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The immune response of human immunodeficiency virus (HIV)-exposed seronegative (ESN) women may be qualitatively different from that in those infected with HIV (HIV(+)). In a cohort of female commercial sex workers in Nairobi, Kenya, we found significantly lower ($P < \text{or} = .01$) levels of CD4(+)-specific immune activation and apoptosis in the ESN women compared with those in the HIV(+) women. Compared with the HIV(+) women, a lower proportion of the ESN women showed p24 peptide pool responses by the short-term, CD4(+)-specific, interferon (IFN)-gamma intracellular cytokine staining assay, whereas the proportion showing responses by the long-term, CD8(+)-depleted T cell proliferation assay was similar. Interestingly, the ESN responders had a 4.5-fold stronger proliferation response ($P = .002$) than the HIV(+) group. These data suggest that, compared with those in HIV(+) women, CD4(+) T cells in ESN women have a much greater ability to proliferate in response to p24 peptides.