new orleans
CIS 2026 ANNUAL MEETING

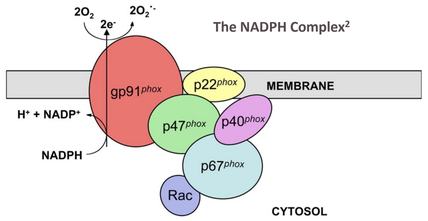
Pre-existing antibodies to virus like particles (VLP) derived from helper dependent adenovirus (HDAd) in patients with Chronic Granulomatous Disease (CGD)

Claire Booth[1,2], Morna Dorsey[3], Jonathan Cotliar[4], Esther Shamir[5], Patrick Au[5], Chris Plescia[5], Andrew C. Dietz[5]*, Siobhan Burns[1,6]*
[1]University College London, [2]Great Ormond Street Hospital, [3]University of California San Francisco, [4]Science 37, [5]Ensoma, [6]Royal Free Hospital

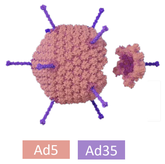
ensoma

Introduction

- CGD is an inborn error of immunity[1]
- Estimated incidence: 1 in 200,000 live births[1]
- Caused by a defect in NADPH oxidase complex[1]
- Patients experience recurrent and severe bacterial or fungal infections, immune dysregulation, and chronic inflammation[1]
- Median life expectancy is ~45 years[1]
- Can be treated by allogeneic hematopoietic stem cell transplantation (allo-HSCT)[1] or experimental gene therapy



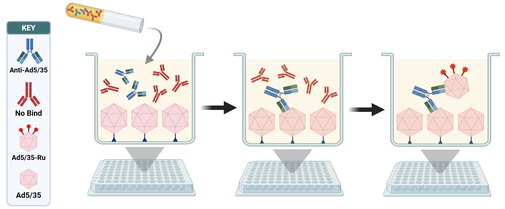
VLP: Helper-dependent adenovirus (HDAd) 5/35++



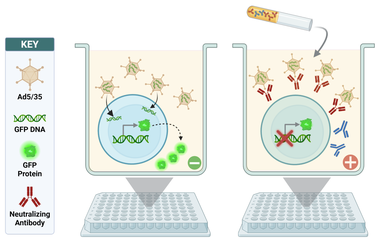
For viral vector based in vivo gene therapy, the presence of pre-existing antibodies to a virus like particle (VLP) derived from helper dependent adenovirus (HDAd) 5/35++ may have an impact on transduction. The prevalence of antibodies against these VLP is previously unknown.

Methods

A single blood draw was obtained in an observational clinical trial (NCT06605378) of patients in the United States and United Kingdom confirmed to have CGD, but who had not previously undergone allo-HSCT or gene therapy. Total antibodies (TAb) were measured by an antibody bridging assay and neutralizing antibodies (NAb) were measured by a transduction inhibition cell-based assay.



Antibody Bridging Assay



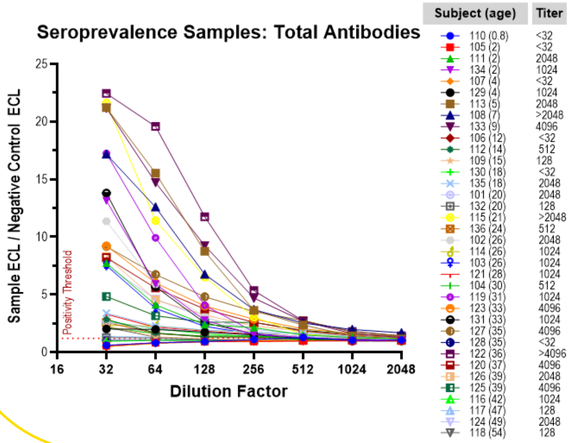
Cell-based Transduction Inhibition Assay

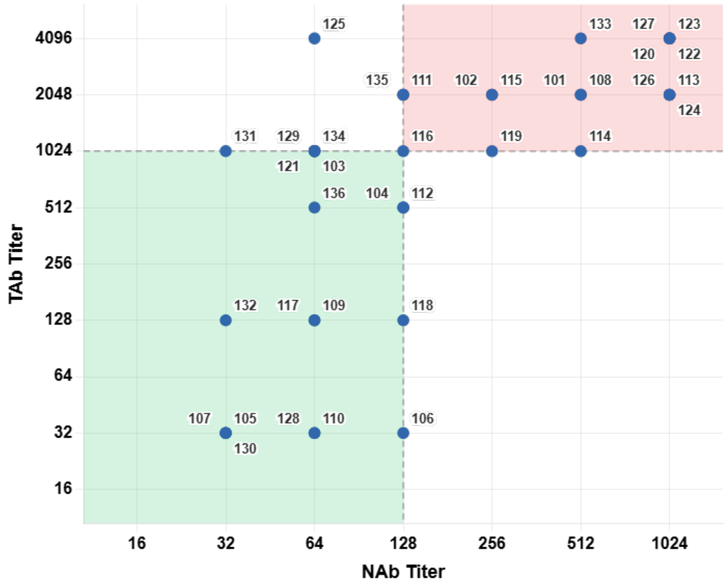
Results

Participant Population

Data Cut Off Oct 2025

Demographic	N = 36
Age (years)	33% <18 (pediatric), 67% ≥18 (adult) Median 26, Range 1-54
Sex	83% male, 17% female
Race/Ethnicity	86% White, 8% Asian, 6% Black 11% Hispanic
Type of CGD	75% X-linked, 25% Autosomal recessive





- Serial dilution curves for NAb appear similar to those show for TAb to the left
- There was good general agreement between NAb and TAb as shown above
- TAb was at or below median titer 67% of the time in pediatrics
- TAb was at or below median titer 54% of the time in adults

Conclusions

- Patients with CGD have varying pre-existing exposure to VLP that appear to increase with age
- Concordance between TAb and NAb in CGD participants was high
- Understanding these results may help to better inform patient selection for *in vivo* gene therapy using HDAd 5/35++ VLP

References

1) Leiding JW, Holland SM. Chronic granulomatous disease. In: Pagon RA, Adam MP, Ardinger HH, et al, eds. GeneReviews®. Seattle, WA: University of Washington, Seattle; 1993-2022.
2) Gardiner, Gail & Deffit, Sarah & Mcletchie, Shawna & Pérez, Liliana & Walline, Crystal & Blum, Janice. (2013). A Role for NADPH Oxidase in Antigen Presentation. Frontiers in Immunology. 4. 295.