Estimated 98% of UK population +ve for antibodies

• Why do people with immunity still get breakthrough infection?
  – GMP Delta challenge agent manufactured (Imperial, hVIVO, Wellcome Trust)
  – Delta challenge study in vaccinated (Imperial) & infected (Oxford) individuals
  – Optimised platform for testing antivirals, diagnostics & next-generation vaccines
What is the role for human challenge in further SARS-CoV-2 vaccine development?

- Rapid, small studies with efficacy readout
  - Reduction in viral load or symptoms
  - Protection from PCR-confirmed infection
  - Comparative studies of different vaccines/regimens
- Non-conventional vaccines
  - Mucosal vaccines
  - T cell-inducing vaccines
- Demonstrating cross-protection
  - Pipeline for future variants

Van der Straten et al. https://doi.org/10.1101/2022.01.03.21268582
Acknowledgments

Chiu group:
Helen Wagstaffe
Nana-Marie Lemm
Steff Ascough
Loukas Papargyris
Pete Dayananda
Ashley Collins
Jo McKenzie
Lydia Taylor
Polly Fox
Emma Bergstrom
Rich McKendry

Imperial:
Emma Smith
Ryan Thwaites
Jie Zhou
Peter Openshaw
Garth Rapeport
Wendy Barclay

hVIVO:
Mariya Kalinova
Alex Mann
Fiona Hughes
Nicolas Noulin
Andrew Catchpole

Oxford:
Helen McShane

Royal Free Hospital:
Ben Killingley
Mike Jacobs

Imperial:

Vaccines Taskforce:
Kate Lindsell
Chris Charman
Priya Mande

Southampton:
Rob Read

DHSC:
Jonathan Van Tam

DSMB:
Stephen Gordon (chair)
Peter Smith (chair)
Anna Durbin
Fred Hayden
David Dockrell