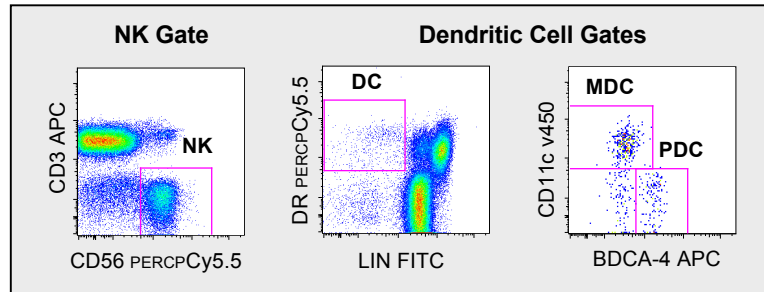
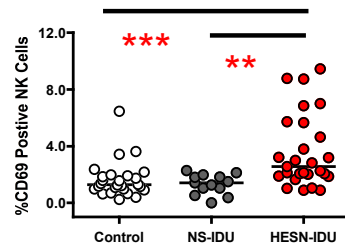
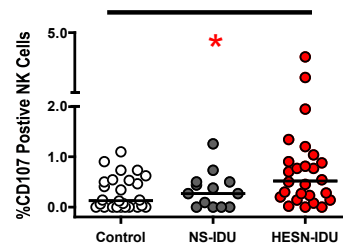
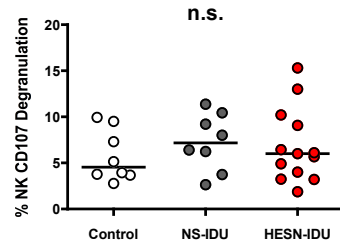
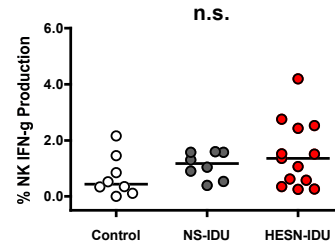
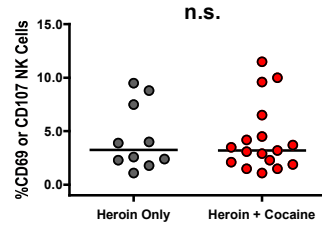


**Supplementary Figure 1.** NK and MDC activation is increased in HESN-IDU subjects and associated with high-risk needle-sharing activity. **(A)** The gating strategy for CD56<sup>+</sup>/CD3<sup>-</sup> NK cells and LIN<sup>-</sup>/HLA-DR<sup>+</sup>/CD11c<sup>+</sup>/BDCA-4<sup>-</sup> MDC cells or LIN<sup>-</sup>/HLA-DR<sup>+</sup>/CD11c<sup>-</sup>/BDCA-4<sup>+</sup> PDC cells is shown from the PBMC of a representative high-risk needle-sharing HESN-IDU subject. **(B-C)** Composite graph of the constitutive CD69 activation **(B)** or CD107a degranulation **(C)** shown independently on CD56<sup>+</sup>/CD3<sup>-</sup> gated NK cells from no-risk control, low-risk NS-IDU and high-risk HESN-IDU subjects **(D-E)** Composite graph of the frequency of K562 target cell-induced CD107a degranulation **(D)** or IFN-gamma production **(E)** shown independently on CD56<sup>+</sup>/CD3<sup>-</sup> gated lymphocytes with quadrant gates set based upon “no target” control cells incubated in the absence of target cells. **(F-G)** Composite graph of the constitutive CD69 activation or CD107a degranulation on CD56<sup>+</sup>/CD3<sup>-</sup> gated NK cells from high-risk HESN-IDU subjects stratified for **(F)** drug use patterns (heroin only or heroin plus cocaine products) and **(G)** high-risk unprotected sexual activity.

**A****B****C****D****E****F****G**