KIR2DS4 promotes HIV-1 pathogenesis: new evidence from analyses of immunogenetic data and natural killer cell function.

BACKGROUND: KIR2DS4 gene variants encode full-length and truncated protein products, with only the former serving as membrane-bound receptors to activate natural killer (NK) cells. We have previously shown that full-length KIR2DS4 was associated with relatively high viral load and accelerated heterosexual HIV-1 transmission. Our objective here was to provide confirmatory data and to offer new insights about the potential mechanisms.

METHODOLOGY/PRINCIPAL FINDINGS: Mixed models for repeated (longitudinal) outcome measurements on 207 HIV-1 seropositive American youth revealed an association of full-length KIR2DS4 with relatively high viral load and low CD4+ T-cell count (p<0.01 for both). Depending on KIR2DS4 expression (presence or absence) on cell surface, NK cells from 43 individuals with untreated, chronic HIV-1 infection often differed in functional properties, including degranulation and secretion of IFN-γ and MIP-1β. In particular, polyfunctional NK cells were enriched in the KIR2DS4-positive subset.

CONCLUSIONS/SIGNIFICANCE: Full-length KIR2DS4 promotes HIV-1 pathogenesis during chronic infection, probably through the maintenance of an excessively pro-inflammatory state.

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