



# When it is no longer null: retrospective review of C04:09N (now C04:09L) cases in our patient population

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## ABSTRACT-AIM

Background  
HLA-C\*04:09N sequence shows a frameshift mutation within its cytoplasmic domain. This results in translation of 32 additional amino acids that were assumed to prevent cell surface expression.

In January 2025, the International ImmunoGenetics Information System (IMGT) reclassified the allele C\*04:09 from null (C\*04:09N) to low expression (C\*04:09L). This reclassification has important clinical implications for transplantation. Donor-recipient pairs previously considered matched due to the null designation may now be at risk for mismatch or the development of donor-specific antibodies (DSA) to C\*04:09L. To evaluate potential clinical impacts, we conducted a retrospective review of cases previously reported as C\*04:09N within our patient population.

## METHODS

- HLA typing information at our center stored in LIS: Histotrac
- 2011-Present included in data set
- HLA-C results queried for HLA-C\*04:09N
- Typing methods used over the date range:
  - CareDx Olerup SSP
  - OneLambda SeCore<sup>TM</sup>
  - OneLambda LABType<sup>TM</sup> SSO
  - Next Generation Sequencing (NGS)
- HLA antibody kit included one C\*04:01 bead specificity
- Clinical significance of C\*04:09N to C\*04:09L was analyzed specifically in the transplant population

## RESULTS

- Identified 26 cases of HLA-C\*04:09N

	Solid Organ transplant=	PBSC transplant=
	11	15
Recipient	6	9
Donor	5	6

- Solid Organ: None of the recipients receiving C\*04:09N donors had pre or post transplant C4 antibodies
- PBSC: All recipients typed as C\*04:09N with donor searches had C\*04:09N donor options

## CONCLUSION

Our review found no clinical impact related to the reclassification of C\*04:09N to C\*04:09L in our patient population.

No new mismatches were identified among stem cell recipients, and no de novo Cw4 antibodies were detected in organ recipients transplanted with C\*04:09L mismatches. Laboratory reporting processes have been updated to reflect the allele's new status. Moving forward, primary NGS testing will standardize the identification of C\*04:09L for both stem cell and organ transplantation cases.

OPTN has in review a 2025 Histocompatibility HLA Table Update for addition of C\*04:09L to the unacceptable antigen equivalencies to align with IMGT.

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cDNA          1080      1090      1100      1100
C*04:01:01:01 TGATGAGTCT CTCATCGCTT GTAAAG|CCTG A
C*04:09L      -----

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