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The distinct pattern of antigen expression during in vitro development of CD56bright and CD56dim NK cell subsets suggests their different origin

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$CD56^{bright}$ and $CD56^{dim}$ NK cell subsets have been proposed to represent either phenotypically and functionally distinct NK cell subsets or, respectively, immature and mature stages of the NK cell lineage. To this regard, using FLT3 ligand, IL-15 and IL-21 cytokine combination, we have recently described the in vitro generation of $CD56^{dim}/CD117^{neg}$ NK cells from $CD34^{+}$ hematopoietic progenitors, but not from immature $CD56^{bright}$ NK cells (Zamai et al. Cytometry A 2012;81:294-302), suggesting that they represent phenotypically and functionally distinct NK subsets. Based on these observations we have analyzed the NK cells developed in vitro from CD34+ progenitors cultured with FLT3-L plus IL-15 and IL-21, trying to distinguish between the two NK cell subsets. $CD56^{bright}$ $/CD117^{+}$ NK cells generated after 15 days of culture, early expressed natural cytotoxicity receptors (NCRs), NKG2D, CD161 and CD244, while only a subset expressed granzyme-B, perforin, LFA-1, and CD94-CD159a heterodimer. Differently, virtually all $CD56^{dim}/CD117^{neg}$ NK cells expressed perforin, granzyme B, CD94 and LFA-1, and only a subset of them expressed NCR and CD16 antigens. After 25 days of culture, we observed a significative expansion of the $CD56^{bright}/CD117^{+}$ compartment, while the "$CD56^{dim}$ NK cell lineage" showed the increase of CD56, CD16 and NCR antigen density, indicating their further maturation and activation. Altogether the data suggest that the two NK subsets originate from two distinct progenitors which, along with their differentiation and activation, generate cells with convergent phenotypes and functions.

Keywords
Human Natural Killer Cell phenotype, NK Cell Differentiation.