

Title: Statistical positivity criteria and multiplicity adjustment methods for the analysis of gated ICS assay data

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Abstract:

To maximize the multi-parameter capability of ICS assays in HIV-1 vaccine development and evaluation, it is generally not sufficient to claim an overall difference in the percentage of positive staining cells between antigen stimulated and negative control wells. We therefore model gated ICS assay data as multivariate binomial distributed, and conduct separate Fisher's exact tests to determine the positivity of each cytokine subset response. In this way, we are able to isolate specific significances and to take into account the sparseness of such data.

In addition, since the number of tests increases linearly with the number of antigens and exponentially with the number of cytokines of interest, we adopt resampling-based multiplicity adjustment methods for multivariate binary data developed by Westfall and Young to control the family wise error rate of these tests. We confirmed in our simulation studies that the power of the tests can be greatly improved using such methods that properly incorporate the discreteness and the dependence structure of the distributions. Results from recent ICS assay validation studies will also be presented.