MICA alleles and MICA-NKG2D interactions: an example of IMGT standardization

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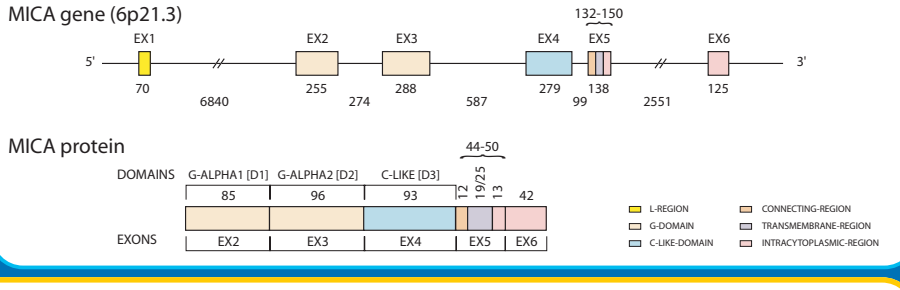
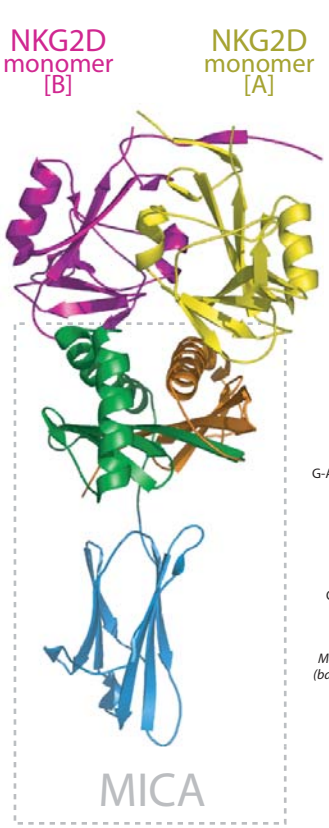
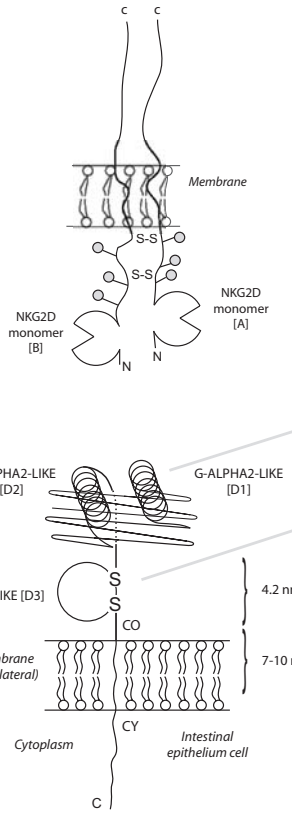
IMGT standardization

IMGT®, the international ImMunoGeneTics information system® http://imgt.cines.fr, is a high-quality integrated knowledge resource specialized in the immunoglobulins (IG), T cell receptors (TR), major histocompatibility complex (MHC), immunoglobulin superfamily (IgSF), major histocompatibility complex superfamily (MhcSF) and related proteins of the immune system (RPI) of human and other vertebrate species, created in 1989 by Marie-Paule Lefranc, at Montpellier (France).

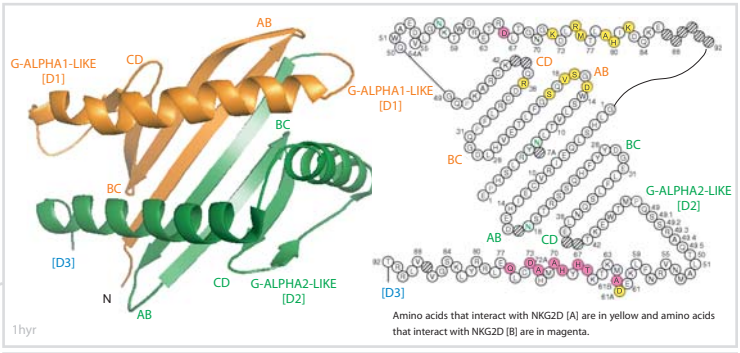




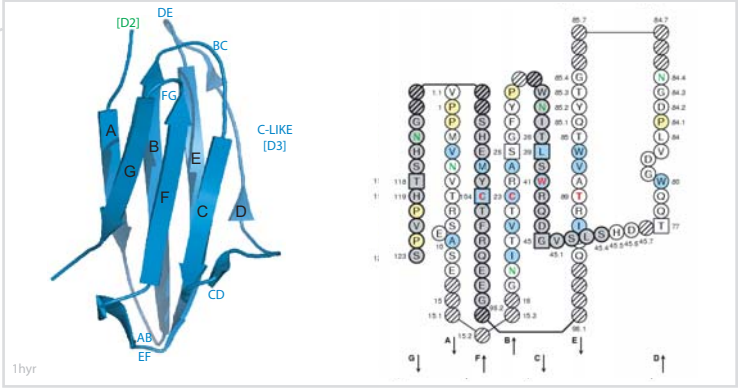


MICA belongs to the:

- MHC superfamily (MhcSF) by its G-LIKE (G-ALPHA1-LIKE [D1] and G-ALPHA2-LIKE [D2]) domains
- immunoglobulin superfamily (IgSF) by its C-LIKE [D3] domain.



Amino acids that interact with NKG2D [A] are in yellow and amino acids that interact with NKG2D [B] are in magenta.



The IMGT Scientific chart is based on IMGT-ONTOLOGY concepts and allows standardization of genomics, genetics and structural IgSF and MhcSF protein data.
Graphical representations or IMGT Colliers de Perles, based on the IMGT unique numbering, enable sequence-structure relations and ligand-receptor interactions approach.
We show how IMGT allows a standardized description:
- of MICA alleles (sequences and microsatellites)
- of G-LIKE and C-LIKE domains (IMGT Collier de Perles)
- of MICA ligand and its NKG2D receptor contacts.
We also standardized MICA literature data in relation with diseases [1].

[1] Frigoul A. and Lefranc M.-P.
Recent Res. Devel. Human Genet. 3: 95-145 (2005)
pdf available on the IMGT® site http://imgt.cines.fr

Examples of MICA allele description

Two kinds of MICA alleles were identified and correlated:
- sequence alleles (MICA*01 to MICA*73)
- EX5 microsatellite alleles (A4 to A10).

IMGT MICA allele names	Other alleles names[a,b] (a)	(b)	Gene functionality[c]	IMGT reference sequences Exons	Accession numbers	Molecule type	EX 5 microsatellite alleles[d]
MICA*01	*001	*001	F	EX 1-6	L14848	cDNA	A4
MICA*02	*00201	*002	F	EX 2-5, EX6	AF336063, AF336064 (AH010545)	gDNA	A9
MICA*03[e]		*003	F	EX 2-4	U56942	gDNA	
MICA*04	*004	*004	F	EX 1-6	X92841	gDNA	A6
MICA*05	*005	*005	F	EX 2-4	U56944	gDNA	

a (a) http://www.ebi.ac.uk/imgt/hla/index.html
b (b) http://mhc-x.u-strasbg.fr/human.htm
c F: FUNCTIONAL. Functionality according to IMGT Scientific chart rules.
d EX5 microsatellite alleles correspond to a repeated sequence (STR) of 4 (A4) to 10 (A10) gct (alanine) codons.

Examples of contacts between MICA and NKG2D

Contacts between MICA amino acids (ligand) and NKG2D homodimer (receptor) are described according to IMGT standardization (IMGT/3Dstructure-DB code 1hyr).

MICA (ligand) DOMAIN	IMGT labels	Amino acid IMGT unique numbering	Name	NKG2D (receptor) Amino acid Name	Position	Monomers	Contact types between MICA and NKG2D amino acids
G-ALPHA1-LIKE [D1]	AB-TURN	15	ASP D	LYS K	186	[A]	H bond
		17	SER S	LYS K			
	B-STRAND	18	VAL V	MET M	184		H bond
							Hydrophobic
				GLN Q	185		H bond
		20	SER S	THR T	205		H bond
	C-STRAND	38	ARG R	ASN N	207		

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