

Functional HIV-1 specific IgA antibodies in HIV-1 exposed, persistently IgG seronegative female sex workers

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Abstract:

Although HIV-specific cellular immune responses are found in a number of HIV highly-exposed, persistently seronegative (HEPS) cohorts, late seroconversion can occur despite pre-existing cytotoxic T lymphocytes (CTL), suggesting that a protective HIV vaccine may need to induce a broader range of HIV-specific immune responses. Low levels of HIV-specific IgA have been found in the genital tract and plasma of the majority of Nairobi HEPS sex workers and appeared to be independent of HIV-specific cellular responses. IgA purified from genital tract, saliva and plasma of most HEPS sex workers were able to neutralize infection of PBMC by a primary (NSI) clade B HIV isolate, as well as viral isolates from clades A and D, which predominate in Kenya. In addition, these IgA were able to inhibit transcytosis of infective HIV virions across a transwell model of the human mucosal epithelium in an HIV-specific manner. Preliminary work in other HEPS cohorts has suggested the recognition of different gp41 epitopes in HEPS and HIV-infected subjects. Although present at low levels, these IgA demonstrated cross-clade neutralizing activity and were able to inhibit HIV mucosal transcytosis, suggesting an important functional role in protection against HIV infection.