Influence of HLA-C environment on the spontaneous clearance of hepatitis C in European HIV-HCV co-infected individuals

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Abstract

Natural Killer (NK) cell functions are regulated by diverse inhibitory and activating receptors including Killer cell Immunoglobulin-like receptors (KIR) which interact with HLA class I molecules. Some KIR/HLA genetic combinations were reported associated with spontaneous clearance (SC) of hepatitis C virus (HCV) but with discordant results, possibly reflecting KIR and/or HLA gene polymorphism according to populations. KIR/HLA genetic combinations associated with both an exhaustive NK and T cell repertoire were investigated in a cohort of HIV-HCV co-infected individuals with either SC (n=68) or chronic infection (CI, n=163) compared to uninfected blood donors (Ctrl, n=100). Multivariate analysis showed that the HLA C2C2 environment was associated with SC only in European HIV-HCV co-infected individuals (OR=4.30[1.57-12.25], p=0.005). KIR2D+ NK cell repertoire and potential of degranulation of KIR2DL1/S1+ NK cells were similar in SC European cohort compared to uninfected individuals. In contrast, decreased frequencies of KIR2DS1+ and KIR2DL2+ NK cells were detected in CI group of Europeans compared to SC and a decreased frequency of KIR2DL1/S1+ NK cells compared to controls. On the T cell side, higher frequencies of DNAM-1+ and CD57+ T cells were observed in SC in comparison to controls. Interestingly, SC subjects emphasized increased frequencies of KIR2DL2/L3/S2+ T cells compared to CI subjects. Our study underlines that the C2 environment may activate efficient KIR2DL1+ NK cells in viral context and maintain KIR2DL2/L3/S2+ mature T cell response in the absence of KIR2DL2 engagement with its cognate ligands in SC group of HCV-HIV co-infected European patients.

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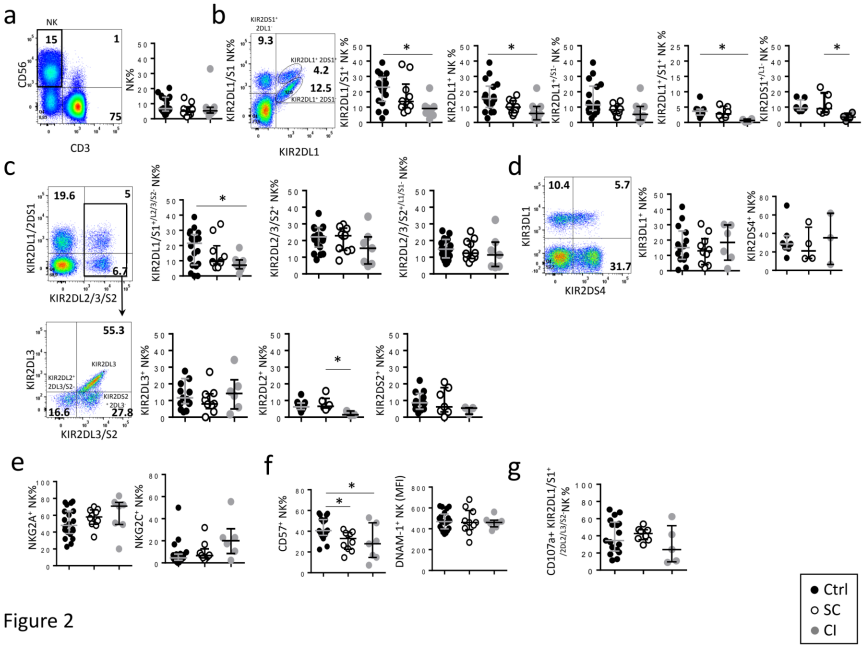

Figure 2

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