

Cytokine Profile in patients with Chronic Granulomatous Disease (CGD)

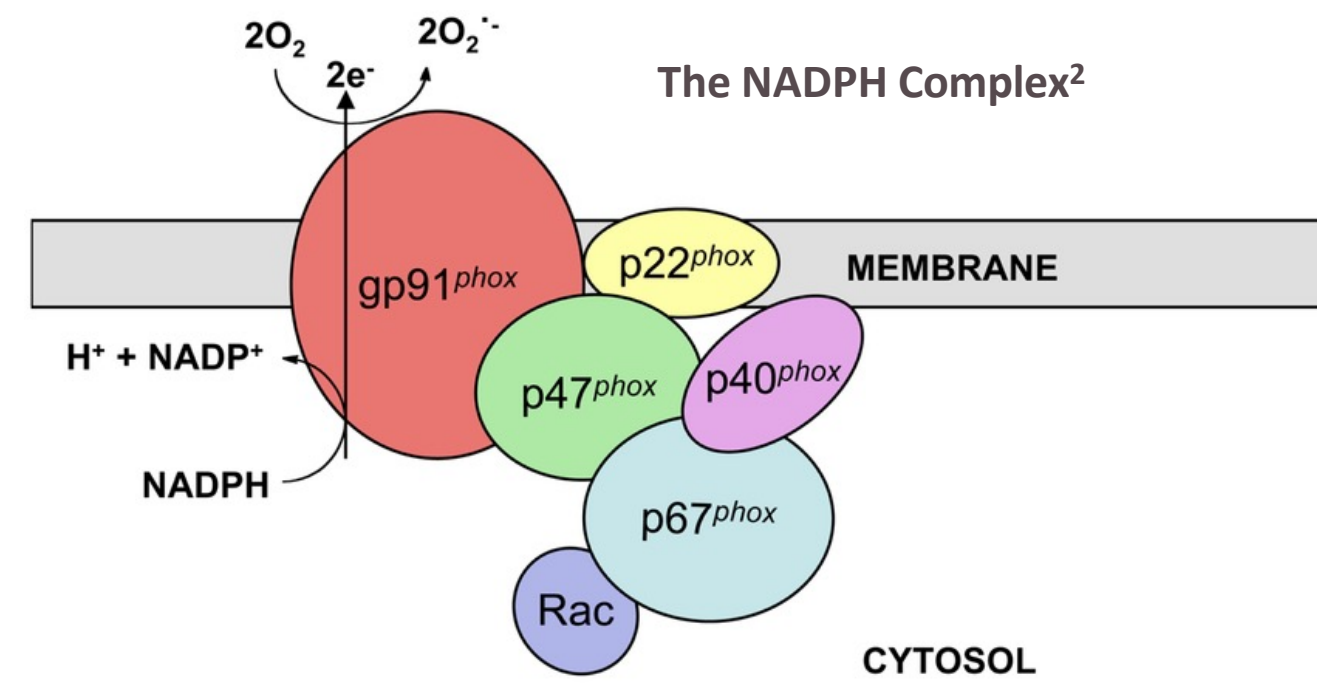
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Introduction

- CGD is an inborn error of immunity¹
- Estimated incidence: 1 in 200,000 live births¹
- Caused by a defect in NADPH oxidase complex¹
- Patients experience recurrent and severe bacterial or fungal infections, immune dysregulation, and chronic inflammation¹
- Median life expectancy is ~45 years¹

There are limited data on serum cytokine levels in patients with CGD, and profiling the cytokine signature may inform allogeneic hematopoietic stem cell transplantation (allo-HSCT) or experimental gene therapy strategies



Subunit (gene)	Mode of inheritance	Frequency
gp91 ^{phox} (CYBB)	X-linked	65-70%
p47 ^{phox} (NCF1)	Autosomal recessive	20-25%
p67 ^{phox} (NCF2)	Autosomal recessive	5-6%
p22 ^{phox} (CYBA)	Autosomal recessive	3-5%
p40 ^{phox} (NCF4)	Autosomal recessive	<1%

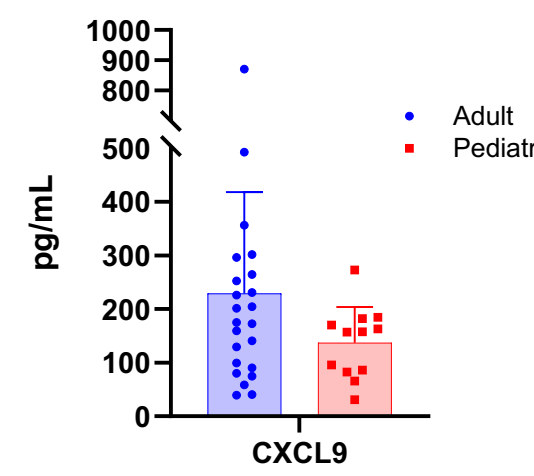
Results

Participant Population

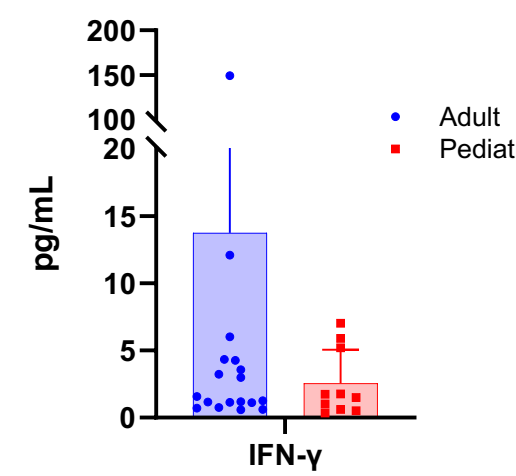
Demographic	N = 36
Age (years)	33% <18 (pediatric) 67% ≥18 (adult) Median 26, Range 1-54
Sex	83% male 17% female
Race/Ethnicity	86% White 8% Asian 6% Black 11% Hispanic
Type of CGD	75% X-linked 25% Autosomal recessive

- Data Cut Off Oct 2025
- Clustering and PCA showed no discrete groups based on cytokine profiles
- IL-1 β , IL-2, IL-4, IL-10, IL-12, IL-13 & TNF- α did not appear elevated and did not show differences between participant groups
- CXCL9, IL-6, and IL-8 & INF- γ , showed differences that appeared to primarily be driven by outlier participants within each cytokine

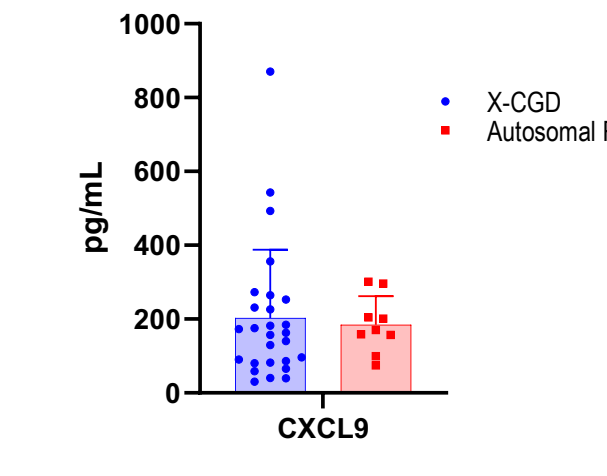
Cytokines by Age (CXCL9)



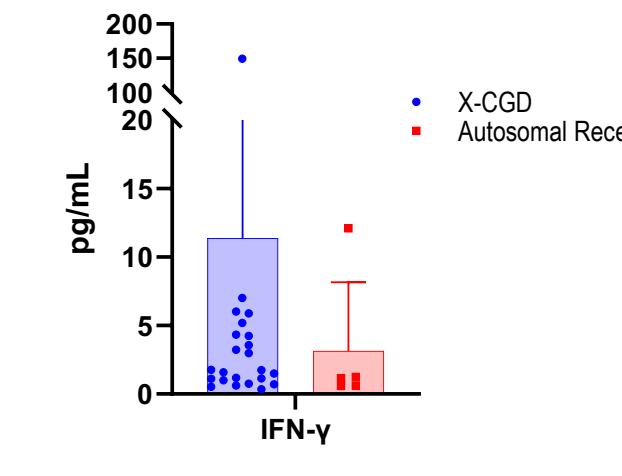
Cytokines by Age (IFN-g)



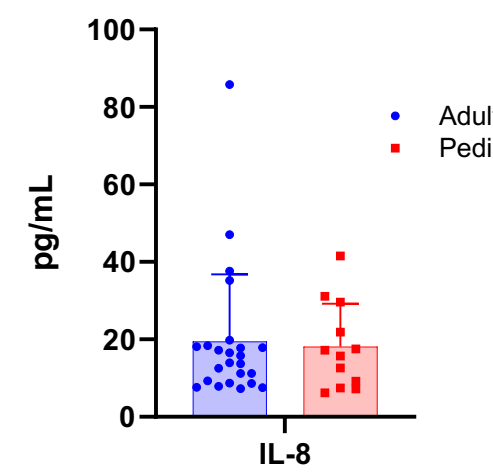
Cytokines by Mutation (CXCL9)



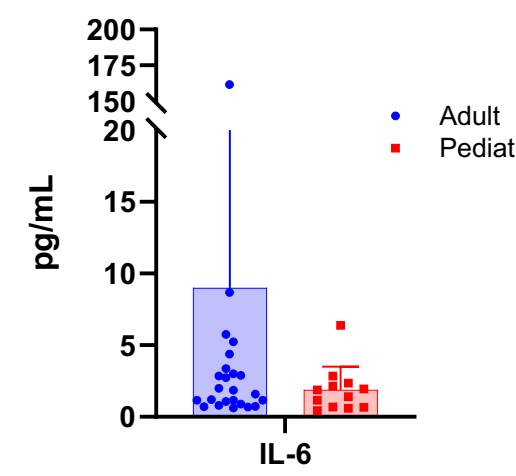
Cytokines by Mutation (IFNg)



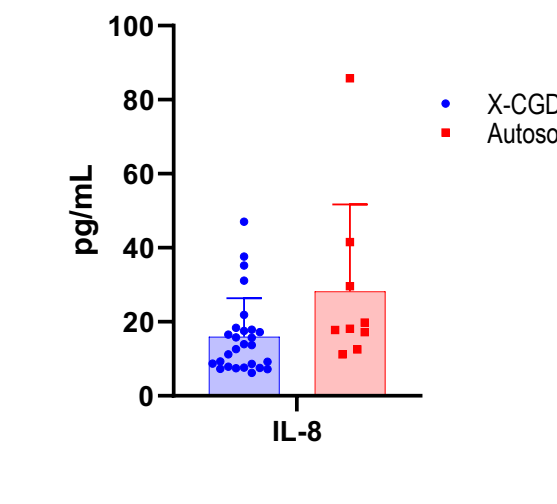
Cytokines by Age (IL-8)



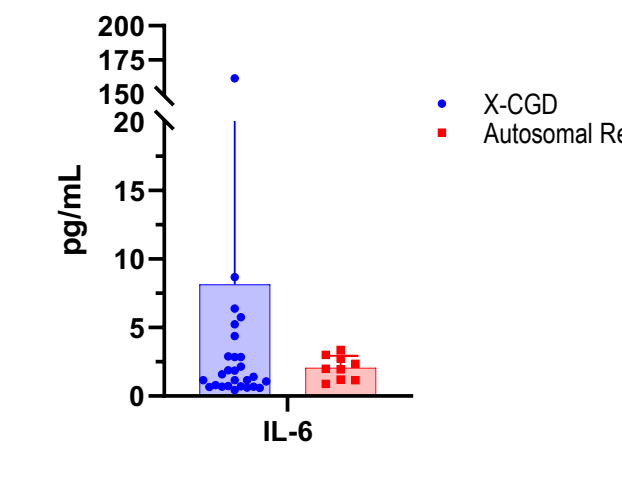
Cytokines by Age (IL-6)



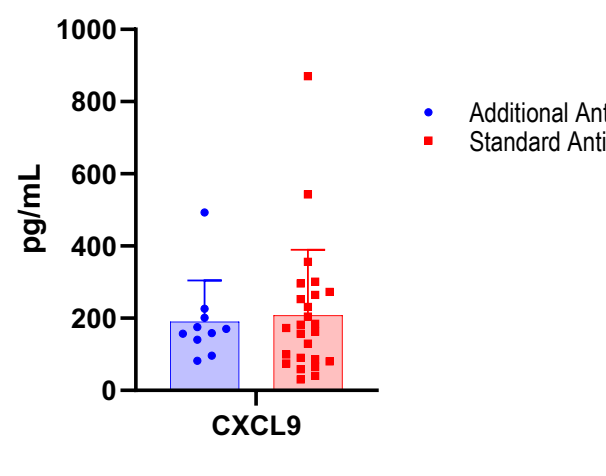
Cytokines by Mutation (IL-8)



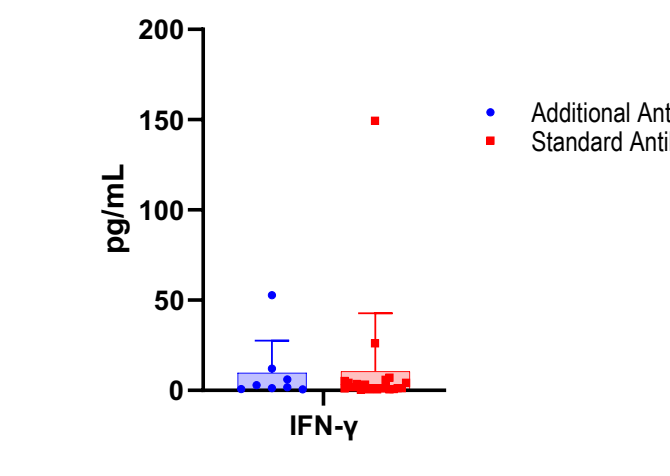
Cytokines by Mutation (IL-6)



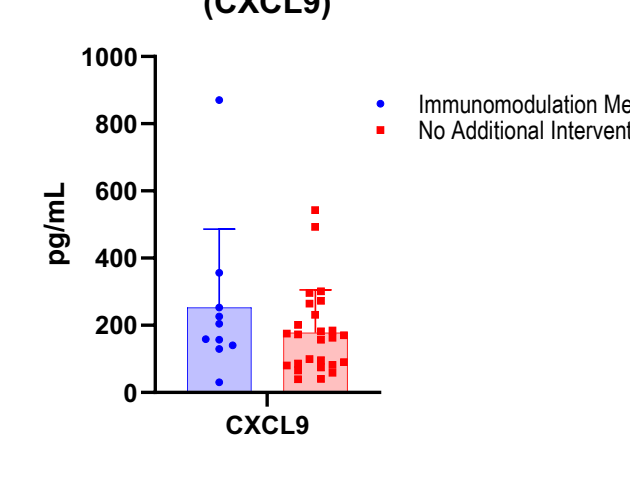
Cytokines by Antibiotic Treatment (CXCL9)



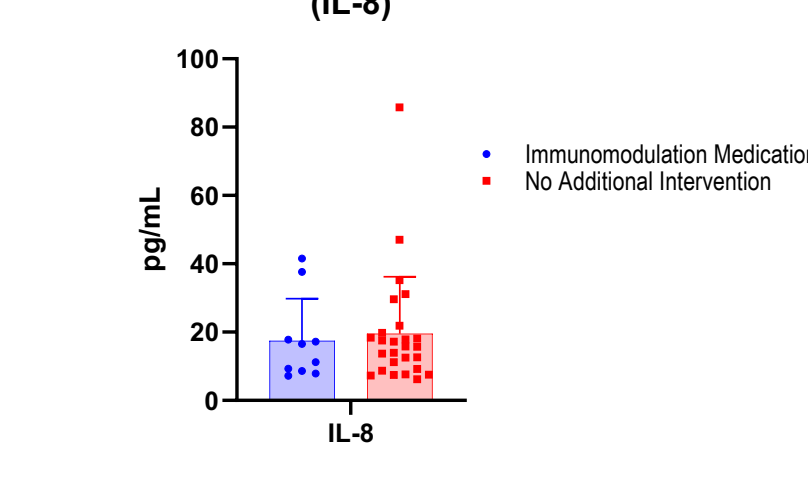
Cytokines by Antibiotic Treatment (IFNg)



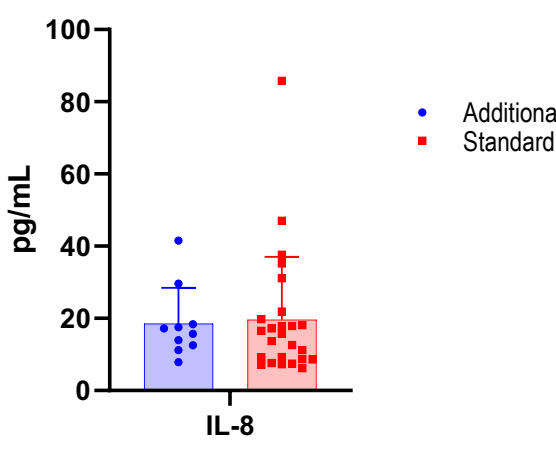
Cytokines by Immuno-modulatory Treatment (CXCL9)



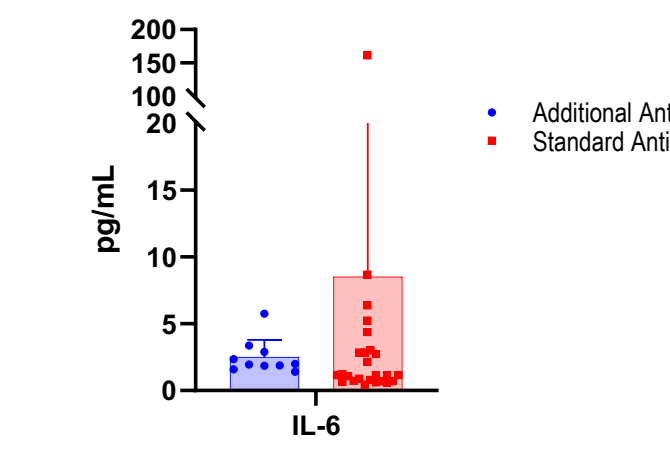
Cytokines by Immuno-modulatory Treatment (IL-8)



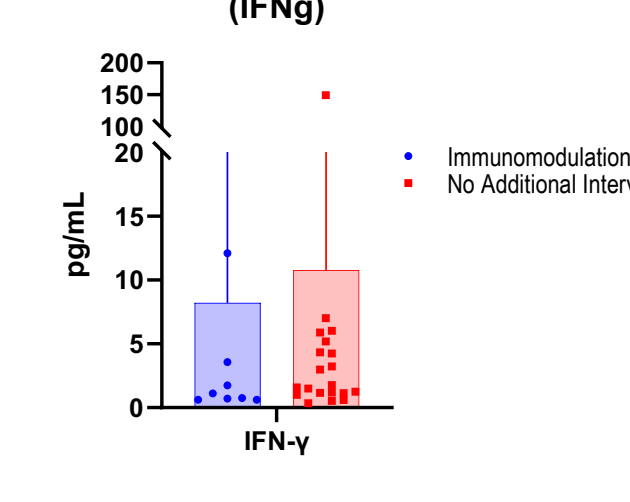
Cytokines by Antibiotic Treatment (IL-8)



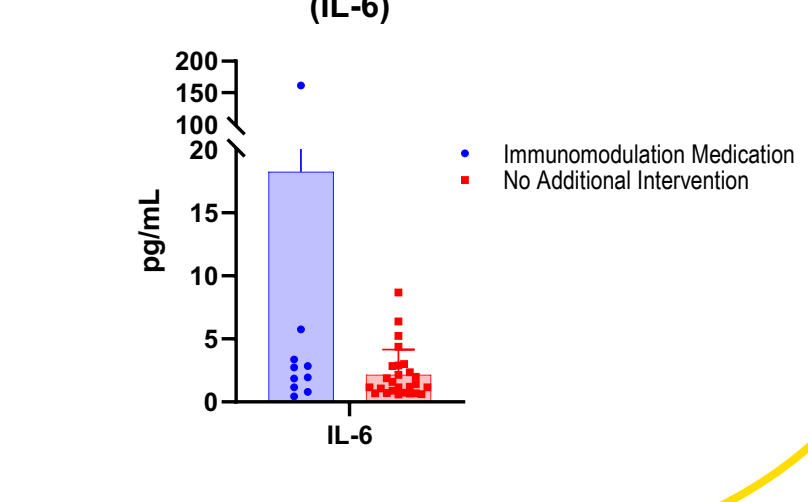
Cytokines by Antibiotic Treatment (IL-6)



Cytokines by Immuno-modulatory Treatment (IFNg)



Cytokines by Immuno-modulatory Treatment (IL-6)



Methods

Serum cytokines were measured from a single blood draw in an observational clinical trial (NCT06605378) of patients in the United States and United Kingdom that were confirmed to have CGD, but who had not previously undergone allo-HSCT or gene therapy.

Cytokines analyzed by Meso Scale Discovery (MSD):

- IL-1 β
- IL-2
- IL-4
- IL-6
- IL-8
- IL-10
- IL-12
- IL-13
- INF- γ
- TNF- α

Cytokine measured by ELISA

- CXCL9



MSD Instrument

Multiplex MSD Plate

Conclusions

- Serum cytokines analyzed here do not clearly identify distinct patterns
- Cytokine profiles in CGD patients may vary with age, genotype and/or clinical status, but differences are mostly driven by outlier values and analysis is limited by small participant numbers
- Additional work is required to more fully understand the impact of serum cytokines on allo-HSCT or gene therapy

References

- 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.
- Gardiner, Gail & Deffit, Sarah & Mclechie, Shawna & Pérez, Liliana & Walline, Crystal & Blum, Janice. (2013). A Role for NADPH Oxidase in Antigen Presentation. Frontiers in Immunology. 4. 295.

Descriptive statistics, clustering, and principal component analysis (PCA) performed. Participants were sorted by age, type of CGD, use of prophylaxis versus treatment antimicrobials, and use of immuno-modulators versus not.