REPORT OF THE 10th UCLA INTERNATIONAL MICA EXCHANGE

May 5, 2010

MICA

37-40

Notice about the new changes to the HLA nomenclature:

As you are aware, the new HLA nomenclature with colon delimited HLA allele names was officially introduced in April, as published in the latest report by the WHO Nomenclature Committee for Factors of the HLA System (1), and implemented with the April 2010 release of the IMGT/HLA Database. To accommodate the increasing number of new HLA alleles, the decision was made by the committee to use colons within the allele names to act as delimiters. The lists of old and new allele names are available in the published

nomenclature report in the April issue of Tissue Antigens, on the IMGT/HLA Database at www.ebi.ac.uk/imgt/hla, and at http://hla.alleles.org.

Our MICA Exchange reports will transition to the exclusive use of the new nomenclature by the end of this year; at this time, you may continue to use the old nomenclature, if needed. Please begin to familiarize yourself with the new nomenclature as you will need to use the new nomenclature to search in the IMGT/HLA Database.

We thank all participating laboratories in the UCLA International MICA Exchange Program. For the 10th MICA Exchange, 4 DNA samples were shipped to 28 laboratories, and MICA typing results were received from 24 of the labs (Table 1). Sixteen laboratories used a reverse sequence-specific oligonucleotide (rSSO) hybridization method, 3 laboratories used sequencing-based testing (SBT), 3 laboratories used sequence-specific priming (SSP) typing, and 1

laboratory used both SBT and rSSO. The number of GCT-repeats in exon 5 was reported by the sequencing laboratories.

We encourage the participating laboratories to resolve any discrepancies so that the information can be shared to improve the reliability and resolution of MICA typing systems.

NEXT MAILING DATE: August 4, 2010

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MICA#037

MICA*010 (A5) was present in this sample. Twelve laboratories reported MICA*010/*054 and 8 labs reported MICA*010. MICA*010 and MICA*054 only differ at position 268 in the $\alpha 3$ domain, where MICA*054 has a glycine and MICA*010 has a serine. Three laboratories reported MICA*016/*019/*033/*056 by rSSOP. MICA*010 differs from MICA*016, MICA*019, MICA*033, and MICA*056 at position 6 (exon 2) in the alpha 1 chain where MICA*010 has a proline while the other MICA alleles (MICA*016/*019/*033/*056) have an arginine. The substitution of proline results in the loss of cell surface expression of MICA*010. MICA*033 also differs from MICA*010, MICA*016, MICA*019, MICA*054, and MICA*056 at position 124, where a threonine is replaced by a serine.

The consensus typing of the second allele is MICA*011 (A6). One laboratory assigned MICA*002. MICA*011 differs from MICA*002 at positions 151 and 271 where MICA*011 contains a valine and an alanine, respectively, compared to methionine and proline in MICA*002.

MICA#038 (Black)

The consensus typing of this sample is MICA*008 and MICA*041. MICA*008 belongs to the MICA-A5.1 group which contains 5 triplet repeats plus 1 additional nucleotide insertion (GGCT/AGCC). This causes a frame shift mutation, which results in premature termination by the stop codon (TAA) at position 304 in the transmembrane domain. MICA*027 has the same nucleotide sequence in exons 2, 3 and 4 as MICA*008, making it difficult to distinguish MICA*027 from MICA*008 if only exons 2-4 are analyzed.

Only 1 laboratory assigned MICA*002, instead of MICA*041 (A9). MICA*002 differs from MICA*041 at position 26 where MICA*002 contains a valine compared to a glycine in MICA*041.

MICA#039 (Black)

MICA*002 (A9) was one allele present in this sample from a Black donor. Two SSP labs reported MICA*002, and MICA*00201 was reported by 4 labs performing SBT and 1 lab using rSSO. One laboratory assigned MICA*015 only, whereas the remaining 16 laboratories reported combinations of the following alleles: *002, *015, *020, *030, and *052. MICA*002, MICA*020, MICA*030, and MICA*052 are identical in their extra cellular domains, but differ in their transmembrane domains.

The consensus typing of the second allele is MICA*015. MICA*015 differs from MICA*002 and MICA*020 at position 114 (exon 3) where an arginine is replaced by a glycine. The transmembrane domain of MICA*015 contains a large polylysine repeat followed by a truncation due to a deletion at the beginning of exon 5 resulting in a frame-shift mutation.

MICA#040 (Black)

MICA*008 (A5.1) and MICA*009 (A6) were present in this sample. MICA*008 was reported in consensus by 16 laboratories, with 3 labs reporting MICA*00801. Another 5 laboratories assigned MICA*008/*058.

Fifteen laboratories reported MICA*009/*049 and 9 labs reported MICA*009 with 5 reporting MICA*00902. MICA*009 is identical to MICA*049 except at position 333 (exon 6) in the transmembrane domain, where MICA*009 has a threonine while MICA*049 has a methionine.

References

1. Marsh SGE, Albert ED, Bodmer WF, et al. Nomenclature for factors of the HLA system, 2010. Tissue Antigens 2010;75:291.

| | Table 1: MICA typing results reported by participating laboratories. | | | | | | |
|-----------|--|---------------------|---------------------|----------------|--------|---------|-----------------------------------|
| MICA #037 | Ctr | Investigator | MICA* allele-1 | MICA* allele-2 | Others | Method | The number of GCT- |
| | 8050 | Baxter-Lowe,Lee | *010 | *011 | *054 | rSSO | repeats (A4, A5, A6, |
| | 3224 | Chen, Dong-Feng | *010/*054 | *011 | | rSSO | A7, A9, A10) or five |
| | 8030 | Davidson&Poulton | *016/*019/*033/*056 | *011 | | rSSO | GCT-repeats with an |
| | 1647 | Gautreaux, Micha | *016/*019/*033/*056 | *011 | | rSSO | additional G (A5.1) |
| | 8040 | Gladman/Pellet/P | *010 | *011 | | SSP | in exon 5 (trans- |
| | 234 | Gomez,Carmen | *010/*054 | *011 | | rSSO | membrane region) are indicated in |
| | 4337 | Kim,Tai-Gyu | *010 | *002 | | SSP | parenthesis |
| | 836 | KuKuruga,Debra | *010/*054 | *011 | | rSSO | (PNAS 1997, |
| | 278 | Lee,Jar-How | *010/*054 | *011 | | rSSO | 94:1298-1303). |
| | 759 | Lopez-Cepero,My | *010/*054 | *011 | | rSSO | 94.1290-1303). |
| | 8055 | Madrigal, J.A. | *010 (A5) | *011 (A6) | | SBT | rSSO - Luminex- |
| | 733 | Mytilineos, Joannis | *010 | *011 | | SBT | based reverse |
| | 5231 | Nelson,Karen | *010/*054 | *011 | | rSSO | sequence-specific |
| | 3966 | Permpikul&Vejbae | *010 | *011 | | SSP | oligonucleotide |
| | 16 | Pidwell/Askar | *010 (A5) | *011 (A6) | | SSP,SBT | hybridization |
| | 8057 | Ray&Balazs | *010/*054 | *011 | | rSSO | method |
| | 3753 | Reed, Elaine F. | *010/*054 | *011 | | rSSO | |
| | 3625 | Rees,Tracey | *010 | *011 | | | SBT - sequencing- |
| | 3798 | Reinsmoen, Nancy | *016/*019/*033/*056 | *011 | | rSSO | based testing |
| | 791 | Stastny,Peter | *010 (A5) | *011 (A6) | | SBT | |
| | 2518 | Tambur,Anat | *010/*054 | *011 | | rSSO | SSP- sequence- |
| | 8053 | Tyan,Dolly | *010/*054 | *011 | | rSSO | specific priming |
| | 3775 | Vidan-Jeras,Blank | *010/*054 | *011 | | rSSO | typing |
| | 1466 | Yu,Neng | *010/*054 | *011 | | rSSO | , · · |

| | Table | 2: MICA typing | results reported by | participating la | boratories. | | |
|-----------|-------|---------------------|----------------------|------------------|---------------|---------|-----------------------------------|
| MICA #038 | Ctr | Investigator | MICA* allele-1 | MICA* allele-2 | Others | Method | The number of GCT- |
| (Black) | 8050 | Baxter-Lowe,Lee | *00801 | *041 | *00804 | rSSO | repeats (A4, A5, A6, |
| | 3224 | Chen,Dong-Feng | *008 | *041 | | rSSO | A7, A9, A10) or five |
| | 8030 | Davidson&Poulton | *008 | *041 | | rSSO | GCT-repeats with an |
| | 1647 | Gautreaux,Micha | *008 | *041 | | rSSO | additional G (A5.1) |
| | 8040 | Gladman/Pellet/P | *00801 | *041 | | SSP | in exon 5 (trans- |
| | 234 | Gomez,Carmen | *008 | *041 | | rSSO | membrane region) |
| | 4337 | Kim,Tai-Gyu | *008 | *002 | | SSP | are indicated in |
| | 836 | KuKuruga,Debra | *008 | *041 | | rSSO | parenthesis |
| | 278 | Lee,Jar-How | *008 | *041 | | rSSO | — (PNAS 1997, — 94:1298-1303). |
| | 759 | Lopez-Cepero,My | *008 | *041 | | rSSO | 94.1296-1303). |
| | 8055 | Madrigal,J.A. | *008(A5.1) | *041 (A9) | | SBT | rSSO - Luminex- |
| | 733 | Mytilineos, Joannis | *00801 | *041 | *00804 | SBT | based reverse |
| | 5231 | Nelson,Karen | *008 | *041 | | rSSO | sequence-specific |
| | 3966 | Permpikul&Vejbae | *008 | *041 | | SSP | oligonucleotide |
| | 16 | Pidwell/Askar | *00801/*00804 (A5.1) | *041 (A9) | | SSP,SBT | hybridization |
| | 8057 | Ray&Balazs | *008/*027 | *041 | | rSSO | method |
| | 3753 | Reed,Elaine F. | *008 | *041 | | rSSO | |
| | 3625 | Rees,Tracey | *008 | *041 | | | SBT - sequencing- |
| | 3798 | Reinsmoen,Nancy | *008 | *041 | | rSSO | based testing |
| | 791 | Stastny,Peter | *00801 (A5.1) | *041 (A9) | *00804 (A5.1) | SBT | |
| | 2518 | Tambur,Anat | *008 | *041 | | rSSO | SSP- sequence- |
| | 8053 | Tyan,Dolly | *008 | *041 | | rSSO | specific priming |
| | 3775 | Vidan-Jeras,Blank | *008 | *041 | | rSSO | typing |
| | 1466 | Yu,Neng | *008 | *041 | | rSSO | |

| | Table | 3: MICA typing | results reported by pa | articipating labo | ratories. | | |
|-----------|-------|---------------------|------------------------|-------------------|------------|---------|---|
| MICA #039 | Ctr | Investigator | MICA* allele-1 | MICA* allele-2 | Others | Method | The number of GCT- |
| (Black) | 8050 | Baxter-Lowe,Lee | *00201 | *015 | | rSSO | repeats (A4, A5, A6, |
| | 3224 | Chen, Dong-Feng | *002/*015/*020/*030+ | *015 | | rSSO | A7, A9, A10) or five |
| | 8030 | Davidson&Poulton | *002/*020 | *002/*020 | | rSSO | GCT-repeats with an |
| | 1647 | Gautreaux, Micha | *002/*015/*020/*030+ | *015 | | rSSO | additional G (A5.1) |
| | 8040 | Gladman/Pellet/P | *015 | *015 | | SSP | in exon 5 (trans- |
| | 234 | Gomez,Carmen | *002/*015/*020/*030+ | *015 | | rSSO | membrane region) are indicated in |
| | 4337 | Kim,Tai-Gyu | *002 | | | SSP | parenthesis |
| | 836 | KuKuruga,Debra | *002/*015/*020/*030+ | *015 | | rSSO | (PNAS 1997, |
| | 278 | Lee,Jar-How | *002/*015/*020/*030+ | *015 | | rSSO | 94:1298-1303). |
| | 759 | Lopez-Cepero,My | *002/*015/*020/*030+ | *015 | | rSSO | rSSO - Luminex- based reverse sequence-specific |
| | 8055 | Madrigal,J.A. | *00201 (A9) | *015 (A9) | *052 (A9) | SBT | |
| | 733 | Mytilineos, Joannis | *00201 | *015 | | SBT | |
| | 5231 | Nelson,Karen | *002/*015/*020/*030+ | *015 | | rSSO | |
| | 3966 | Permpikul&Vejbae | *002 | *015 | | SSP | oligonucleotide |
| | 16 | Pidwell/Askar | *00201 (A9) | *015 (A9) | | SSP,SBT | hybridization |
| | 8057 | Ray&Balazs | *002/*020 | *015 | *052, *055 | rSSO | method |
| | 3753 | Reed, Elaine F. | *002/*015/*020/*030+ | *015 | | rSSO | |
| | 3625 | Rees,Tracey | *015/*00201/*020/*052+ | *015 | | | SBT - sequencing- based testing |
| | 3798 | Reinsmoen, Nancy | *002/*015/*020/*030+ | *015 | | rSSO | |
| | 791 | Stastny,Peter | *00201 (A9) | *015 (A9) | | SBT | |
| | 2518 | Tambur,Anat | *002/*015/*020/*030+ | *015 | | rSSO | SSP- sequence- |
| | 8053 | Tyan,Dolly | *002/*015/*020/*030+ | *015 | | rSSO | specific priming typing |
| | 3775 | Vidan-Jeras,Blank | *002/*020/*030/*052+ | *015 | | rSSO | |
| | 1466 | Yu,Neng | *002/*015/*020/*030+ | *015 | | rSSO | |

| | Table | | | | | | |
|-----------|-------|---------------------|----------------------|----------------|---------------|---------|-----------------------------------|
| MICA #040 | Ctr | Investigator | MICA* allele-1 | MICA* allele-2 | Others | Method | The number of GCT- |
| (Black) | 8050 | Baxter-Lowe,Lee | *027 | *00901 | *049 | rSSO | repeats (A4, A5, A6, |
| | 3224 | Chen, Dong-Feng | *008/*058 | *009/*049 | | rSSO | A7, A9, A10) or five |
| | 8030 | Davidson&Poulton | *008 | *009/*049 | | rSSO | GCT-repeats with an |
| | 1647 | Gautreaux, Micha | *008 | *009/*049 | | rSSO | additional G (A5.1) |
| | 8040 | Gladman/Pellet/P | *00801 | *00901/02 | | SSP | in exon 5 (trans- |
| | 234 | Gomez,Carmen | *008 | *009/*049 | | rSSO | membrane region) are indicated in |
| | 4337 | Kim,Tai-Gyu | *008 | *009 | | SSP | parenthesis |
| | 836 | KuKuruga,Debra | *008 | *009/*049 | | rSSO | (PNAS 1997, |
| | 278 | Lee,Jar-How | *008 | *009/*049 | | rSSO | 94:1298-1303). |
| | 759 | Lopez-Cepero,My | *008 | *009/*049 | | rSSO | 94.1290-1303). |
| | 8055 | Madrigal, J.A. | *008 (A5.1) | *00902 (A6) | | SBT | rSSO - Luminex- |
| | 733 | Mytilineos, Joannis | *00801 | *00902 | *00804 | SBT | based reverse |
| | 5231 | Nelson,Karen | *008/*058 | *009/*049 | | rSSO | sequence-specific |
| | 3966 | Permpikul&Vejbae | *024 | *009 | | SSP | oligonucleotide |
| | 16 | Pidwell/Askar | *00801/*00804 (A5.1) | *00902 (A6) | | SSP,SBT | hybridization |
| | 8057 | Ray&Balazs | *008/*027 | *009/*049 | | rSSO | method |
| | 3753 | Reed,Elaine F. | *008/*058 | *009/*049 | | rSSO | |
| | 3625 | Rees,Tracey | *008 | *00902 | | | SBT - sequencing- |
| | 3798 | Reinsmoen, Nancy | *008 | *009/*049 | | rSSO | based testing |
| | 791 | Stastny,Peter | *00801 (A5.1) | *00902 (A6) | *00804 (A5.1) | SBT | |
| | 2518 | Tambur,Anat | *008/*058 | *009/*049 | | rSSO | SSP- sequence- |
| | 8053 | Tyan,Dolly | *008 | *009/*049 | | rSSO | specific priming |
| | 3775 | Vidan-Jeras,Blank | *008/*058 | *009/*049 | | rSSO | typing |
| | 1466 | Yu,Neng | *008 | *009/*049 | | rSSO | |