

Identification of novel T cell antigens through directed delivery of the *Chlamydia trachomatis* ORFeome to antigen presentation pathways in human monocyte-derived dendritic cells

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Antibody Responses

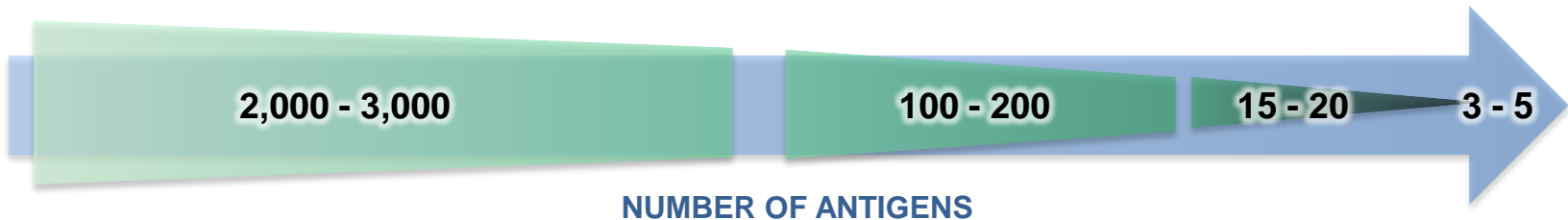
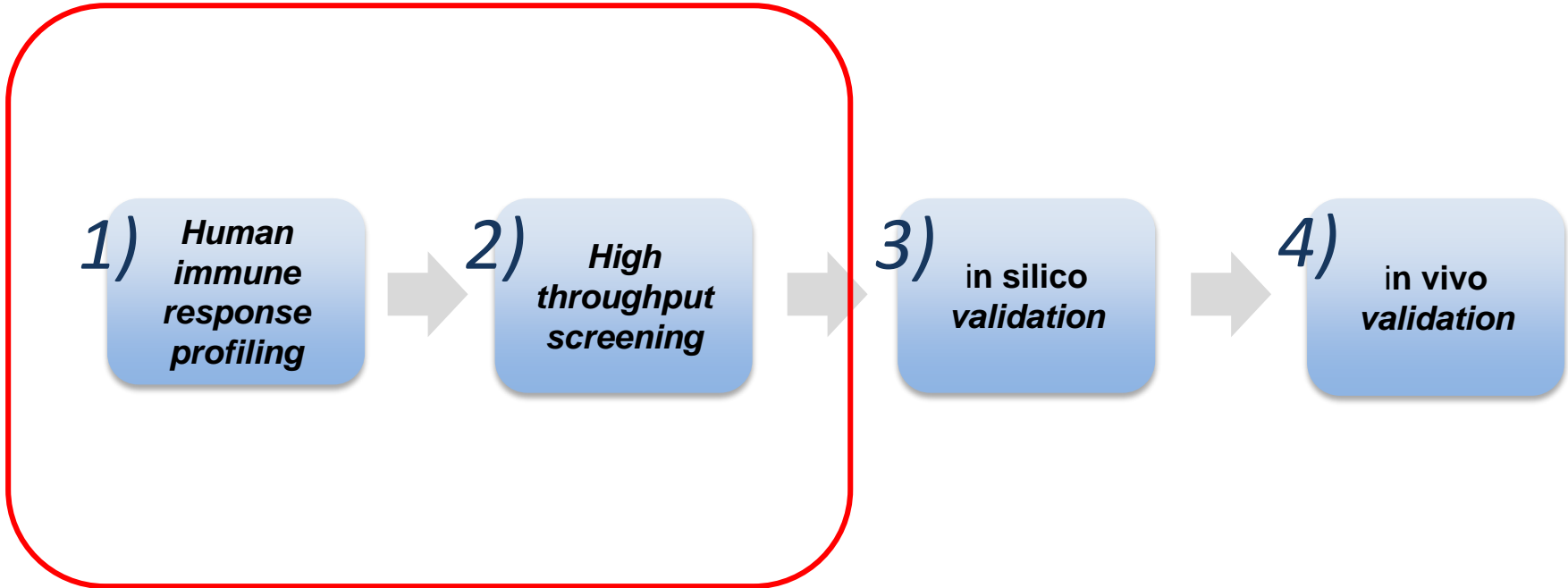
- Antibodies purified from human eye secretions can neutralize trachoma in a monkey ocular challenge model
- Inverse correlation of IgA and titer of *Chlamydia* in endocervix

T Cell Responses

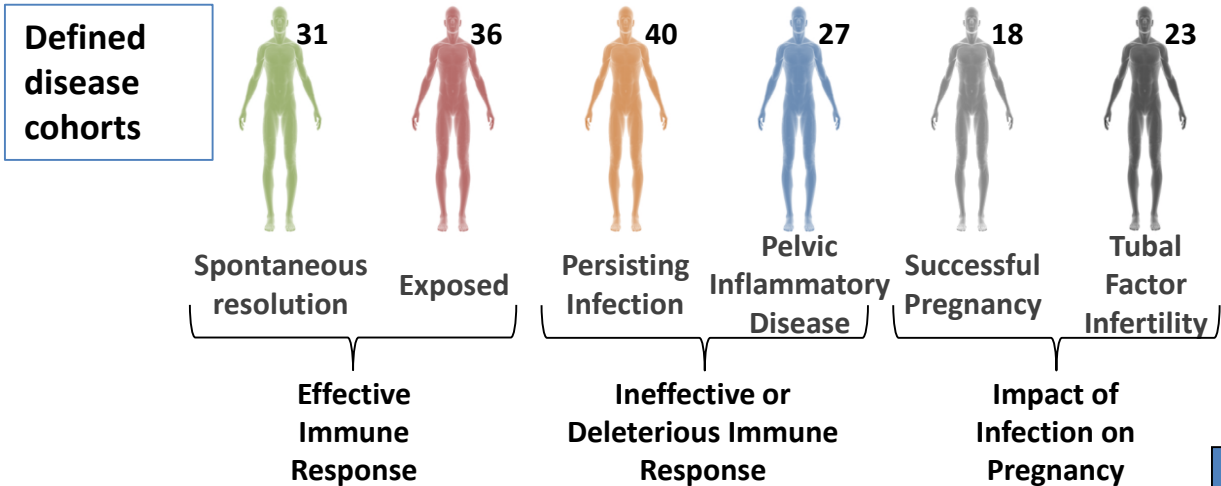
- Both CD4⁺ and CD8⁺ T cells are recruited to endocervix during infection and resolve within 3-4 weeks of clearance
- Low CD4⁺ T cell counts are correlated with highest risk of developing Chlamydia complications

T cell responses appear to be important in control of infection
How do we identify which proteins, out of the hundreds of possible candidates, are able to induce protective T cell responses in exposed humans?

Genocea Antigen Discovery Platform



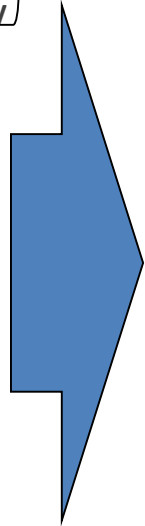
1) Human Immune Response Profiling



Collected patient blood

Diversified Human Samples

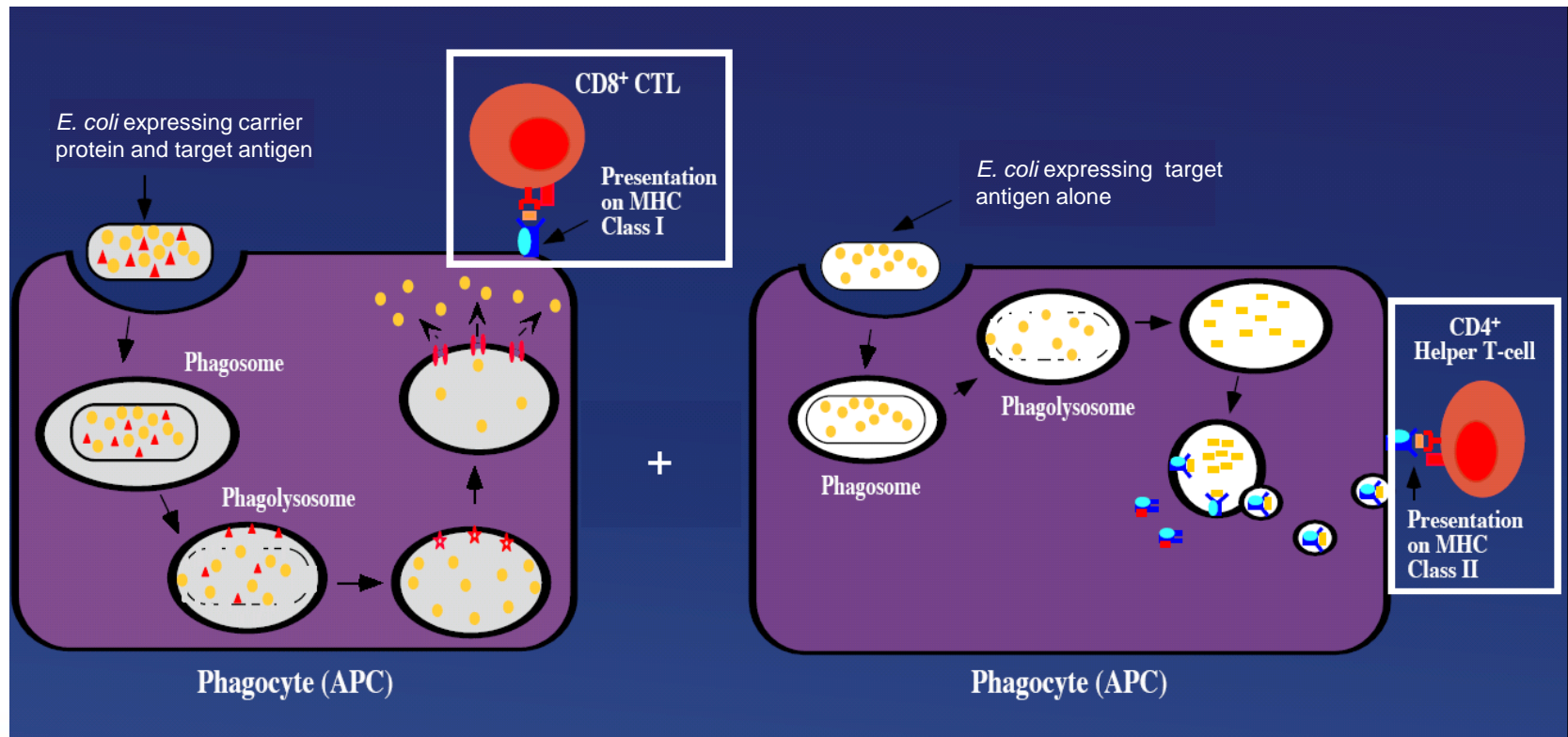
Gender	Female	164
	Male	37
Race	White	73
	African American	113
	Other	15
Age [median (range)]		26 (15-60)
Months since diagnosis [median (range)]		13 (1-332)
Prior CT # [median (range)]		1 (1-6)



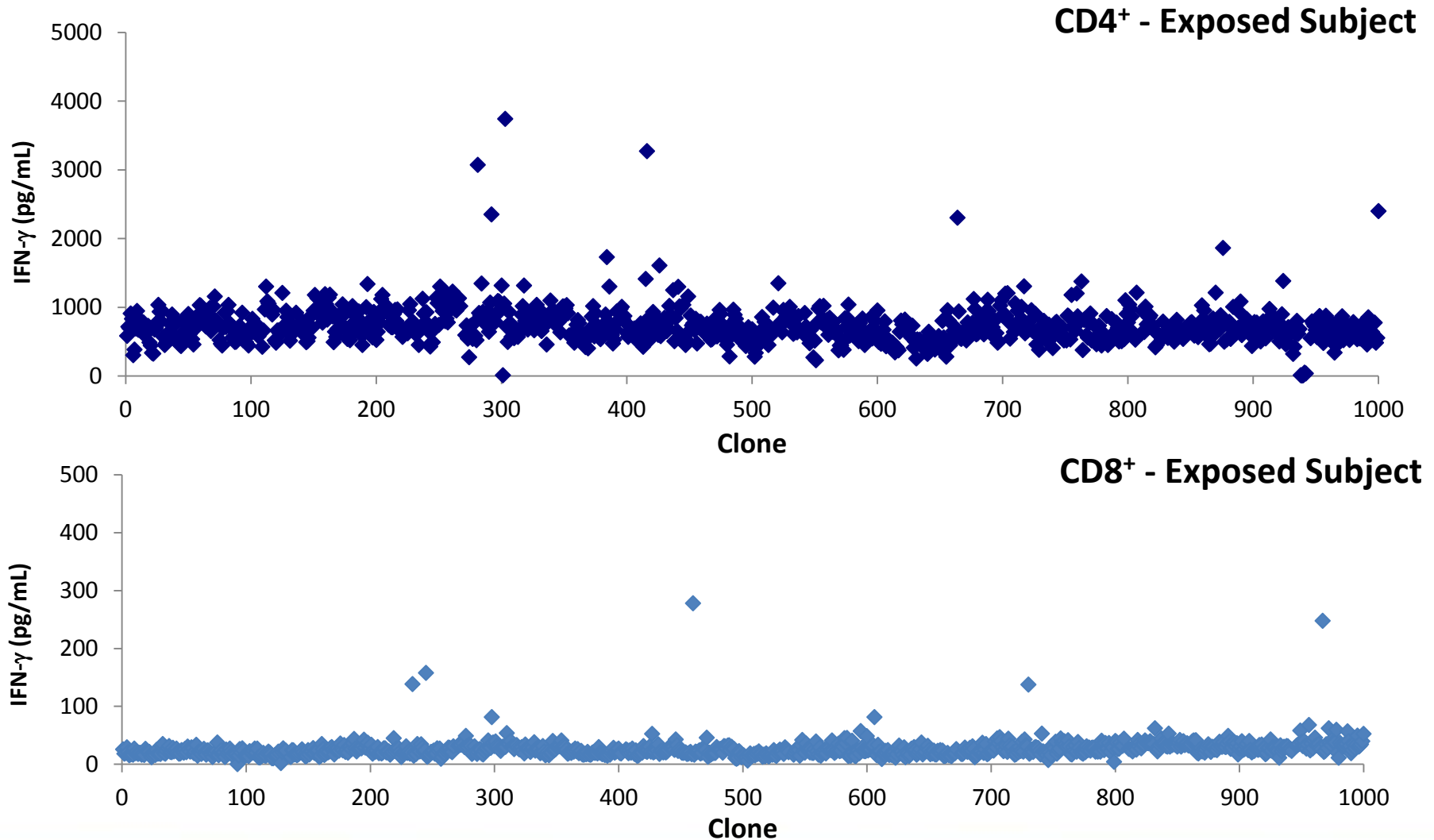
- Develop clinically meaningful basis for understanding immune response differences

2) High Throughput Screening

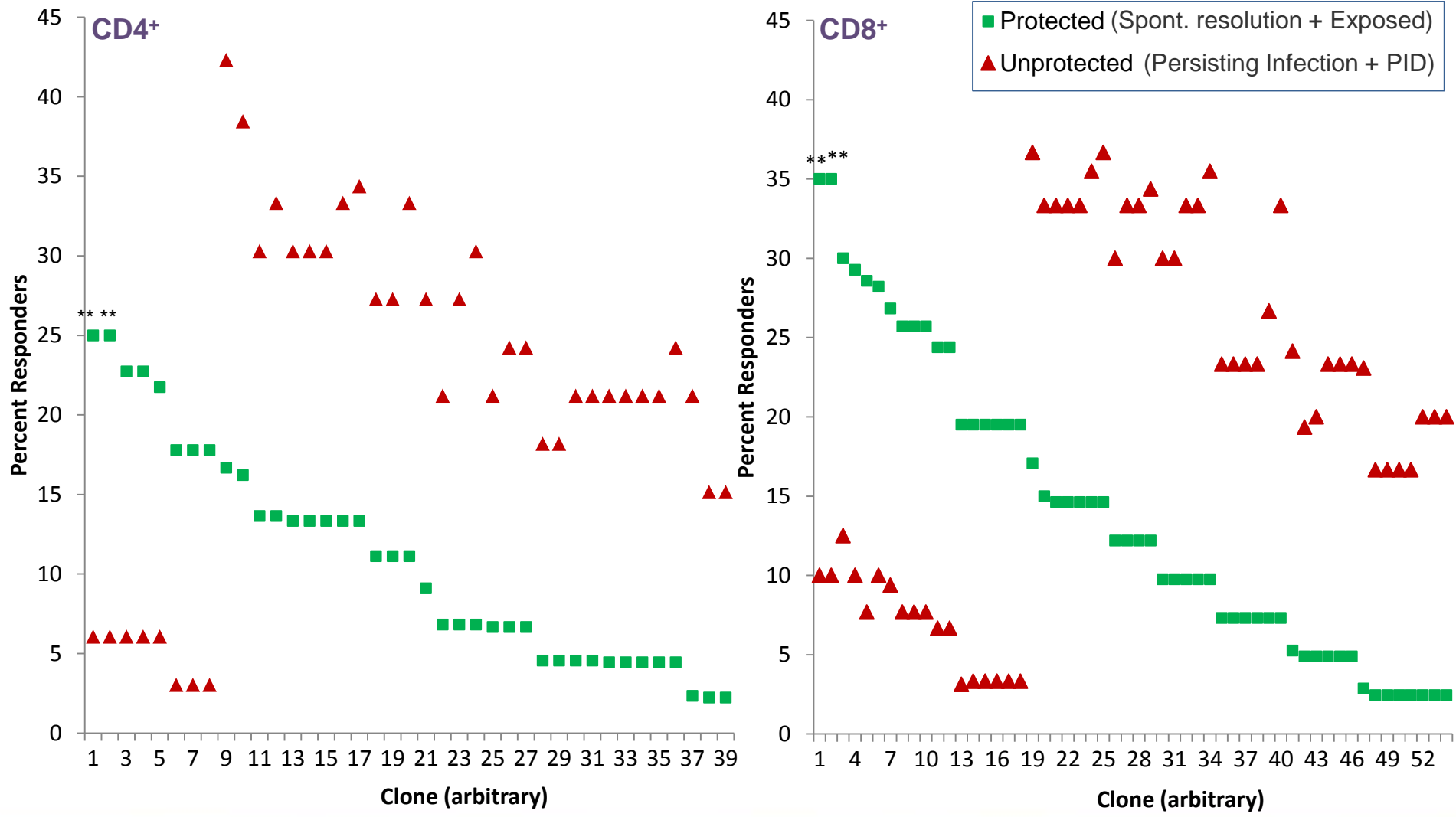
- Built full library containing 1017 clones from *C. trachomatis* serovar D
- Validated full-length protein expression through a surrogate assay
- Separately screened both CD4⁺ and CD8⁺ T cells from donors with diverse HLA types



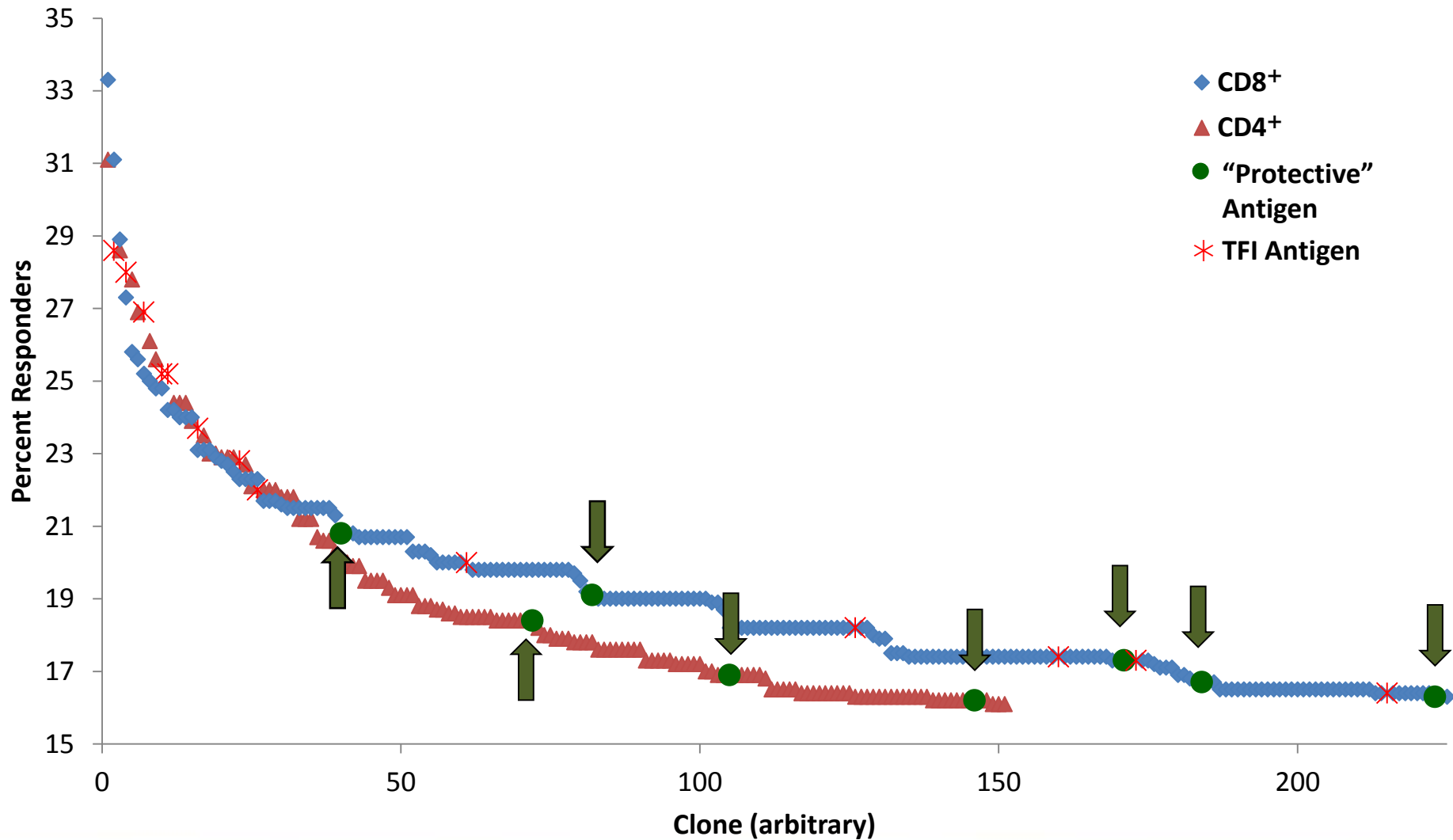
Representative Screens to Identify Chlamydia Antigens from Humans



Statistically Significant Differences Identified in Frequency of Antigens Recognized in Protected vs. Unprotected Cohorts



Most Frequently Recognized Antigens May Not Correlate to Protection



- PBMC from Chlamydia-exposed or -infected donors were screened against a full proteomic library
 - CD4⁺ and CD8⁺ T cells screened separately
 - Results were segregated by donor clinical outcome
 - Plasma saved to separately probe protein microarrays for B cell antigens
- A subset of 25 T cell antigens were more frequently recognized by T cells from donors who controlled infection compared with those who did not
 - No overlap identified in antigens between T cell subsets
 - ✓ Eighteen antigens with greater CD8⁺ T cell frequencies in “controllers”
 - ✓ Seven antigens with greater CD4⁺ T cell frequencies in “controllers”
 - Four “protective” antigens were also identified in TFI cohort
- Several of the most frequently recognized antigens were also highly represented in the TFI cohort

- Evaluate top T cell antigens as vaccine candidates in intravaginal challenge model:
 - Top antigens associated with clinical control
 - Top antigens overall
 - TFI-associated antigens
- Evaluate vaccines containing T cell antigens in combination with B cell antigens identified through screens of plasma

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