medical genomics

Effect of genetic inconsistencies on duo parentage testing using COrDIS Plus DNA marker system

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ISFG 2007 Recommendations

In case of inconsistencies between DNA profiles of C and AP the decision as to parentage exclusion should be based on *comparing the obtained CPI value for the case with the threshold CPI value adopted by the laboratory* and not on the number of inconsistent loci observed between the two DNA profiles.

The Purpose of the Study

Evaluation of the effect of small number of genetic inconsistencies on duo parentage cases using COrDIS Plus STR marker system

13 CODIS STR

1-2 inconsistencies – inconclusive result

3 inconsistencies – CPI ~ $^{1}/_{4,600}$ (exclusion)

COrDIS Plus

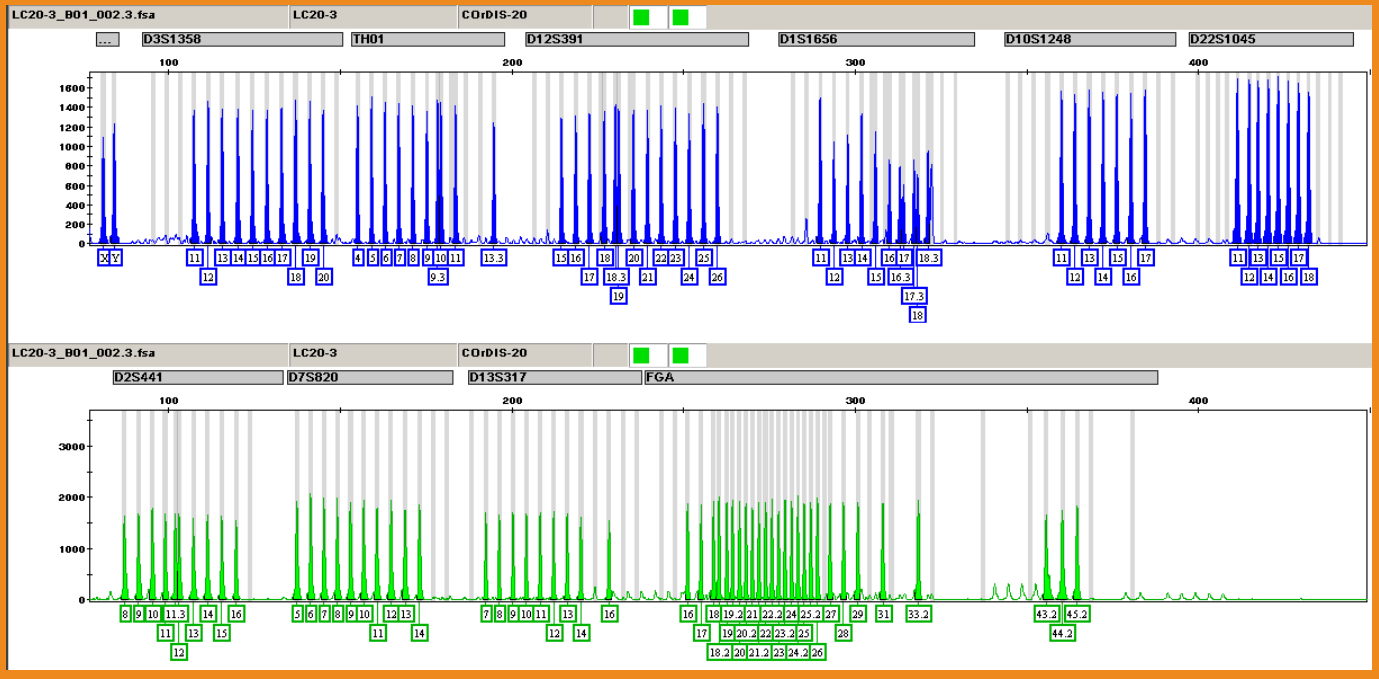
(GORDIZ Ltd, Russia)

19 Autosomal loci + AMEL

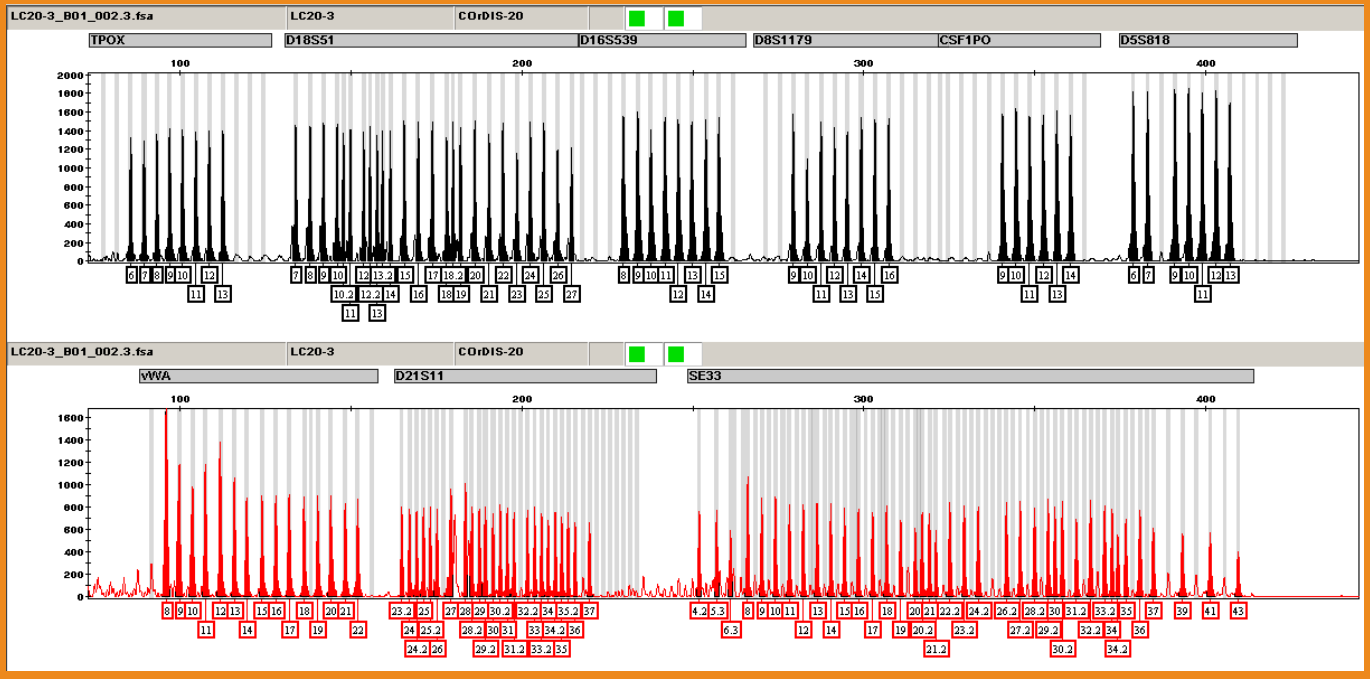
D3S1358	TPOX
TH01	D18S51
D12S391	D16S539
D1S1656	D8S1179
D10S1248	CSF1PO
D22S1045	D5S818
D2S441	VWA
D7S820	D21S11
D13S317	SE33
FGA	AMEL

Widely used by paternity laboratories and the Investigative Committee of the Russian Federation and for forensic casework. Also used in Latvia, Iran and several other countries

Allele and size ranges of COrDIS Plus loci



Allele and size ranges of COrDIS Plus loci



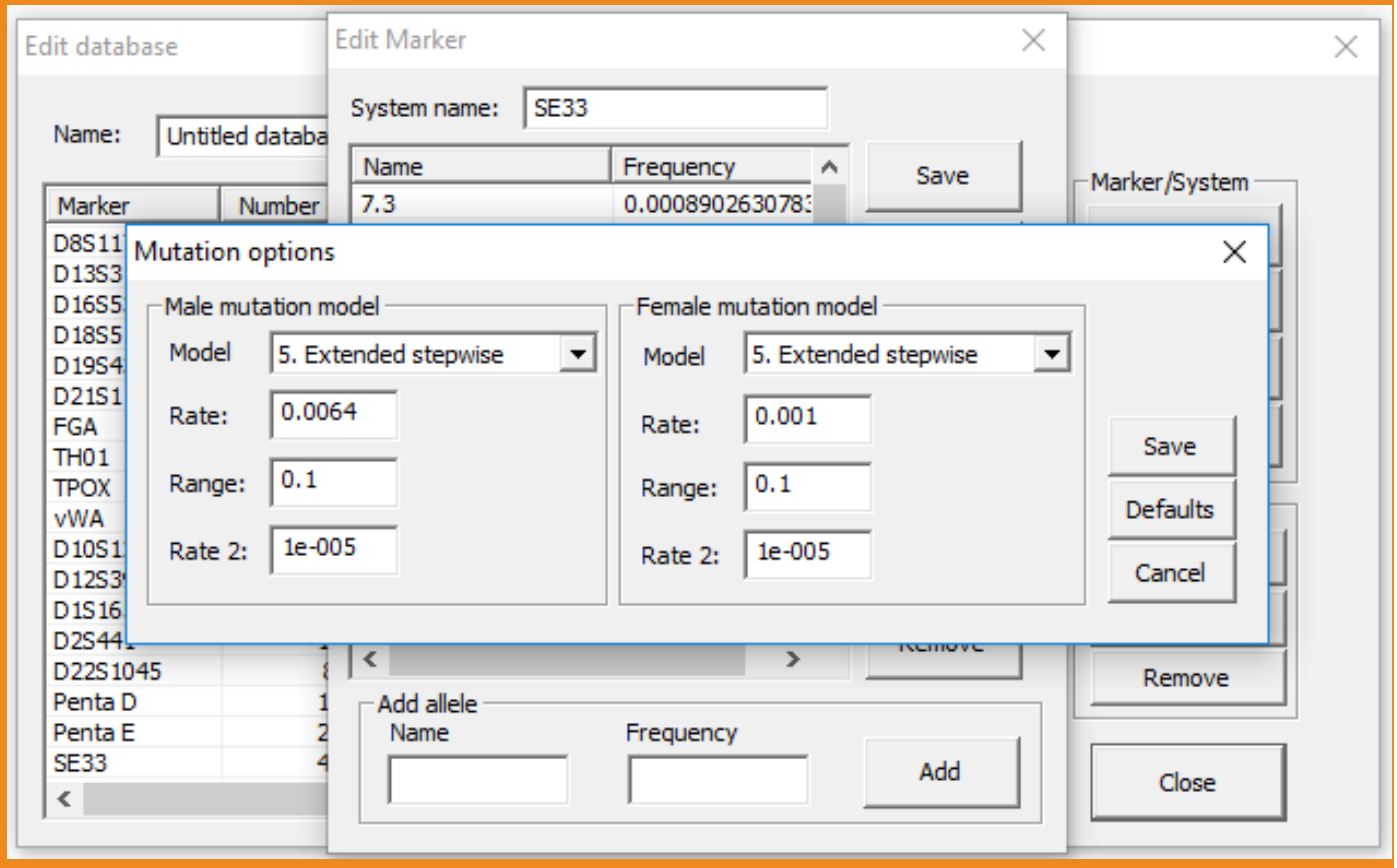
Experimental Design

3,129 duo parentage tests:

paternity - 3,080

maternity - 49

- Source of DNA - buccal swabs
- PCR – ABI 2720 and SureCycler 8800
- Genetic analyser - ABI PRISM® 3500
- Analysis software - GeneMapper ID-X 1.4
- Calculation of CPI - J. Buckleton, Ch. M. Triggs and S. J. Walsh (2005)
- Familias 3 used for CPI calculations in cases with inconsistencies
- STR mutation rates - AABB 2003 Annual Report
- STR mutation rates for D12S391, D1S1656, D10S1248 - 0.001


Edit database
Name:
Untitled databa
Marker
Number
D8S11
D13S3
D16S5
D18S5
D19S4
D21S1
FGA
TH01
TPOX
vWA
D10S1
D12S3
D1S16
D2S44
D22S1045
Penta D
Penta E
SE33
Edit Marker
System name:
SE33
Name
Frequency
7.3
0.0008902630783
Save
Add allele
Name
Frequency
Add
Marker/System
Remove
Close
Mutation options
Male mutation model
Model
5. Extended stepwise
Rate:
0.0064
Range:
0.1
Rate 2:
1e-005
Female mutation model
Model
5. Extended stepwise
Rate:
0.001
Range:
0.1
Rate 2:
1e-005
Save
Defaults
Cancel

Results

No genetic inconsistencies between the child and the alleged parent were observed in 2,446 (78.17%) cases (minimum CPI=2,404)

Paternity - 632 inconsistent cases out of 3,080 cases (20.5%)

Maternity - 2 inconsistent cases (1 inconsistency) out of 49 cases (4.1%)

In 609 cases (19.47%) > 4 genetic inconsistencies

In 74 cases (2.36%) ≤ 4 genetic inconsistencies:

- 1 inconsistency – 48+3* (minimum CPI=241)
- 2 inconsistencies – 3 (minimum CPI=$^{1}/_{14}$)
- 3 inconsistencies – 2+3* (maximum CPI=$^{1}/_{27,395}$)
- 4 inconsistencies – 10+5* (maximum CPI=$^{1}/_{1,758,652}$)

* Incomplete profile in one of the participants. Not taken for analysis

Single Inconsistency (48 cases)

2 maternity cases

46 paternity cases

Single Inconsistencies per Locus

Locus	# of cases
D12S391	7
SE33	6
D5S818	5
D18S51	5
D8S1179	4
VWA	3
D21S11	3
FGA	3
D3S1358	2
D16S539	2
CSF1PO	2
D10S1248	2
D1S1656	1
D7S820	1
D13S317	1
TPOX	1
TOTAL	**48**

Locus	# of cases
TH01	0
D22S1045	0
D2S441	0

Silent Alleles (dropouts?)

Case	Locus	COrDIS Plus		GlobalFiler®	
		Child	AF	Child	AF
Case 1*	D8S1179	13, 13	14, 14	13, 15	14, 15
Case 2*	D10S1248	13, 13	16, 16	13, 14	14, 16
Case 3*	D18S51	12, 12	13, 13	12, 20	13, 20
Case 4*	FGA	18, 18	21, 21	18, 24.1	21, 24.1
Case 5 (Null allele or 3 step mutation, PI=0.0007)	TPOX	8, 8	11, 11	8, 8	11, 11

* - Samples sent to the kit manufacture for sequencing

Two Inconsistencies (3 cases)

Two Inconsistencies
Case #1

Locus	Child	AF	PI
FGA	19, 24	21, 22	**0.0007**
SE33	18, 28.2	17, 19	**0.0247**
	COrDIS Plus CPI		**467**

2 Repeats difference

Testing additional markers did not reveal further inconsistencies

Two Inconsistencies
Case #2

Locus	Child	AF	PI
D12S391	18, 19.3	17, 18.3	**0.0073**
D7S820	8, 14	10, 13	**0.0501**
COrDIS Plus CPI			**24.22**

Testing additional markers did not reveal further inconsistencies

Two Inconsistencies
Case #3

Locus	Child	AF	PI
D12S391	21, 27	18, 26	**0.0200**
D5S818	10, 12	11, 11	**0.0041**
COrDIS Plus CPI			$^{1}/_{14.06}$

Testing additional markers did not reveal further inconsistencies

Three Inconsistencies (2 cases)

Three Inconsistencies Case #1

Locus	Child	AF	PI
D7S820	10, 12	8, 9	**0.0001**
D5S818	10, 13	9, 11	**0.0034**
FGA	20, 25	21, 22	**0.0002**
COrDIS Plus CPI			**$1.7*10^{-6}$ ($1/592,287$)**

Additional testing with biological mother revealed 2 further inconsistencies (D18S51, CSF1PO)

Three Inconsistencies Case #2

Locus	Child	AF1	PI
TPOX	9, 9	8, 8	**0.0007**
D8S1179	11, 14	12, 13	**0.0037**
D21S11	28, 29	30, 32.2	**0.0010**
COrDIS Plus CPI			**$3.7*10^{-5}$ ($1/_{27,395}$)**

Additional testing with AF2 (biological son of AF1) resulted in non-exclusion of AF2 (all loci are consistent)

Four Inconsistencies (10 cases)

Four Inconsistencies

In 23 out of 40 inconsistent loci – 1 repeat difference between alleles of the Child and AF

4 inconsistent loci – integer / non integer allele

13 inconsistent loci – 2-5 repeats difference

The maximum CPI = $^{1}/_{1,758,652}$

Conclusions

- For all the cases with 1 and 2 inconsistencies for COrDIS Plus STR results are in favour of parentage in question
- If the threshold value of CPI=1/1,000 is adopted results for all the cases with $\geq$ 3 inconsistencies for COrDIS Plus STR will be in favour of exclusion of parentage in question
- For all duo cases with $\leq$ 3 genetic inconsistencies for cases with CPI>1/1000 testing the biological parent and/or alternative alleged parent as well as testing extra STR loci not in the COrDIS Plus panel is required to confirm the results of initial testing

Acknowledgments

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