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Titel des Beitrags: Coordinated acquisition of inhibitory and activating receptors and functional properties by developing human natural killer cells.

Abstract: The stages of human natural killer (NK) cell differentiation are not well established. Culturing CD34(+) progenitors with interleukin 7 (IL-7), IL-15, stem cell factor (SCF), FLT-3L, and murine fetal liver cell line (EL08.1D2), we identified 2 nonoverlapping subsets of differentiating CD56(+) cells based on CD117 and CD94 (CD117(high)CD94(-) and CD117(low/-)CD94(+) cells). Both populations expressed CD161 and NKp44, but differed with respect to NKp30, NKp46, NKG2A, NKG2C, NKG2D, CD8, CD16, and KIR. Only the CD117(low/-) CD94(+) population displayed cytotoxicity and interferon-gamma production. Both populations arose from a single CD34(+)CD38(-) Lin(-) cell and their percentages changed over time in a reciprocal fashion, with CD117(high)CD94(-) cells predominating early and decreasing due to an increase of the CD117(low/-)CD94(+) population. These 2 subsets represent distinct stages of NK cell differentiation, since purified CD117(high) CD94(-) cells give rise to CD117(low/-)CD94(+) cells. The stromal cell line (EL08.1D2) facilitated the transition from CD117(high)CD94(-) to CD117(low/-)CD94(+) via an intermediate phenotype (CD117(low)CD94(low/-)). EL08.1D2 also maintained the mature phenotype, preventing the reversion of...
CD117(low/-)CD94(+) cells to the intermediate (CD117(low)CD94(low/-)) phenotype. An analogous population of CD56(+)CD117(high)CD94(-) cells was found in cord blood. The identified stages of NK-cell differentiation provide evidence for coordinated acquisition of HLA-specific inhibitory receptors (ie, CD94/NKG2A) and function in developing human NK cells.