

# MICA AND MICB TYPES OF 51 INTERNATIONAL HISTOCOMPATIBILITY WORKSHOP CELL LINES



WELSH BLOOD SERVICE  
*GWASANAETH GWAED CYMRU*

WELSH TRANSPLANTATION AND  
IMMUNOGENETICS LABORATORY



M. T. REES, J. DOWNING AND C. DARKE

## Introduction

Extensive testing of new PCR sequence-specific primers against known reference material is an essential and vital step in their validation.

International Histocompatibility Workshop (IHW) B-cell lines provide readily available reference material which can be easily compared with others' findings. As part of the validation of our PCR-SSP typing system for MICA and MICB we typed 51 IHW cell lines.

## Methods

Our MIC typing system used the same PCR-SSP parameters as our routine HLA-A,B,C typing system and detects 54 MICA and 17 MICB alleles. All allele families are differentiated except MICA\*00201/020 and MICA\*00701/026.

MICA and MICB cell line reference types were obtained from the IMGT/HLA Database, 3 published reports and personal communications from 2 laboratories. This provided 172 MICA and 127 MICB types. Thirty-eight of the cell lines were typed for MICA and MICB, 12 for MICA only and 1 for MICB only and covered 25/54 MICA alleles and 14/17 MICB alleles. The methods used by these 'reference' laboratories included PCR-SSP, PCR-SSOP and sequencing.

## Results

Our typing concurred with 43/46 of the MICA types listed on the IMGT/HLA database, and largely determined by sequencing.

The 'bio-identity' of the 3 discrepant cell lines was confirmed using HLA-A,B,DRB,DQB1 typing. Our MICA typing for 2 of these cell lines, EHM and WDV, concurred with other laboratories. Importantly, EHM used as the only reference for MICA\*036, typed as MICA\*00201/020 MICA\*009 suggesting that this allele may not exist. The third cell line had only been typed by one laboratory and the discrepancy is still unresolved.

We found two other MICA discrepancies typed by a single laboratory. One included an additional allele in a cell line previously reported as homozygous and the other was found to be the wrong cell line following 'bio-identity' checks.

We were unable to amplify the MICB-01023 allele in the reference cell line RML. This finding accords with others and supports the view that this allele is a sequencing artifact.

Importantly, a comparison of the MICA types of the 51 lines (Table 1) from all laboratories, excluding the 5 above, identified 12 types which were discordant with at least two other laboratories – a disagreement rate of 6.9%.

All our MICB types matched at least one other reference type. However, when comparing the reference MICB types 5 did not concur with the consensus type, determined by at least two other laboratories – a disagreement rate of 3.9%.

**Table 1. 51 IHW cell lines used for validation of our MICA and MICB typing system.**

DUCAF	BSM	SWEIG007
EJ32B	IBW9	FH71*
AMAI	LWAGS	WEWAKI
WT49	LKT3	M7
PF97387	HOKKAIDO	LUY
KAS116	OMW	KIME
BM92	FPAF	PAR
FH6	DBB	RSH
FH8	DEM	CLA
MGAR	WJRO76	DOP-ND
LEO23	BM16	OLL
SAVC	31227AB0	J0528239
JHAF	D0208915	JY
RML*	CF996	EHM*
MANNIKA	WT51	LS40*
AMALA	DHIF	WDV*
BOLETH	HOM-2	DKB*

\*Unconfirmed cell types

## Comments

Typing for MIC polymorphism is a relatively new endeavor and the availability of well typed reference material is limited. The readily available IHW B-cell lines provide a good source of reference MIC typed material to establish and validate a MIC typing system. The lines include examples of all MICA and MICB alleles with a frequency of >1.0% and some rarer alleles such as MICA\*033.

This study also highlights the importance of confirming the 'bio-identity' of material used for validation and the problems of consensus typing of emerging polymorphic systems particularly of the rarer/new alleles. Consensus types are available from MTR.