

I-Familia: Identifying Missing Persons Globally Through Family DNA Kinship Matching

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ISHI
INTERNATIONAL SEARCH AND IDENTIFICATION

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Missing persons: a global phenomenon

600,000/year (USA)
20,000/year (EU)
3,000,000/year (India)
100,000/year (Japan)
80,000/year (Brazil)
30,000/year (South Africa)
25,000/year (Australia)

25% of missing person cases have a transnational dimension
(European Parliament 2016)

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International police cooperation via INTERPOL

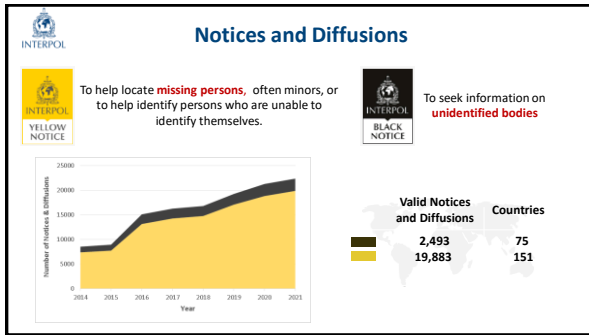
- International organization established in 1923
- INTERPOL General Secretariat in Lyon, France
- Legal framework and technical infrastructure for secure international police data exchange (I-24/7)
- National Central Bureau in each member country

19 MEMBER COUNTRIES CONNECTED THROUGH A SECURE NETWORK

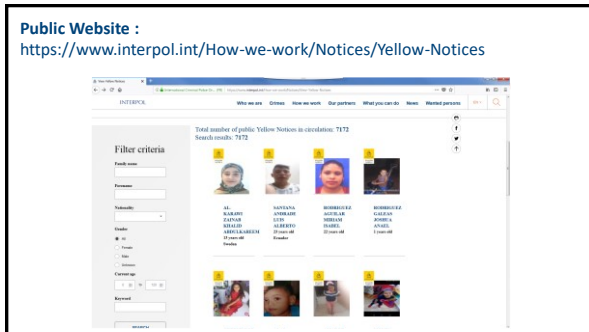
DATABASES

19 MEMBER COUNTRIES
114 DATABASES
9 MEMBER OFFICES
0.5 MEMBER UNITS

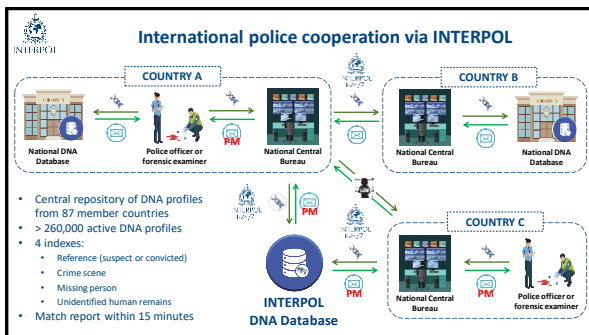
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International DNA matching in INTERPOL Databases

DIRECT MATCHING

DNA from missing person: prior medical sample or personal item

DNA from unidentified body or human remains

INTERPOL DNA Database

SINCE 2004 PROVEN SUCCESS

DNA of the missing person international requests (Lauri)

- Case is too old
- No personal item/med
- No DNA capabilities in

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The 3 components of I-Familia

I-Familia DNA database

- No criminal DNA data
- No nominal information (only biological relationships, date and DNA profiles)
- Only accessible to the INTERPOL DNA Unit
- Retention period: 5 years for family DNA and 15 years for unidentified human remains

DNA kinship matching software

- Compare ante-mortem and post-mortem DNA data
- All pedigrees accepted
- Calculation of likelihood ratio (LR)
- Propose a list of potential biological associations

Statistical interpretation

- Interpretation tables developed by INTERPOL
- Quickly evaluate the statistical relevance of the proposed associations
- Report to countries / Reject / Additional information required

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Challenges of international DNA kinship matching

• **First challenge : the choice of method to perform DNA kinship matching computations**

$LR = \frac{P(E|H_1)}{P(E|H_2)}$

BONAPARTE SMART

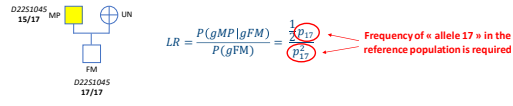
- Bayesian networks
- Likelihood Ratio (LR) computed for any pedigree to measure the fit with any UHR profile
- Rank potential matches by probability of match

Police data (24 autosomal STRs)
Independent loci
Close relatives only

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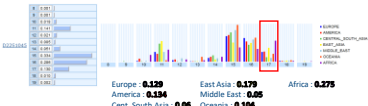
Challenges of international DNA kinship matching

• **Second challenge : Avoid the bias of using the wrong reference population**



$$LR = \frac{P(gMP|gFM)}{P(gFM)} = \frac{1}{2 \cdot p_{17}}$$

Frequency of « allele 17 » in the reference population is required

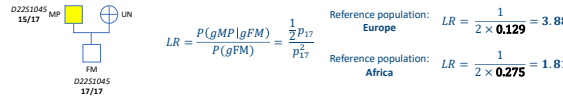
Europe : **0.129** East Asia : **0.179** Africa : **0.275**
 America : **0.184** Middle East : **0.05**
 Cent. South Asia : **0.06** Oceania : **0.104**

Amigo et al. (2009)

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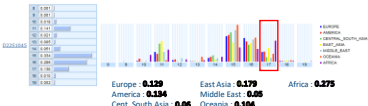
Challenges of international DNA kinship matching

• **Second challenge : Avoid the bias of using the wrong reference population**



$$LR = \frac{P(gMP|gFM)}{P(gFM)} = \frac{1}{2 \cdot p_{17}}$$

Reference population: Europe $LR = \frac{1}{2 \times 0.129} = 3.88$
 Reference population: Africa $LR = \frac{1}{2 \times 0.275} = 1.81$

Europe : **0.129** East Asia : **0.179** Africa : **0.275**
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Amigo et al. (2009)

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Challenges of international DNA kinship matching

• **Second challenge : Avoid the bias of using the wrong reference population**

- « Worldwide allele frequencies »
- Compilation of data from Buckleton et al. 2016
 - 369 reference populations
 - 183k individuals
 - 2.5 million typed alleles (813 unique alleles)
- Theta (θ) correction factor (0.03)
- Λ -dependent factors for common, rare, and new alleles

Clusters	Number of reference populations	Number of individuals	Weight in Worldwide population
Africa	36	7344	4.02%
Asian	72	14522	9.03%
AsiaAb	17	15637	8.54%
Caucas	151	82579	45.13%
Hispa	39	30403	16.45%
IndPa	26	3276	1.79%
Inuit	2	209	0.11%
Nordam	23	2795	1.52%
Polyn	4	24184	13.22%
Total	369	182999	100.00%

Laurent et al. (2022)

- Virtually applicable to any international DNA kinship matching request regardless of ancestry
- Confirmation by using national or continental allele frequencies to determine the true LR value

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Challenges of international DNA kinship matching

- Third challenge : The number of available overlapping STR loci for comparison

STR	LHM	Son of MP	LR
1	10,12	10,12	1
2	24,25	24,25	1
3	2,3	2,3	1
4	9,10	9,10	1
5	11,12	11,12	1
6	16,17	16,17	1
7	18,19	18,19	1
8	21,22	21,22	1
9	23,24	23,24	1
10	25,26	25,26	1
11	27,28	27,28	1
12	29,30	29,30	1
13	31,32	31,32	1
14	33,34	33,34	1
15	35,36	35,36	1
16	37,38	37,38	1
17	39,40	39,40	1
18	41,42	41,42	1
19	43,44	43,44	1
20	45,46	45,46	1

Butler et al. (2012)

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Butler et al. (2012)

- Minimum overlap required in I-Familia = 6 STRs

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Challenges of international DNA kinship matching

- Fourth challenge : LR interpretation and report of potential biological relationships

LR = 0.054
LR = 1.456
LR = 774.741

Unrelated LR distribution Related LR distribution

False negatives
False positives

LR ≥ threshold = report match
LR < threshold = reject match

LR threshold

A unique arbitrary LR threshold is often applied to all DNA kinship cases regardless of the pedigree

LR threshold = 10,000

Laurent et al. (2022)

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Challenges of international DNA kinship matching

Fourth challenge : LR interpretation and report of potential biological relationships

Legend:
 □ Family Member (FM)
 ● Missing Person (MP)
 ○ Unidentified Human Remains (UHR)

Step 1: Generation of 100,000 full pedigrees with full DNA profiles (26 STRs) using worldwide allele frequencies. = 100,000 Full pedigrees

Step 2: One FM profile is compared into a LR profile to create a LR search in LR database. The rest of the family members compare the pedigree. = 100,000 LRH + 100,000 Pedigrees with MP

Step 3: Random selection of full to create 10 sub-profiles per LR containing 6 to 26 loci. = 100,000 x 10 Sub-profiles = 1,000,000 LRH

Step 4: \log_{10} computation to measure strength of every LR to reach pedigree using worldwide allele frequencies. = 10 Sub-profiles LRH = 100,000 Pedigrees x 1 = 1,000,000 'Volume' of $\log_{10} LR$
 = 10 Sub-profiles LRH = 100,000 Pedigrees x 10,000 = 100,000,000,000 'Normalized' $\log_{10} LR$

Laurent et al. (2022)

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Challenges of international DNA kinship matching

Scenario = A : 6 STRs. **Scenario = B :** 14 STRs. **Scenario = C :** 10 STRs / 24 STRs.

Legend:
 ■ Reject the match
 ■ Additional DNA data may be required
 ■ Review the potential biological association
 ■ Further interpretation may be required

Laurent et al. (2022)

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Streamlined interpretation of kinship matching results

Interpretation table for scenario « C »

Legend:
 ■ Reject the match
 → $\log_{10} LR$ value is too low to be considered

Laurent et al. (2022)

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Streamlined interpretation of kinship matching results

INTERPOL

Interpretation table for scenario « C »

Reject the match
 → $\log_{10}LR$ value is too low to be considered

Additional DNA data may be required
 → More than 50 adventitious matches (on average) per 100,000 UHR
 → High risk of heavy workload
 → Suggest adding another relative to the pedigree or include additional typed loci

Laurent et al. (2022)

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Streamlined interpretation of kinship matching results

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Review the potential biological association
 → Less than 50 adventitious matches (on average) per 100,000 UHR
 → Compare ante mortem and post mortem data

Laurent et al. (2022)

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Streamlined interpretation of kinship matching results

INTERPOL

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Review the potential biological association
 → Less than 50 adventitious matches (on average) per 100,000 UHR
 → Compare ante mortem and post mortem data

Further interpretation may be required
 → Risk of germinal mutation or drop-out
 → Pedigree may not be accurate (half-siblings)

Laurent et al. (2022)

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Scientific validation and transparency

Case file available at [Interpol](#)

Forensic Science International: Genetics

Research paper
Streamlining the decision-making process for international DNA kinship matching using Worldwide allele frequencies and tailored cutoff log₁₀L_R thresholds

François-Xavier Laurent^{1,*}, Andrea Fischer^{2,3}, Robert F. Old⁴, Neer Kausharwamy⁵, John S. Buckleton⁶, Susana Huchin⁷

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First international confirmed match with I-Familia

October 2020

- Request from NCB Rome
- Missing Person since April 2004
- No DNA profile available for the missing person
- DNA profile from 2 children
- Upload of pedigree information to I-Familia

- April 2004**
- Body found in Adriatic Sea by Croatian Police
- No fingerprints or face data
- DNA profile from human remains
- No match in National DNA database
- DNA profile shared by NCB Zagreb in April 2004

Confirmation of the missing person's identity by both NCBs

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Extraction of national UHR DNA profiles

CODIS-to-INTERPOL export function

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Extraction of national biological relatives DNA profiles

XLSX2XML SPREADSHEET

This Excel document can be used to extract DNA profiles to mass upload to the INTERPOL DNA Database and/or Family. Please use the correct spreadsheet depending on the type of DNA profile (paternal, maternal, mitochondrial, Y-chromosome, or X-chromosome).

Instructions include:

- Include DNA profile per row.
- First name to change the order of 1-10, please specify the same order to all data.
- Minimum requirements for DNA profiles from missing persons and unidentified human remains (not including biological relatives).
- Both alleles must be entered for Y-chromosome (Y-DNA).
- Submit profiles with exactly 18 STR markers, except for the Y-DNA, Y-chromosome (not including biological relatives).
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1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50

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Acknowledgments

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 Sree Kanthaswamy
 John Buckleton

3 anonymous reviewers of our published manuscript
 Member countries which provide the DNA data
 Families of missing persons

DNA@interpol.int

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INTERPOL's new service : I-Familia

Efficiency of worldwide allele frequencies and tailored LR thresholds confirmed using simulated DNA profiles

Forensic Science International: Genetics
 Communications
 Contributions to I.L.G. Population Data for IP Automated DNA Loci (Shenolik, Sci. Ser. Genet. 7 (2019) 482-485)
 Author(s): Shenolik, Shoshita, G. Gallo, Marilouise G. Loring, Adam M. Todd
 Copyright: Elsevier B.V. All rights reserved. https://doi.org/10.1016/j.fsig.2019.04.001

NIST 1038 Revised U.S. Population Dataset (July 2017)
 African-American / Asian / Caucasian / Hispanic

Isolated populations:
 Native Americans (Ng et al, 2016)
 Mexican-Mestizo population from Northwest Mexico (Martinez-Cortes et. al, 2019)
 Circassian subpopulation in Jordan (Al-Eitan et. al, 2020)

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INTERPOL's new service : I-Familia

Classification efficiency of related and unrelated matches using the a specific threshold vs. tailored thresholds

Matched against 1,000 simulated matches (LR = 1,000) (10,000 matches)	Matched against 1,000 simulated matches (LR = 1,000) (10,000 matches)																																																												
<table border="1"> <thead> <tr> <th>Population</th> <th>LR threshold</th> <th>True Positives</th> <th>False Positives</th> <th>True Negatives</th> <th>False Negatives</th> </tr> </thead> <tbody> <tr> <td>African-American</td> <td>1,000</td> <td>9,999</td> <td>1</td> <td>9,999</td> <td>1</td> </tr> <tr> <td>Asian</td> <td>1,000</td> <td>9,999</td> <td>1</td> <td>9,999</td> <td>1</td> </tr> <tr> <td>Caucasian</td> <td>1,000</td> <td>9,999</td> <td>1</td> <td>9,999</td> <td>1</td> </tr> <tr> <td>Hispanic</td> <td>1,000</td> <td>9,999</td> <td>1</td> <td>9,999</td> <td>1</td> </tr> </tbody> </table>	Population	LR threshold	True Positives	False Positives	True Negatives	False Negatives	African-American	1,000	9,999	1	9,999	1	Asian	1,000	9,999	1	9,999	1	Caucasian	1,000	9,999	1	9,999	1	Hispanic	1,000	9,999	1	9,999	1	<table border="1"> <thead> <tr> <th>Population</th> <th>LR threshold</th> <th>True Positives</th> <th>False Positives</th> <th>True Negatives</th> <th>False Negatives</th> </tr> </thead> <tbody> <tr> <td>African-American</td> <td>1,000</td> <td>9,999</td> <td>1</td> <td>9,999</td> <td>1</td> </tr> <tr> <td>Asian</td> <td>1,000</td> <td>9,999</td> <td>1</td> <td>9,999</td> <td>1</td> </tr> <tr> <td>Caucasian</td> <td>1,000</td> <td>9,999</td> <td>1</td> <td>9,999</td> <td>1</td> </tr> <tr> <td>Hispanic</td> <td>1,000</td> <td>9,999</td> <td>1</td> <td>9,999</td> <td>1</td> </tr> </tbody> </table>	Population	LR threshold	True Positives	False Positives	True Negatives	False Negatives	African-American	1,000	9,999	1	9,999	1	Asian	1,000	9,999	1	9,999	1	Caucasian	1,000	9,999	1	9,999	1	Hispanic	1,000	9,999	1	9,999	1
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As stringent against false-positive reports as a LR threshold of 1,000

Efficient identification of real matches with a false-negative rate similar to a LR threshold of 1

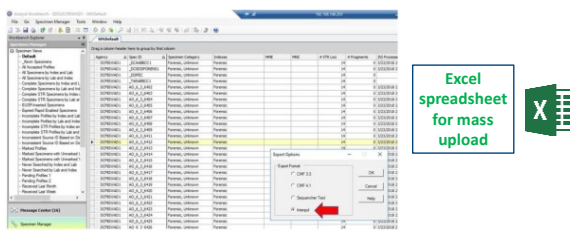
Lauren et al. under review

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Mass-upload options

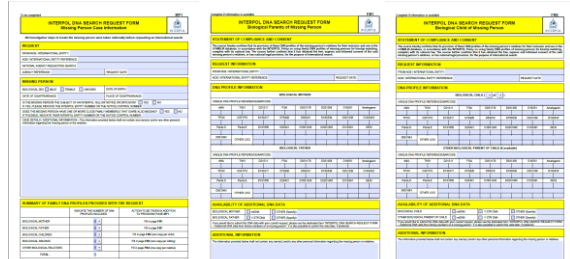
CODIS-to-INTERPOL export function XLSX-to-INTERPOL export function



Excel spreadsheet for mass upload

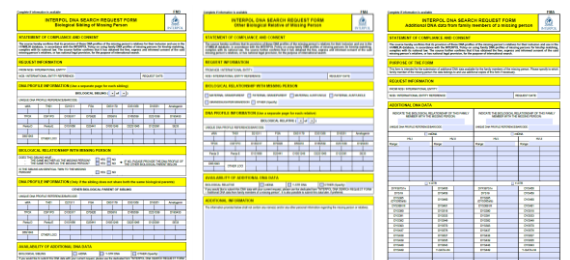
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How can you help ?



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How can you help ?



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