aaBB Accreditation Relationship Testing News

January 2018 Volume 13, Number 1

In This Issue

Do you have an interesting case or question you would like to share? Email us at nikkib@aabb.org

Proposed Parentage Calculations in Cases with a Chimera – Part 1 of 3

Robert E. Wenk MD, Debra Davis PhD and Michael Baird PhD

I. Detection and Confirmation of Human Chimera

A *congenital chimera* is an individual composed of two cell populations derived from early dizygotic twin embryos that have fused together or by inter-twin transfusion or cell migration. Fusion produces a "tetragametic" chimera, a misnomer because all chimera, including those produced by transplantation, contain the genomes of four gametes. Cell migration from mother to child or from one DZ twin embryo to another are other ways to generate chimera, but fewer cells distribute to fewer tissues and fewer cells implant. Actually, little is known about their natural genesis in humans.

Human chimerism is detected so infrequently that its prevalence hasn't been established. Few cases have been recognized despite suspicion that chimera may be far more prevalent than published cases suggest. There are several reasons why this is so: 1) Common analytical methods exhibit poor sensitivity. Typical PCR amplification of STRs as used in relationship testing laboratories may fail to amplify DNA of the minor cell population. 2) The tissue distribution of a chimera's DZ cell populations is highly variable. Whereas some tissues contain two populations of cells, other tissues appear to contain only one. Sampling DNA from an apparently monozygotic tissue has resulted in false exclusions of parentage.[1,2,3] 3) Observing the alleles of two genomes has been mistaken for sample contamination. One prenatal paternity test sample of maternal plasma was initially considered contaminated, when, in fact, the plasma contained the fetal DNA of a congenital chimera (D. Davis, unpublished).

Sometimes, human congenital chimerism is suggested by clinical observations of bi-colored skin or hair, differently colored eyes (iris heterochromia) or physical evidence of intersex, but these findings are not specific. Unexplained 'mixed field agglutination' found by a blood bank is similarly nonspecific, but by 1973 'mixed field' reactions had led to diagnosis of seventy congenital 'blood chimera', of which almost half were attributed to DZ twin transfusion.[4]. (Blood chimera are so-named because that was the only tissue examined.) Chromosomal heteromorphisms can diagnose congenital chimera, but past cytogenetic studies were ordered after clinical recognition of intersex.[5] Molecular genetics laboratories have detected or diagnosed chimera at loci of blood groups, HLAs and STRs. Molecular diagnosis of chimera depends on demonstrating 3-4 alleles/locus at loci on different chromosomes. Otherwise, mosaicism and single chromosomal anomalies (duplications, trisomy) may produce extra alleles at a locus on that chromosome.

If a chimera's two cell populations are sampled and a genetic (STR) profile is obtained, every genetic locus necessarily carries four alleles, but the four are not always observed. The reasons are:

1) An uneven tissue distribution of DZ cells. Not every tissue contains cells from both zygotes so that sampling the wrong tissue causes only one genome to be examined. No tissue is known to provide an optimal site for collecting cells of both populations.

2) Analytical Insensitivity. Cells of one population may be too few to obtain sufficient DNA for analysis. Alleles of the minor cell population may not be observed after PCR amplification.

3) Allele Duplication. Second, third and fourth copies of an STR allele cannot be observed separately from the first copy. For example, a duplicate STR allele in an ordinary homozygote is not visible as a discrete marker. The two-alleles are seen as one because both copies migrate to the same location in an electrophoretic gel. (Only a greater fluorescent signal after PCR amplification suggests that more than one copy of an allele may be present.) Thus, duplicate alleles are not "visible" as separate from alleles already identified in a chimera's phenotype. Suspected duplicates of an allele seen in a chimera's phenotype will be termed "invisible" alleles in this article.

Allele duplication occurs for two reasons. Either the genotype from one cell population is homozygous at a locus or the locus genotypes of the two cell populations share identical alleles. Since the DZ twins comprising a chimera are full siblings they inherit 50% of their alleles identical by descent from common parents. Our experience has shown that most of a chimera's STR loci exhibit three visible locus alleles; a minority of loci exhibit four; fewer loci exhibit two; and rarely does a locus exhibit one.

REFERENCES

Yu N et al. (16 May 2002). Disputed Maternity Leading to Identification of Tetragametic Chimerism. New England Journal of Medicine. 346 (20): 1545–1552.

Sheets, K et al. A Case of Chimerism-Induced Paternity Confusion: What ART practitioners can do to prevent future calamity for families. Journal of Assisted Reproduction and Genetics. (In press.)

Tippett P. Blood group chimeras. A review. Vox Sang. 1983; 44(6):333-59.

Lee KF et al. The identification of spontaneous 47, XX, +21/46 chimeric fetus with male genitalia. BMC Medical Genetics. 2012 13 (85): 2-6.

Wenk RE and Davis D. Paternity Probabilities When a Child is a Congenital Chimera. Transfusion. 2017 57(11):2814-5

NOW AVAILABLE

AABB and the American Association for Laboratory Accreditation (A2LA) have joined forces to offer the AABB/A2LA Accreditation Program to the relationship testing and forensics communities.

- **Two assessments in one**, covering – AABB Relationship Testing Standards and ISO 17025:2005, reducing laboratory staff time
- **An ISO standard that is not prescriptive** and can be implemented based on your work culture and processes
- **Internationally-recognized accreditation** through ILAC (A2LA) and ISQUAa (AABB)
- **Value-added assessments by quality-focused technical experts** in the areas they are assessing resulting in an opportunity for all involved
- **Partners in accreditation** that will provide friendly, responsive staff to assist laboratories in navigating the accreditation landscape

For more information on how to enroll in this program, please contact the AABB Accreditation and Quality Dept. at 301-215-6492 or accreditation@aabb.org.

Available Now!

Standards for Relationship Testing Laboratories

13th edition

Print Only

And

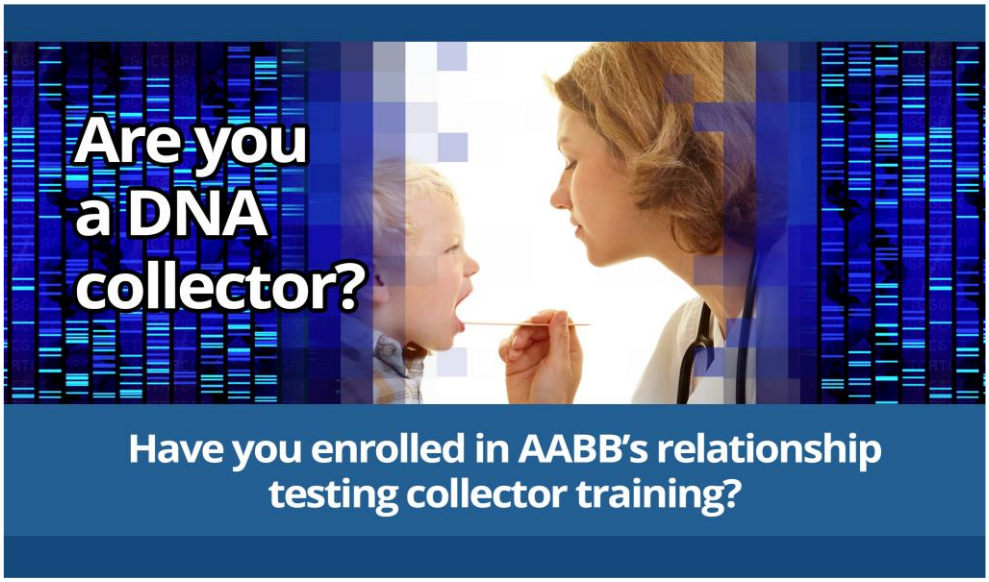
BUNDLE: Standards for Relationship Testing Laboratories 13th edition

Print and Portal

The effective date January 1, 2018

New from AABB

Relationship Testing Collector Training and Certificate



This self-paced online course teaches individuals the proper methods to collect, process, and submit high quality DNA samples. Successful individuals will earn a Certificate of Training from AABB and be included on the list of qualified collection professionals given to AABB Accredited Relationship Testing laboratories nationwide.

LEARN MORE AND ENROLL TODAY!

www.aabb.org/DNAcollector

For more information:
Phone: +1.301.215.6482 • Email: professionaldevelopment@aabb.org

Registration Fees

November 17, 2017 – December 31, 2018: $99
January 1, 2019 – June 30, 2019: $59
July 1, 2019 – December 15, 2019: $29

Find more information or to register, please visit the AABB RT Collector Training web page.

To obtain a FREE copy
Click below

The AABB Relationship Testing Annual Report Summary

GREAT RESOURCES

- NEW E-Cast: AABB Standards for Relationship Testing, 13th Edition Changes – Coming February 1, 2018

- Available E-Cast: **Human Chimera**
  Describes different kinds of chimera and mosaics, how natural chimera arise in an embryo and how human chimera are discovered and proven by genetic tests. Limitations in detection and testing are discussed and indicate why the frequency of chimerism is not easily determined. To purchase the Human Chimera E-Cast visit our Marketplace.

- AABB has launched the newest edition of the Collector Training certificate course for individuals who would like to be recognized as AABB-trained sample collectors for relationship testing purposes. For more information visit the AABB RT Collector Training web page.

Misleading Claims of Accreditation and Logo Misuse

With the explosion of advertising on the internet, there has been increasing misuse of AABB's trademarked logos and misleading claims of AABB accreditation. We are renewing our efforts to stop such practices and are actively searching out these organizations so that we can address this problem on a more global scale. These efforts benefit accredited laboratories by preserving the strong value of AABB accreditation and by ensuring that customer attention is focused on laboratories that actually are accredited. Our facilities work hard to achieve and maintain accreditation and deserve the maximum benefit of that accreditation. Increased vigilance will also benefit laboratories' customers by ensuring that they get the accredited-laboratory test that they have paid for. You can aid these efforts by bringing to our attention instances of logo misuse or misleading statements regarding accreditation. Please advise AABB's Accreditation Department (accreditation@aabb.org) by providing the offending Web site and briefly describing the issue. It would be particularly helpful if you copy and email the actual link from your browser's address bar, as some offending organizations maintain multiple Web sites. The AABB Trademark Usage Guideline as well as Language for use by Third Party Collectors can found on the AABB Website.

2017-2018 RTAC Members

Robert Wenk, MD Chair

Charles Kelly, PhD
Michelle Beckwith, BS
Harmeet Kaur, PhD
Brandt Cassidy, PhD
George Maha, JD, PhD
John Peterson, PhD

2017-2018 RTSC Members

George Maha, JD, PhD
Chair

David Baumgarten
Kelly Beatty, MS
Debra Davis, PhD
Donna Housley, PhD
Megan S. Mackenzie, PhD
Christopher Miles
Jane Prichard, BS, MT(ASCP), CLSp(MB)
Meghan Nemeth, JD
Zahra Mehdizadeh Kashi, PhD
Maureen Dunn
Kaitlin Keating

WANTED

Audio Conference Content

Would you like to repurpose your old talks or presentations?

Share your content as part of AABB's 2018 RT Audio Conference Series.

Please let us know if you have given a talk or presentation in the last 2-3 years on a topic that you think may be of interest to the relationship testing community. Topics of interest may include but are not limited to calculations, new technologies, expert systems, court room basics, forensics, DNA etc. If you decide to submit your content, you can choose to moderate the audio conference or we can assign a speaker for you.

For more information or to submit your content, contact Nikki Bass at nikkib@aabb.org

Articles

Do you have an interesting case or question you would like to share through this newsletter? Or is there a topic or issue you would like us to write about? Email us at nikkib@aabb.org

RTAC or RTSC Member

- Are you interested in ensuring that assessment/audit procedures are in consistent with AABB policies established by the AABB Accreditation Program Committee?
- Are you interested in working with U.S. Citizenship and Immigration Service and/or the Dept. of State as it relates to RT?

If these issues are of interest to you, the **Relationship Testing Accreditation Committee** would like to have you as a member.

- Are you currently an AABB Member?
- Would you like to be involved in creating and revising the Relationship Testing Standards?
- Would you like to be involved in creating and revising the Guidance for the Standards?

If these issues are of interest to you, the **Relationship Testing Standards Committee** would like to have you as a member.
To get involved, please contact Nikki Bass at the AABB National Office at nikkib@aabb.org.