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Epitope specificity appears to be an important determinant of in vivo killing ability of simian immunodeficiency virus (SIV)-specific CD8+ T Cells

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Background

CD8+ cytotoxic T lymphocytes (CTL) are a critical component of antiviral immunity and play an important role in the control of lentiviral infection.

Methods

We have developed an in vivo CTL assay to directly measure the killing capacity of MHC-restricted SIV-specific CTL in rhesus macaques (RM). In order to evaluate the in vivo efficacy of different epitope-specific CTL, we compared the in vivo killing capacity of Mamu-A*02-restricted Nef YY9 and Gag GY9 CD8+ T lymphocytes in three RM vaccinated with a recombinant HSV prime/DNA boost SIV vaccine regimen.

Results

Tetramer frequencies of Mamu-A*02-restricted Nef YY9-specific CD8+ T-cells were at least 10-fold higher than Mamu-A*02-restricted Gag GY9-specific CD8+ T-cells in individual animals both pre- and post-challenge. Prior to SIV challenge, both CTL populations showed poor and incomplete killing (22-35%) of target cells over 18 hours. Seven weeks post-challenge, there was a marked increase in the CTL killing capacity of both Nef YY9 and Gag GY9-specific CTL with 26-38% killing occurring over the first two hours and up to 100% killing over 18 hours. Surprisingly, Gag GY9-specific CTL consistently showed equivalent or greater in vivo killing when compared to Nef YY9-specific CTL even though the percentages of IFN-γ secreting and degranulating cells upon peptide stimulation were comparable.

Conclusion

These data suggest that epitope specificity rather than tetramer frequency determines the ability of SIV-specific CTL to kill infected cells. Taken together, these data may have important implications for the development of a successful HIV vaccine.

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