



**ASHI Standards and Accreditation:
Impact on the Quality of Laboratory Testing
In the 20 Years of CLIA
CLIAC Meeting, February 20, 2008**

Presented by Marilyn S. Pollack, Ph.D., D(ABHI)

Program Director, ASHI Accreditation Review Board (2007-08)

Dept. of Pathology, Univ. of Texas Health Science Center San Antonio

Early History of HLA, the ASHI Organization and the Standards and Accreditation Process

- 1952- Dausset – wbc agglutination ← transfusion pt. serum, MAC ('58)
- 1958- van Rood – 2 Loci; Payne – antibodies ← Pregnancy
- 1960-63 – First human kidney transplants – limited success
- 1964- Amos – 1st Intl. Histocompatibility Workshop at Duke - Terasaki – Microlymphocytotoxicity Test – crossmatch test = prediction of immediate rejection
- 1970's HLA Typing Sera NIH Trays – not commercially available
- 1975– NIH Tray Users → AACHT (Am. Assoc. Clin. Histo. Testing)
- 1976- BOB of FDA HLA Workshop
- 1977- FDA Guidelines for licensure of Leukocyte Typing Sera
- 1978– First AACHT (AACHT-NIAID) Standards and Lab Accreditation (Transplantation Proceedings)
- 1979-80- First Proficiency Testing (jointly with the CAP)
- 1984- Name change: Am. Soc. for Histocompatibility & Immunogenetics

Early Efforts to Ensure Test Quality: Workshops, Exchanges of Sera, Comparison of Test Methods



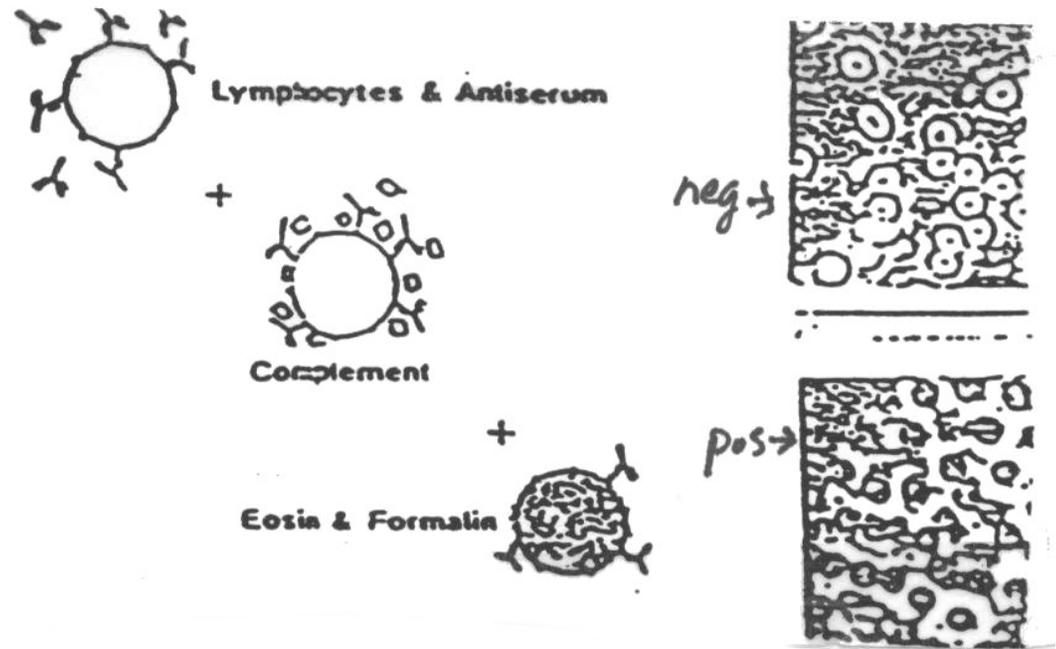
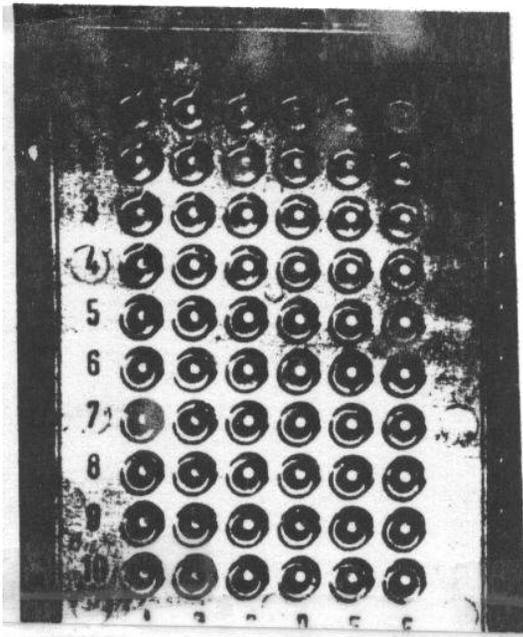
*First
Workshop
Durham 1964*

*Paul
Terasaki
and
microtest*

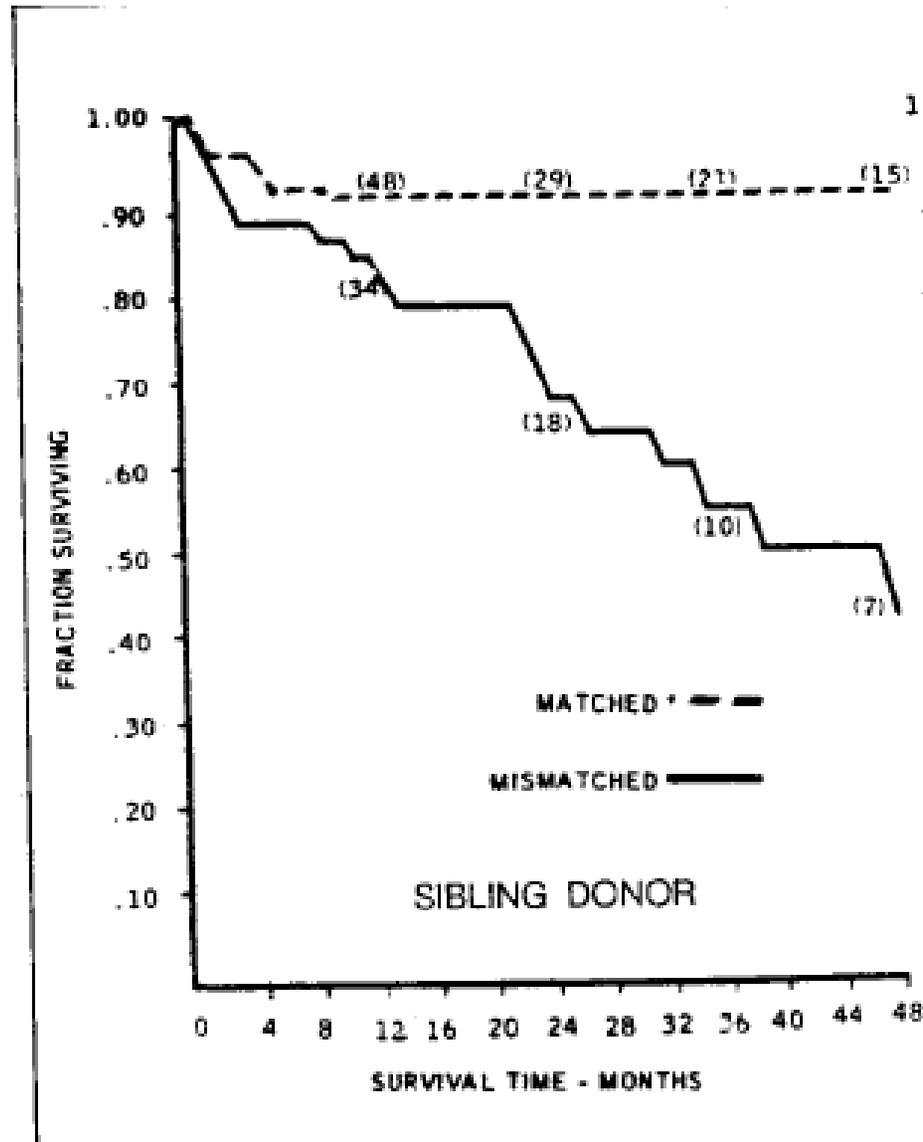
*Parviz
Lalezari*

THE MICROLYMPHOCYTOTOXICITY TEST METHOD

- Optimum use of limited reagents
- Reproducible and standardization of test conditions



Role of HLA in Kidney Transplant Outcome (Terasaki, 1968)



From the ASHI Web Site (www.ashi.hla.org)



About ASHI

Patient care is our first priority.

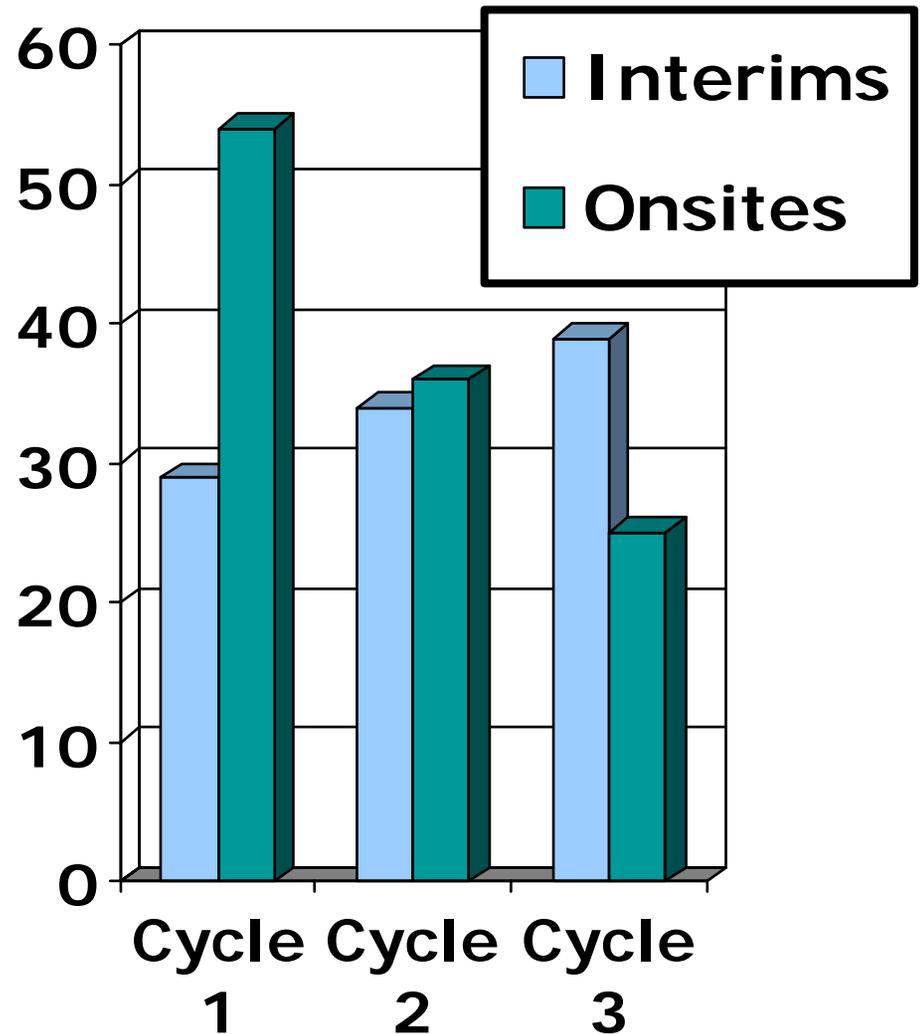
The American Society for Histocompatibility and Immunogenetics (ASHI) is a not-for-profit association of clinical and research professionals including immunologists, geneticists, molecular biologists, transplant physicians and surgeons, pathologists and technologists. As a professional society involved in histocompatibility, immunogenetics and transplantation, ASHI is dedicated to advancing the science and application of histocompatibility and immunogenetics; providing a forum for the exchange of information; and advocating the highest standards of laboratory testing in the interest of optimal patient care.

Recent ASHI History/ Accreditation Process

- ASHI Accredits Labs for UNOS and the NMDP
- ASHI (has an independent) Proficiency Testing Program
- Accreditation for
 - Organ Transplantation (living and deceased donors)
 - HPC transplantation (related and unrelated donors)
 - Non-transplant clinical purposes (disease risk, relationship testing)
 - Multiple Technologies: molecular, serological, crossmatching, chimerism, immune function, non-HLA polymorphisms, etc.
- 1999 CMS approval of ASHI as an Accrediting Org.
- 2005 CMS re-approval for 6 years (longest period)
- 2005-06 Initiated web-based re-accreditation applications
- 2006-07 Web-based Inspector Training Updates
- 2007 Minimally announced inspections
- 2008 (anticipated) Electronic PT Summaries

Laboratory Statistics 2007

- **Cycle 1**
 - January-August
 - 83 Labs (19 Foreign)
- **Cycle 2**
 - May-December
 - 65 Labs (4 Foreign)
- **Cycle 3**
 - September-April
 - 62 Labs (5 Foreign)



210 Labs Total

Why ASHI Made/Makes a Difference

- Reagents for HLA Typing are NOT FDA Approved
 - Pregnancy Sera- uncontrolled specificity/potency
 - Experience Required for Interpretation of Results
- Every Transplant Program has Different Requirements
 - Directors must consider Immunosuppression levels
 - Different Test Requirements for Different types of Patients
- Technologies Change Rapidly
 - New standards needed yearly
 - SSP, SSOP, Microarrays, Chips
- Medical Technologist Training does not include HLA
- On the job training for new Directors, Supervisors and technologists
- Peer Review by EXPERTS is Essential for Quality

ASHI-ARB Policies to Ensure Lab Quality

- New Inspectors Must Have
 - 3 years of Specific HLA Laboratory Experience
 - 1 full-day on-site Inspector Training Workshop
 - 1-2 Training Inspections with a trained Inspector, successful review
- Trained Inspectors must have continuing re-training
 - ½ day workshop every 2 years, or
 - On-line training modules
- Re-accreditation process
 - On-site inspection every 2 years
 - Interim Assessment of actual PT results
 - Multi-tiered review: Inspector, Commissioner, Co-Chair, Full-ARB
- Commissioners serve 2-4 years; Co-Chairs serve 3 years
- Audit-based inspections – NO Checklist
- Corrective Action Follow-up (Contingency Lists)
 - Submission of PT to Commissioner
- Ad Hoc Inspections for New Directors, Re-locations (can be waived)

Recent Changes in ARB Policies ← CMS

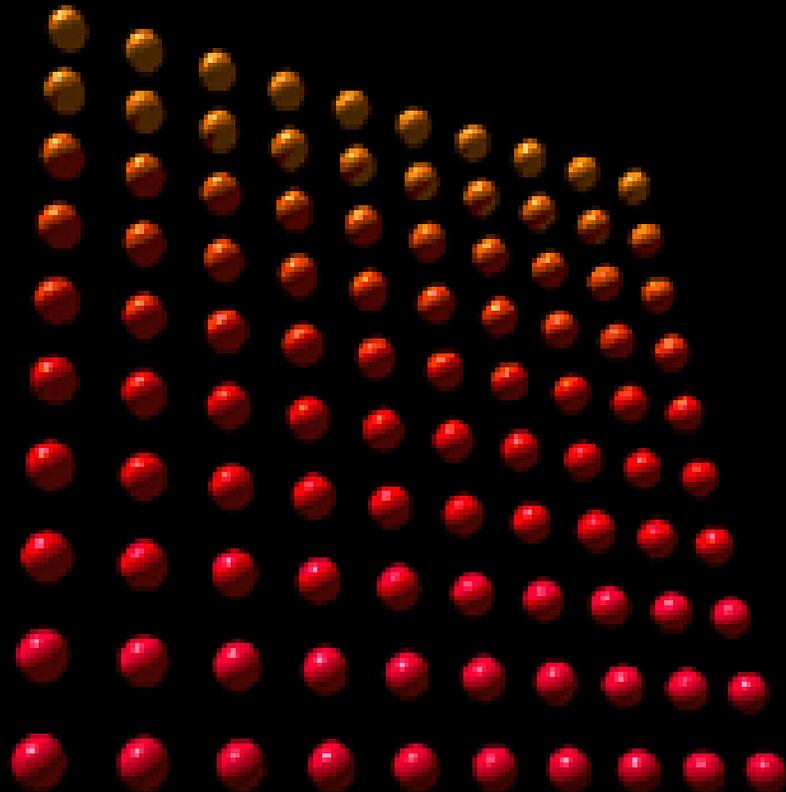
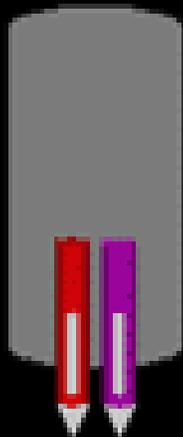
- Minimally Announced (2 weeks) Inspections (2007)
 - Intended to improve quality of assessment
 - Lab Directors (still) expected to be on site, if possible
- Instructions to Inspectors Re: “Research Tests” (NEW)
 - If tests are within ASHI purview (e.g., immune function, KIR)
 - If results are reported to physicians with patient identifiers
 - If U.S. Lab
 - Labs need to submit test validation to Commissioner
 - Check for participation in PT or equivalent
- Partial Testing using an Instrument in another Lab has the same requirements as referred testing

Suggested Changes in CLIA Regulations

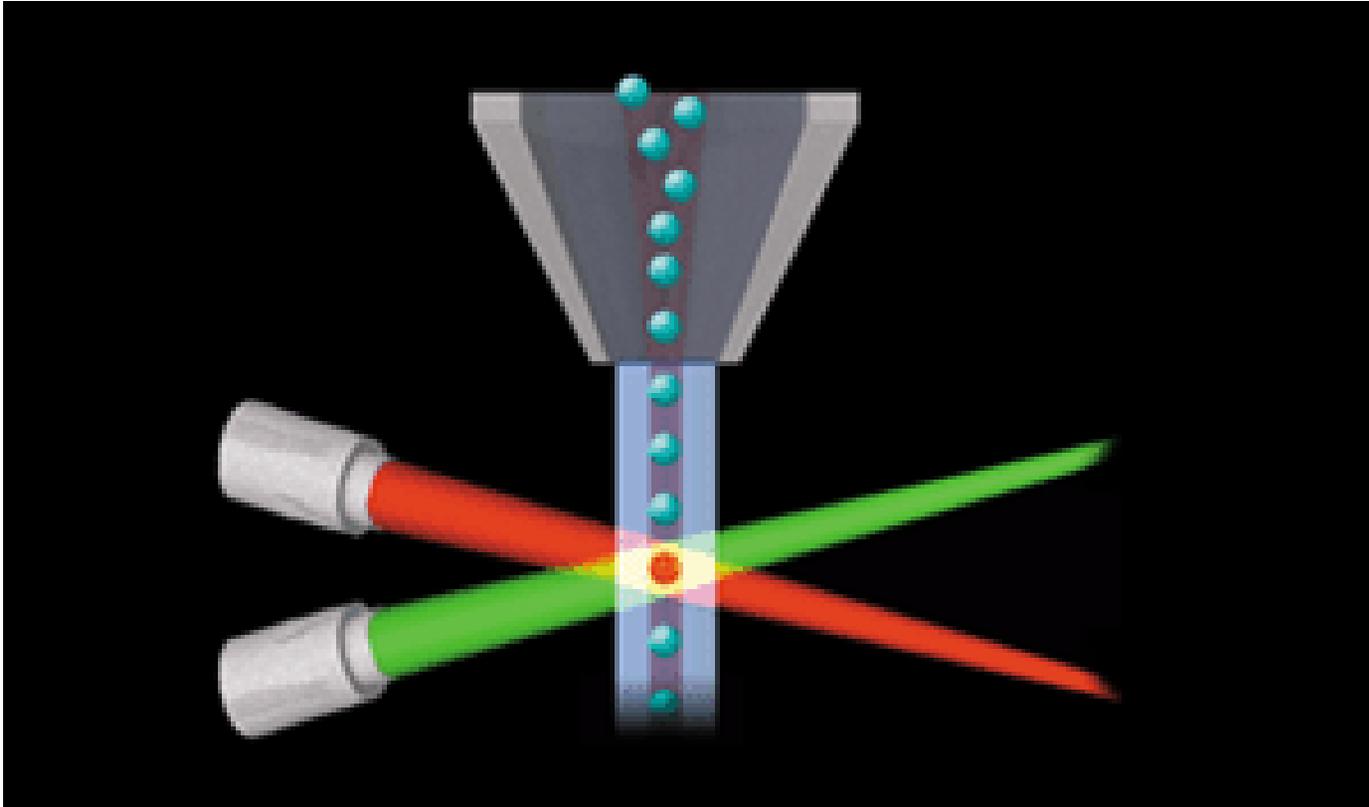
- Technology Changes: Some Regulations Outdated
 - Relevant Antibody Identification now Always Possible
 - Pre-transplant Crossmatch prolongs ischemic time
- Current CLIA Regulations require a pre-transplant crossmatch for renal transplantation
 - 493.1278 Standard: Histocompatibility (f)(2) For renal allotransplantation and combined organ and tissue transplants in which a kidney is to be transplanted, have available results of final crossmatches before the kidney is transplanted.
- A positive crossmatch in the absence of HLA antibodies could be clinically irrelevant – deny transplant
- Consider situation for an imported “0 mismatched” kidney

HLA Antibody Identification with Microarrays – Single Alleles

**100 Color-codes =
100 Simultaneous Tests**

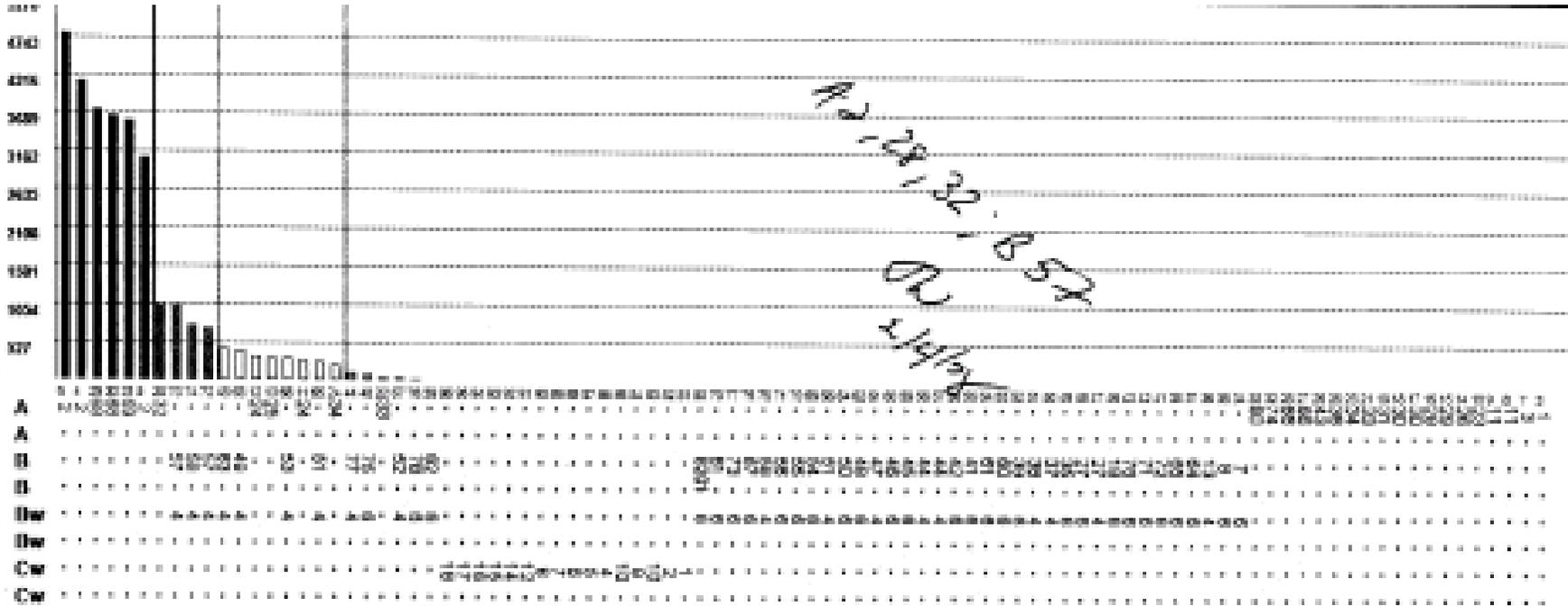


Fluidics align the microspheres to flow, in single file, through two focused laser beams



One Laser Excites the Beads
The Second Laser Excites the Reporter Fluor
Fluorescence Intensity Quantitatively Reflects
Binding of Target to the bead.

Example of Class I Microarray Antibody Identification Results



Conclusions

- ASHI is an effective CMS partner for Lab Quality
- ASHI Standards and Policies ensure compliance with CLIA Regulations
 - Crosswalks performed after every change
 - Interpretive CMS Assistance is regularly sought
- ASHI expertise helps ensure appropriate validation and use of new technologies to improve test accuracy and clinical outcomes.