Abstract Template – BHIVA Annual Conference 2016

Title:	Gag- and Nef- specific responses are associated with increased proportions of regulatory T cells in treated chronic HIV-1 infection

- ***Please do not add the names of authors or affiliations on this form***
- *Use a concise title that indicates the nature of the study.*
- *Please capitalise the first letter of the title and use lower case for the rest of the title (with the exception of proper nouns or abbreviations).*
  e.g. **Recall of men who have sex with men diagnosed with bacterial sexually transmitted infections for retesting: a feasible and effective strategy?**
- *Please do not use a full stop at the end of the title*

Abstract:

- Your abstract **must** be pasted into the space to the right and use the Arial font in size 10.
- Your abstract must not exceed a maximum of 2,500 characters (including spaces and tables).
- Please follow the general outline ***Background, Methods, Results and Conclusion*** where applicable.
- Please ensure that your abstract is thoroughly **proof read** for grammatical inaccuracies.

Background: Interventions directly targeting the HIV-1 reservoir to achieve a cure (induction, immune recognition and clearance) are required, and CD4 T cells, mediators of HIV-1-specific response, are central to this. Functional and phenotypic immune profiles associated with slower progression rates have been demonstrated. Early and robust CD4 T-cell responses to Nef and a preserved Gag p24 proliferative response are associated with better disease prognosis. Furthermore, long-term non-progressors have less generalized CD4 T-cell immune activation compared to rapid progressors. This study aims to determine the relationship between virus-specific responses and regulatory T cell (Treg) frequency in treated chronic HIV-1 infection.

Methods: Peripheral blood mononuclear cells from ART-treated HIV-1^+ individuals were assessed in IFN-γ and IL-2 ELISpot assays, for their functional responses following stimulation with overlapping pools of Gag and Nef peptides. Subjects were characterized as being responders to Gag (n=5), Nef (n=3), both Gag and Nef (n=2), or as non-responders (n=7). Functional responses were then compared to the immunophenotypic profiles using flow cytometry and markers of Tregs (CD4, CD25, CD45RO). Analysis of seronegative donors was also undertaken (n=10). Statistical analysis was performed using the Mann-Whitney U test.

Results: All patients had CD4 T-cell counts >350 cells/μl blood and plasma HIV-1 RNA <50 copies/ml. Percentage CD4 Treg subset was significantly higher in the HIV-1^+ subjects compared to seronegative donors ($p<0.0001$). Responders tended to have higher proportions of Tregs, and non-responders lower proportions, albeit higher than observed for seronegative controls. Treg frequencies did not differ between Gag and/or Nef responder groups.

Conclusion: Functionally classified responders have increased levels of Tregs during treated infection. This may indicate dysfunction of Treg-mediated suppression. Conversely, elevated Tregs may protect from excessive activation and exhaustion. As Tregs may represent a population enriched for the HIV-1 reservoir in virally suppressed individuals, it is key that the role of Tregs is understood to allow accurate therapeutic targeting in chronically infected individuals. Further in-depth studies, focussing on functional and phenotypic complexity of Tregs during HIV-1 infection and/or therapeutic interventions, are warranted.