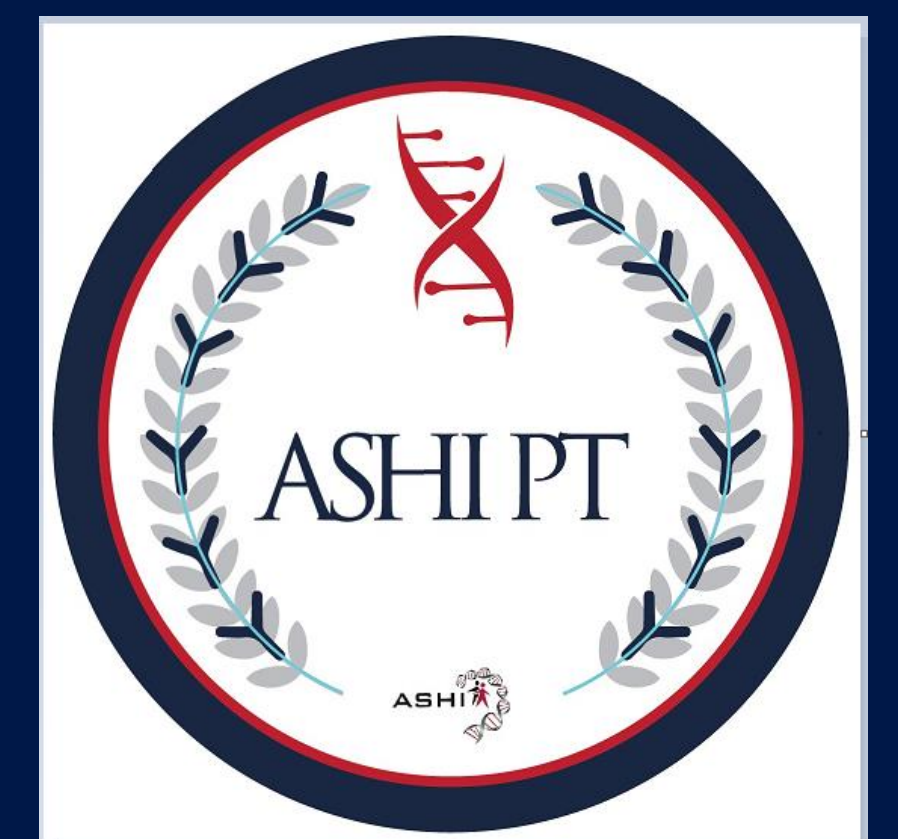


Changes in HLA typing methods and correlation with typing discrepancies observed in the ASHI proficiency testing HLA Typing Survey



Reut Hod Dvorai¹; Anna Greenshields²; Alan Sanfilippo³, Olga Timofeeva⁴, on behalf of the PT Committee

¹SUNY Upstate Medical University, Syracuse, NY; ²Dalhousie University, Halifax, Canada; ³Piedmont Transplant Institute, Atlanta, GA; ⁴UCLA, Los Angeles, CA

Introduction

Human leukocyte antigen (HLA) typing is a critical component in the matching of donors and recipients for solid organ and hematopoietic stem cell transplants, identification of donor-specific antibodies, virtual crossmatch compatibility assessments, and evaluation of disease associations and the risk for drug hypersensitivity. Over the years, the methods used for HLA typing have evolved, revealing the enormous complexity and polymorphic nature of the HLA genes.

The ASHI HLA Typing (HT) Survey is designed to assess laboratory performance in HLA typing by any method. We aimed to evaluate the changes in HLA typing methods, common types of discrepancies and the correlation between discrepancies and typing methods by analyzing ASHI Proficiency Testing (PT) HT survey results.

Methods and Materials

HLA typing data were extracted from the ASHI PT Data Center. The analytes in the HT survey are defined as low resolution (LR) HLA Class I, LR HLA Class II, high resolution (HR) HLA Class I, and HR HLA Class II typing by molecular methods. Prior to 2024, HLA class I and HLA class II typing results were also reported by serology, however, in 2024 this was discontinued due to lack of participation. HLA typing results were graded based on 80% consensus among participating laboratories. Results that did not agree with consensus were graded Discrepant. Sub-consensus grading was applied when 80% consensus for a single allele was not reached. Data from 2018-2024 were analyzed to assess trends in HLA typing methods. Analysis of HLA typing discrepancies was performed for 30 HT specimens tested across the 2023 and 2024 surveys.

Results

The number of participants in the HT survey between 2018 and 2024 was stable and ranged from 160 to 168. During this timeframe, a decline in the reporting of typing by SSO, SSP and SBT and an increase in the use of NGS was observed (Figure 1).

Common indications for discrepant grade assignment included the miscalling of P/G groups (e.g. not reporting the P/G group or reporting a non-existent P/G group) and data entry errors in cases of homozygosity in the DRB345 loci or when the typing included a Not Preset/Absent DRB345 allele.

Higher rates of discrepancies were observed for HLA Class II than HLA Class I (76% vs 24%, respectively), as well as for HR versus LR typing (79.7% vs 20.3%, respectively) with DPB1 being the most common locus to be graded Discrepant (Table 1).

Of the 71 laboratories receiving discrepant grades for any locus during 2023-2024, 47 labs (66.2%) reported testing by low/intermediate resolution typing methods, 14 (19.7%) by high resolution typing methods and 10 (14.1%) by a combination of low- and high-resolution typing methods (Table 2).

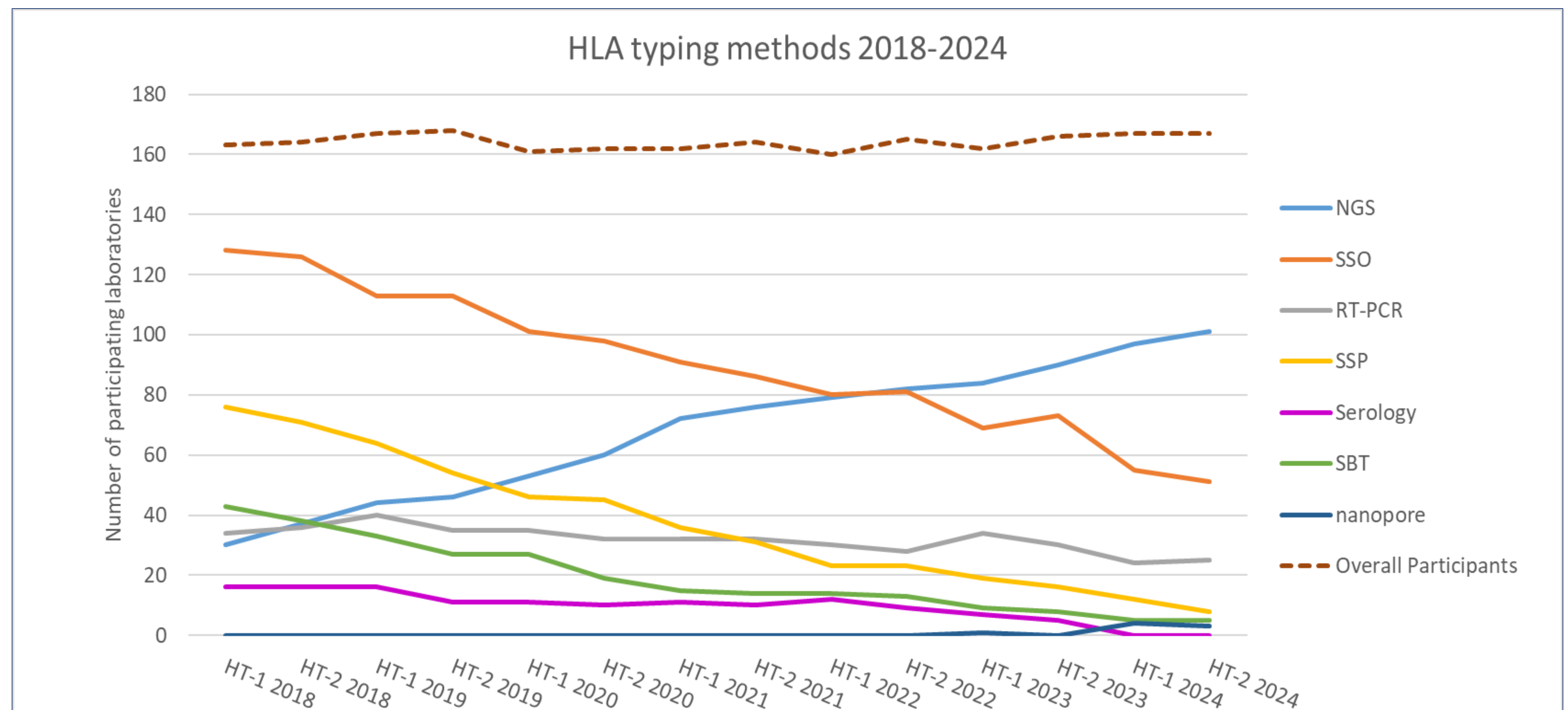


Figure 1: HLA typing methods used by the participants of the HT survey between 2018 and 2024

Table 1. HLA typing discrepancies stratified by HLA loci and typing method resolution.

	HT-1 2023	HT-2 2023	HT-1 2024	HT-2 2024	Total
	10 specimens	10 specimens	5 specimens	5 specimens	30 specimens
# discrepant assignments	n=37	n=64	n=70	n=16	n=187
class I LR, n(%)	3 (8.1%)	5 (7.8%)	3 (4.3%)	5 (31.25%)	16 (8.5%)
class I HR, n(%)	3 (8.1%)	14 (21.9%)	10 (14.3%)	2 (12.5%)	29 (15.5%)
class II LR, n(%)	6 (16.2%)	5 (7.8%)	6 (8.6%)	5 (31.25%)	22 (11.8%)
class II HR, n(%)	25 (67.6%)	40 (62.5%)	51 (72.8%)	4 (25%)	120 (64.2%)
A	2	5	5	5	17
B	4	12	4	2	22
C	0	2	4	0	6
DRB1	2	2	2	2	8
DRB345	4	5	10	1	20
DQA1	7	2	0	3	12
DQB1	10	13	11	1	35
DPA1	2	1	4	1	8
DPB1	6	22	30	1	59

Table 2: Laboratories with discrepancies stratified by typing method used for testing

	HT-1 2023	HT-2 2023	HT-1 2024	HT-2 2024	Total
# participating labs	162	166	167	167	-
# labs with discrepancies	15	26	22	8	71
Low/intermediate resolution method, n(%)	7 (46.7%)	15 (57.7%)	19 (86.4%)	6 (75%)	47 (66.2%)
High resolution method, n(%)	5 (33.3%)	6 (23.1%)	2 (9.1%)	1 (12.5%)	14 (19.7%)
Combination (low and high), n(%)	3 (20%)	5 (19.2%)	1 (4.5%)	1 (12.5%)	10 (14.1%)

Conclusions

The use of NGS typing to report PT results has significantly increased over the last 6 years while the use of methods providing lower resolution has decreased. Most discrepant grades were associated with the reporting of high resolution and HLA class II typing results, specifically DPB1. Interestingly, in many cases discrepancies were due to the assignment of high resolution typing results without P/G group nomenclature from data obtained using a low/intermediate resolution typing method.

Contact

Reut Hod Dvorai, PhD, F(ACHI)
 Email: hoddvorr@upstate.edu
 ASHI PT Website: <https://www.ashi-hla.org/page/PT>

Acknowledgement:

We thank the Proficiency Testing Committee members who perform evaluation and review of data., and Cheryl Hartman, the PT Program Administrator

The authors have no conflict of interest.