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Oral presentation

0A07-01. HIV-specific CD8+ T-cells of vaccinees exhibit proliferative and cytotoxic capacities comparable to those of progressors

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Background

HIV-specific CD8+ T-cells of long-term nonprogressors (LTNP) exhibit extraordinary per-cell cytotoxic capacity. To adapt cytotoxicity assays for vaccine trials, we compared HIV-specific CD8+ T-cell cytotoxic capacity with proliferation and perforin expression using cells from LTNP, viremic progressors, antiretroviral recipients with <50 HIV RNA copies/ml plasma (Rx<50) and seronegative individuals who had or had not received the Merck Ad5 trivalent vaccine.

Methods

HIV-specific CD8+ T-cell cytotoxic responses to HIV_{SF162}-infected CD4+ T-cell targets were measured at 1 hour by flow cytometric detection of granzyme (Gr) B delivery to live targets or infected CD4 elimination (ICE). Cytotoxicity, IFN-γ production, perforin expression, and proliferation of HIV-specific CD8+ T-cells were examined following a 6-day stimulation with HIV_{SF162}-infected CD4+ T-cell targets.

Results

The HIV-specific CD8+ T-cell cytotoxic responses of vaccinees (medians 16.8% GrB activity, 37.2% ICE) were clearly distinguishable from those of seronegative controls (1.7% GrB activity, $p < 0.001$; 0.3% ICE, $p < 0.001$), but were comparable to those of progressors (16.6% GrB activity, $p > 0.5$; 37.4% ICE, $p > 0.5$). Among vaccinees, those with the protective alleles HLA B*27, B*57, or B*58 tended to have higher responses. Vaccinee responses were significantly less than those of LTNP (50.7% GrB activity, $p < 0.001$; 82.5% ICE, $p < 0.001$). GrB activity and ICE were strongly correlated with HIV-specific CD8+ T-cell proliferation ($R = 0.85$, $p < 0.001$ and $R = 0.87$, $p < 0.001$, respectively) and perforin expression ($R = 0.86$, $p < 0.001$ and $R = 0.9$, $p < 0.001$, respectively). When measured on a per-cell basis, cytotoxicity of most vaccinees remained at the level of progressors, even with higher effector:target ratios.

Conclusion

GrB activity and ICE correlate strongly with CD8+ T-cell proliferation and perforin expression in expanded cells suggesting these parameters are reasonable surrogate measurements of CD8+ T-cell-mediated killing requiring fewer cells. GrB activity and ICE of vaccinees were similar to those of progressors, suggesting these low responses might contribute to suboptimal control in cases of HIV infection following vaccination.