

NK cells: receptors and functions

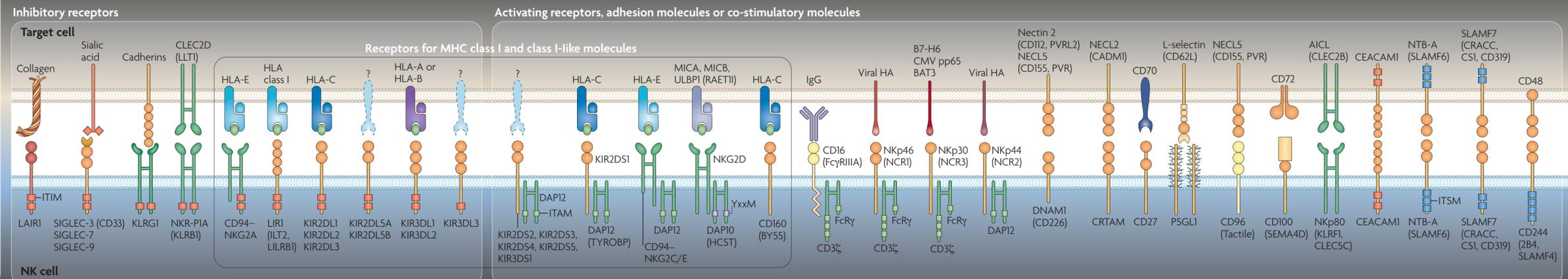
Eric Vivier and Sophie Ugolini

Natural killer (NK) cells were identified in 1975 as lymphocytes of the innate immune system that can kill tumour cells. Since then, NK cells have been shown to kill an array of 'stressed' cells and secrete cytokines that participate in shaping adaptive immune responses. A key feature of NK cells resides in their capacity to distinguish stressed cells (such as tumour cells, infected cells and damaged cells) from normal cells. Although NK cells are generally considered to be components of early innate immune defence,

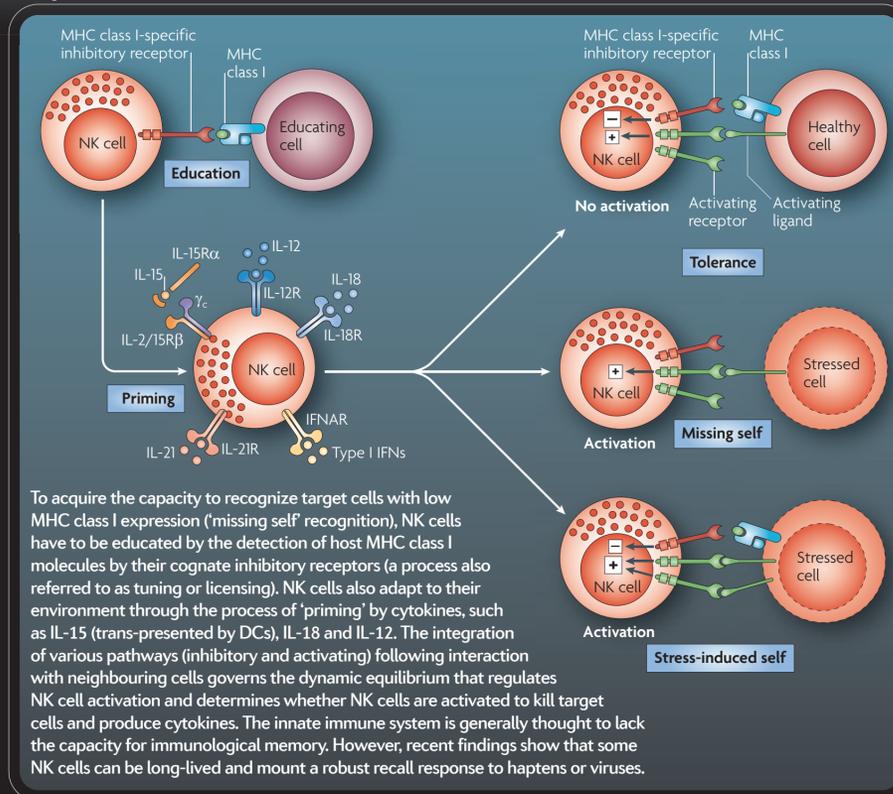
many processes that were originally restricted to adaptive immunity, such as priming, education and memory, are now known to occur in NK cells. Indeed, NK cells undergo sophisticated processes of adaptation that allow them to be tuned to their environment. There is also a growing interest in manipulating NK cells in innovative therapeutic settings. For example, the understanding of NK cell inhibition by MHC class I-specific receptors has prompted the design of innovative anticancer therapies.

The NK cell detection system includes numerous receptors, the engagement of which dictates the quality and intensity of the NK cell response. NK cells use inhibitory receptors to gauge the absence of constitutively expressed self molecules on susceptible target cells. As a consequence, NK cells can recognize 'missing self' on haematopoietic cells. By interacting with MHC class I molecules that are constitutively expressed by most healthy cells under steady-state conditions but that may be lost under conditions of stress, MHC class I-specific inhibitory receptors provide a way for NK cells to remain tolerant to healthy self cells while being toxic towards stressed cells. By contrast, NK cell activating receptors detect self molecules that are expressed under conditions of cell stress. Only human NK cell receptors are shown and the list is not exhaustive. There are several differences in NK cell receptors between mice and humans. In mice, inhibitory MHC class I-specific receptors are lectin-like dimers of the Ly49 family. Although several activating NK cell receptors are present in humans and mice (such as CD16, NKp46, DNAM1 and NKG2D), commonly used mouse strains lack orthologues of NKp30 and NKp44.

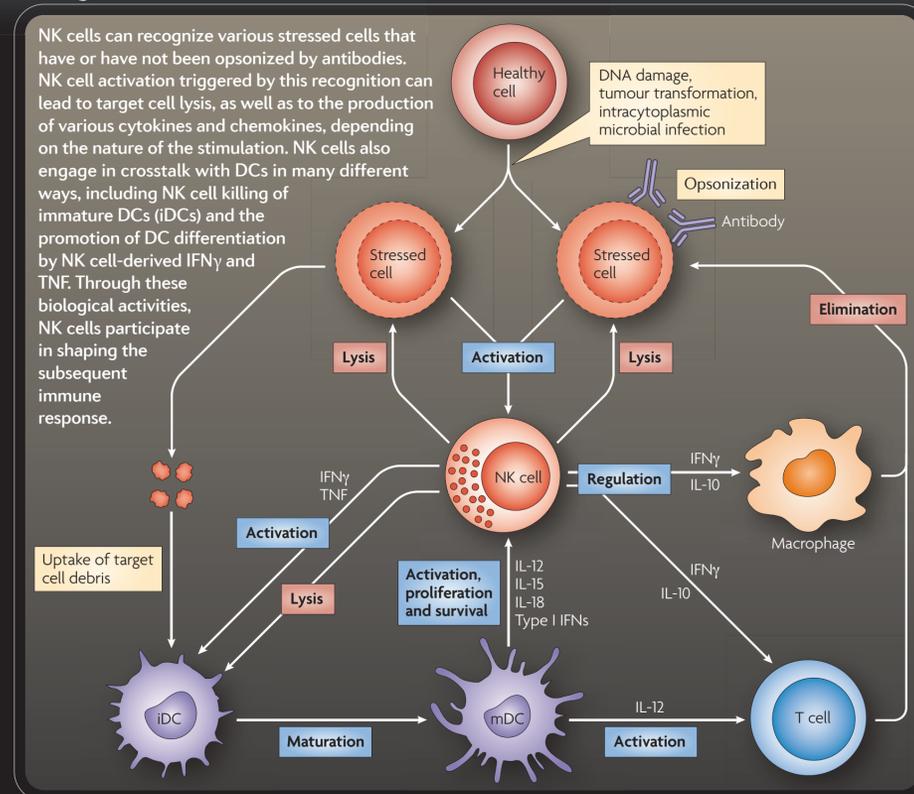
Key receptors on human NK cells



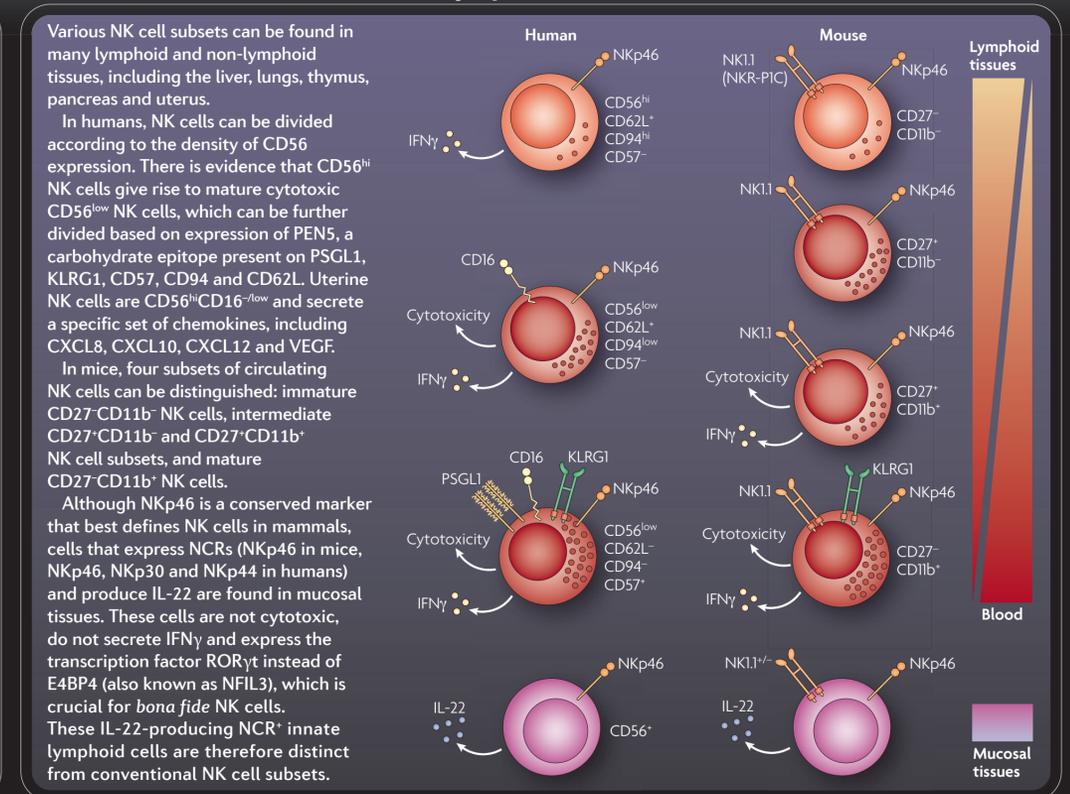
Acquisition of NK cell function



Biological function of NK cells and cellular crosstalk



NK cell subsets and NK-like innate lymphoid cells



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Species	Selection	Starting Sample	Product	Catalog #
Human	Negative	PBMC	EasySep™ Human NK Cell Isolation Kit	17955
		Whole Blood	EasySep™ Direct Human NK Cell Isolation Kit	19665
			RosetteSep™ Human NK Cell Enrichment Cocktail	15025
	Positive	PBMC	EasySep™ Release Human CD56 Positive Selection Kit	17755
			EasySep™ Human CD56 Positive Selection Kit II	17855
		Buffy Coat	EasySep™ Human Buffy Coat CD56 Positive Selection Kit	18085
Mouse	Negative	Spleen or other tissues	EasySep™ Mouse NK Cell Isolation Kit	19855
	Positive		EasySep™ Mouse CD49b Positive Selection Kit	18755

Abbreviations

γ_c, common cytokine receptor γ-chain; AICL, activation-induced C-type lectin; BAT3, HLA-B associated transcript 3; CADM1, cell adhesion molecule 1; CD62L, CD62 ligand; CEACAM1, carcinoembryonic antigen-related cell adhesion molecule 1; CLEC, C-type lectin domain family; CMV, cytomegalovirus; CRACC, CD2-like-receptor activating cytotoxic cells; CRTAM, class I MHC-restricted T cell-associated molecule; CSI, CD2 subset 1; CXCL, CXC-chemokine ligand; DC, dendritic cell; DNAM1, DNAX accessory molecule 1; E4BP4, E4 promoter binding-protein 4; FcR, Fc receptor; HA, haemagglutinin; HCST, haematopoietic cell signal transducer; IFN, interferon; IL, interleukin; ILT, immunoglobulin-like transcript; ITAM, immunoreceptor tyrosine-based activation motif; ITIM, immunoreceptor tyrosine-based inhibitory motif; ITSM, immunoreceptor tyrosine-based switch motif;

KIR, killer cell immunoglobulin-like receptor; KLRG, killer cell lectin-like receptor subfamily G; LAIR1, leukocyte-associated immunoglobulin-like receptor 1; LIR1, leukocyte immunoglobulin-like receptor 1; LLT1, lectin-like transcript 1; mDC, mature DC; MIC, MHC class I polypeptide-related sequence; NCR, natural cytotoxicity receptor; NECL, nectin-like; NFIL3, nuclear factor IL-3-regulated protein; NKG2, NK group 2; NKR-P1A, NK cell receptor protein 1A; NTB-A, natural killer, T and B cell antigen; PSGL1, P-selectin glycoprotein ligand 1; PVR, poliovirus receptor; R, receptor; RAET1L, retinoic acid early transcript 1; RORγt, retinoic acid receptor-related orphan receptor-γ; SEMA4D, semaphorin 4D; SIGLEC, sialic acid-binding immunoglobulin-like lectin; SLAM, signalling lymphocyte activation molecule family; TNF, tumour necrosis factor; TYROBP, TYRO protein tyrosine kinase-binding protein; ULBP1, UL16-binding protein 1; VEGF, vascular endothelial growth factor.

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The authors declare competing financial interests: see Web version for details.

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