Abstract
Syndromic and local (oral mucosal) immune responses in acutely infected HIV+ subjects before the initiation of HAART have not been well characterized. Protein microarrays were used to analyze saliva and plasma from HIV-infected and uninfected subjects to identify new biomarkers for HIV disease progression and pathogenesis.

Methods
A 507 protein microarray was employed to provide a broad view of cytokines and chemokines in saliva and plasma of acutely infected HIV subjects as compared to uninfected subjects. A custom array derived from the initial results was utilized to further define the potential for biological impact.

Results
Microarray data indicated that the cytokines MIG and RANTES induced by HIV (pp65-1L-2) were increased in saliva and plasma of HIV-infected subjects relative to uninfected controls. Microarray data for four cytokines (angiotensin, MIG, MIP-1α, and RANTES) were confirmed by ELISA or chemiluminescent assay.

Background
In vitro studies have provided valuable information on potential HIV suppressive properties of several cytokines, in particular the ß-chemokines (1-2). Cocci et al (1) showed that several factors, including SDF-1α and CCL3, are expressed in saliva of long term HIV-infected individuals. This study provides a solid understanding of the role of these factors in the oral cavity of HIV infected and uninfected individuals.

To analyze saliva and plasma from HIV infected and HIV uninfected controls to identify host immune proteins that were altered during HIV infection. In vivo studies have provided valuable information on potential HIV suppressive properties of several cytokines, in particular the ß-chemokines (1-2). Cocci et al (1) showed that several factors, including SDF-1α and CCL3, are expressed in saliva of long term HIV-infected individuals. This study provides a solid understanding of the role of these factors in the oral cavity of HIV infected and uninfected individuals.

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Figure 1. A 507 protein microarray was employed to provide a broad view of cytokines and chemokines in saliva and plasma of acutely infected HIV subjects as compared to uninfected subjects. A custom array derived from the initial results was utilized to further define the potential for biological impact.

Figure 2. A 507 protein microarray was employed to provide a broad view of cytokines and chemokines in saliva and plasma of acutely infected HIV subjects as compared to uninfected subjects. A custom array derived from the initial results was utilized to further define the potential for biological impact.

Figure 3. Horizontal full changes observed with the 40 protein cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects. The x-axis represents the fold change of the cytokine in the saliva or plasma of HIV-infected and HIV-uninfected subjects.

Figure 4. HIV+ and HIV- comparison in saliva and plasma of 15 acutely infected subjects, pattern of cytokine expression (Cytokine Array Assay) and correlation of cytokine expression compared to a control subjects. Median fold changes observed with cytokine expression.

Figure 5. A representative image of a cytokine microarray showing the probe intensity (fold change) of each cytokine in saliva and plasma. The x-axis represents the fold change of the cytokine in the saliva or plasma of HIV-infected and HIV-uninfected subjects.

Figure 6. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 7. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 8. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 9. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 10. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 11. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 12. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 13. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 14. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 15. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 16. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 17. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 18. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 19. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 20. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

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Figure 24. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 25. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 26. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 27. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 28. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

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Figure 31. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

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Figure 45. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 46. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 47. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 48. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 49. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.

Figure 50. Median fold changes observed with the Custom 40 cytokine array in saliva and plasma. Fold changes in cytokine expression in saliva and plasma of HIV-infected and HIV-uninfected subjects.