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Oral presentation

OA06-04. The role of early T-cell responses in subjects with acute HIV-1 infection

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Background

Previous studies have shown that T-cells play an important role in the maintenance of virus set-point in early and chronic HIV-1 infection. This study investigates the role of the first T-cell responses in selecting virus escape and controlling the early peak of viremia.

Methods

To identify the single transmitted/founder virus full-length single genome amplification (SGA) virus sequencing was performed when patients were screened before seroconversion during peak viremia. Virus evolution was monitored by further serial SGA sequencing. *Ex vivo* IFN-γ enzyme-linked immunospot assays and multi-parameter flow cytometry were used with peptides matching the founder virus sequence to comprehensively map the HIV-1 specific T cell responses in subjects at serial time points over the first 12 months post-screening.

Results

T-cell assays showed that HIV-1 specific T-cell responses selected non-synonymous sequence changes at different rates across the whole of the HIV-1 proteome. The first detectable T-cell responses induced virus escape within 18–34 days of screening. However, these T-cell responses were subsequently lost or diminished after the escape variant became fixed within the virus population. The majority of the later HIV-1 specific T-cell responses induced a slower rate of escape, whilst a minority did not select for escape variants over the study period. Selected sequence changes could also be attributable to reversion, compensatory mutations, other immune responses and linkage to other selected sites. Ongoing studies are exploring the mechanisms behind the few rapid sequence changes found where no T cell response could be identified.

Conclusion

The data shows that the first HIV-1 specific T-cell responses can induce rapid virus escape at times earlier than previously described. Appearing during the decline of viral load from peak viremia these T-cell responses provide some evidence that they contribute to this fall. The role of these first HIV-1 specific T-cell responses will have an impact on vaccine design.