



Nanoparticle Based Biobarcode Amplification Assay (BCA) for Sensitive and Early Detection of Human Immunodeficiency Type 1 (HIV-1) Capsid (p24) Antigen

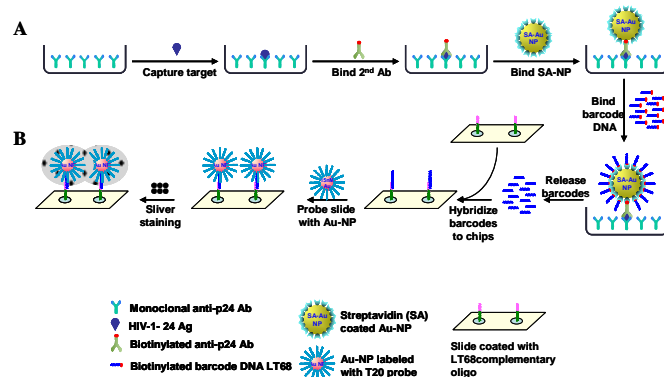
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Introduction

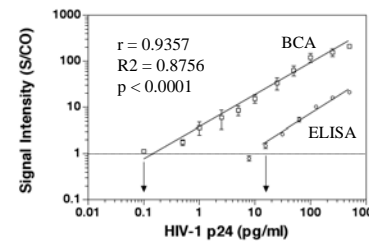
A possible alternative to testing for HIV-1 RNA is HIV-1 p24 antigen which is usually detected by enzyme-linked immunosorbent assay (ELISA). It has been found that HIV-1 p24 may be a useful marker for predicting CD4⁺ T cell decline and disease progression. They may also be useful for early detection of HIV-1 infection resulting in early diagnosis and improved patient management. Other potential applications are in testing the blood supply in regions of the world where HIV-1 RNA testing is not available or practical provided the further improvement of the test sensitivity. Over the past decade, certain nanotechnology-based techniques have been widely evaluated in medical testing and could provide new tools for clinical diagnosis due to their potential for high degrees of sensitivity, high specificity, multiplexing capabilities and ability to operate without enzymes. In particular, an ultra sensitive nanoparticle (NP)-based assay, called the biobarcode amplification (BCA) assay, uses oligonucleotides (the biobarcode) as surrogates for the indirect amplification of the disease markers, and a microarray-based chip detection method, which utilizes NP probes and a silver amplification process for signal enhancement and optical readout. The assay, in certain settings, allows one to detect proteins such as prostate specific antigen (PSA) with an LOD of 30 aM or nucleic acid targets at the level of 500 zM. In principle, this ultra sensitive NP-based testing system, when applied to HIV-1 p24, could provide more sensitive alternative to the ELISA based systems, provided it performs well in the relevant sample types. Herein we report a BCA assay for sensitive and early detection of HIV-1 p24 antigen.

Methods

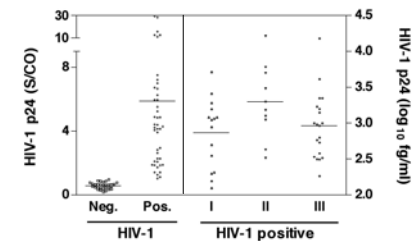


Results

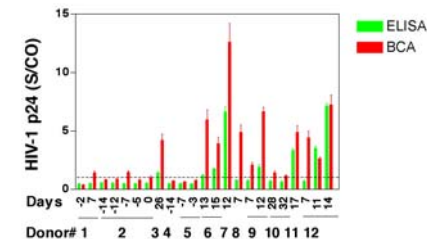
1. BCA is more sensitive than ELISA



2. BCA showed high sensitivity and specificity



3. BCA can detect HIV-1 p24 3 days earlier than ELISA



Conclusion

- ♦ For detection of HIV-1 p24, BCA assay could detect 0.1 pg/ml of HIV-1 p24 antigen compared with 15 pg/ml by conventional p24 antigen capture assays (ELISA), indicating that the current first generation BCA assay may be 150-fold more sensitive than the conventional ELISA. There is a linear relationship between the concentration of p24 antigen and the signal intensities at the range of 0.1 ~ 500 pg / ml.
- ♦ No false positive results were seen with 30 HIV-1 negative samples while all 45 HIV-1 positive samples were HIV-1 p24 positive by BCA assay.
- ♦ BCA assay can detect HIV-1 p24 at least 3 days earlier than conventional ELISA.

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