FINAL PROGRAM AND ABSTRACTS

THE SIXTH ISABS CONFERENCE ON HUMAN GENOME PROJECT BASED APPLICATIONS IN FORENSIC SCIENCE, ANTHROPOLOGY AND INDIVIDUALIZED MEDICINE

June 1-5, 2009
Split, CROATIA

ISABS

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ISABS

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Welcome note

Dear Colleagues,

Welcome to the 6th ISABS Conference on Human Genome Project Based Applications in Forensic Science, Anthropology and Individualized Medicine.
The conference is next in the series of biennial events organized by the International Society for Applied Biological Sciences, a society dedicated to the promotion of applied molecular biology (www.isabs.hr).

Since the initiation of the series in 1997, we have strived both to focus and broaden the scope of the conferences. The focus has been on the application of cutting-edge analytical methodology in forensic science. However, since 2007 we have broadened the area of interest by the introduction of molecular anthropology that, in large part, shares the methodology with forensic genetics. In 2009, we are introducing selected topics from individualized medicine, another applied discipline based on the advances in mapping of the human genome.

As before, the conference is structured to allow close interaction of the international faculty and attendees. Together with formal presentations, there will be meet-the-professor sessions, a day trip and other social occasions that are meant to enhance opportunities for scientific intercourse, but also to introduce the participants to the city of Split, the ancient maritime capital of Croatia and a vibrant modern Mediterranean city.

Enjoy!

Moses Schanfield
Dragan Primorac
Stanimir Vuk-Pavlović
Program/Conference Directors

CONFERENCE ORGANIZER

Organizer:

International Society for Applied Biological Sciences
e-mail: info@isabs.hr
http://www.isabs.hr

Program/Conference Directors:

Moses Schanfield, George Washington University, Washington, DC, USA
Dragan Primorac, University of Split, Split and Josip Juraj Strossmayer University, Osijek, Croatia
Stanimir Vuk-Pavlović, Mayo Clinic College of Medicine, Rochester, MN, USA

Program Committee:

Damir Marjanović (Institute for Genetic Engineering and Biotechnology (INGEB), Sarajevo, BH and Genos and Forensic DNA laboratory, Zagreb, Croatia)
Pavao Rudan (University of Zagreb, Zagreb, Croatia)
Stanimir Vuk-Pavlović (Mayo Clinic College of Medicine, Rochester, MN, USA)

Local Organizing Committee:

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Ante Ivkošić
Dalibor Marijanović
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Zrinka Romić
Ante Vulić

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VenEvent
Gundulićeva 3, 10000 Zagreb, Croatia
www.venevent.com
tel 01 48 200 48
fax 01 48 200 49
info@venevent.com
ID Code: HR-A-01-080443208

Nima Splita do Splita

Uvik kad se čuje da se di u nas oli u svitu dogaja čakod gruboga - kad su orkani, veliki vali, trusi, poplave, vulkani - mi se Splićani uvik i iznova sitimo Dioklecijana i falimo ga kako je bija pripametan kad je zna za naše misto izabrat baš ovi pozicjun.

Vazmite balotu zemajsku, okrićite je, vrtite je ka trotul, vižitajite je od Sivernoga do Južnoga pola, od Japana do Amerik i vidit ćete da nidir njanci iz bliza nima takoga pozicjuna. Idealnoga u svemu. Jemamo sve, sve na ruku i sve na okupu.

Jemamo more i odisprid otoke, da nikad ne moredu bit perikulani vali i da jemamo di gradit vikendice i odit na đite.

Jemamo i riku, ali ne veliku, divlju i opaku, vengo naše Jadro da nan daje vodu za razvodnit vino i oprat oči od krmeji. I di je, kad je fiera u Solin, lipo sidit na travicu i bacivat košćice o janjca u riku.

Usrid grada jemamo planinu i to ne divje brdo vengo najlipji uzorak, kampjun brda koji se da zamislit. I na Marjanu šumu di se mladost more izgubit u škuribandu činit jubav.

I pored toga ča jemamo i more i brda i riku i šume, od svi nji nikakvi nan perikul ne priti i uvik smo ka u škatulicu.

A ča se klime tiče, ne triba njanci govorit. Najsunčaniji smo grad u cilu Evropu. A jopet nismo žejni ni kiše, vengo smo je i štufi. Svake dvi-tri godine pade koja šaka sniga da nan dica i moredu vidit. Liti, kad je puno vruće jemamo mestral za razladit se. Bura nan puše da nan očisti arju.
Ne priti nan nikakva pogibej ni od trusa jer jemamo tle od elastične tupine koja se rastiže ka laštik i jedino se moremo malo gingolavat.

Da je bilo dat inženjerima da na kartu nacrtadu jedno ovako idealno misto, ne bi ovo ispalo jer bidu čakod zaboravili oli falili. Ne reče se zaludu: nima Splita do Splita.

A mi se još tužimo kako je u Split sve skupo! Budimo sritni i mučimo jer i bez šolda u žep svi smo ovod di smo - miljarderi!

MILJENKO SMOJE

SPLIT, 07. 10. 1964.

There's no place like Split!

Whenever we hear of something dire happening near or far away – be it hurricanes, storms, quakes, floods, volcanoes – we cannot help but recall Diocletian and praise him for his great wisdom in choosing such a fine place for this city of ours.

Were you to take the globe, turn it around, spin it like a whirligig, visit every place from the North Pole to the South, from Japan to the Americas, you would see there is nothing so perfectly positioned as this. Ideal in everything. We've got it all, all at hand and all close.

We've got the sea and the islands in front, to shield us from the perilous waves and give us somewhere to build our summer houses and take excursions.

It is not only the sea that we hold dear, but our river as well. River *Jadro* is not one of those great rivers that run wild and unpredictable, but rather one that gives us clean water to mix with our wine and wash our eyes of sleep. A place where it is oh so nice, when there is a fiesta in small city close to Split, *Solin*, to sit on the grass and fling lamb bones into the river after delicious meal.

In the heart of the Split we have a mountain, and not just any mountain but a most beautiful specimen with the finest peak imaginable. And on this *Marjan* mountain, woods whose darkness holds secrets of young loves forged, hidden away from inquisitive eyes.

And though we have the sea and the hills and the river and the woods, none of them are a menace to us, making us feel well sheltered instead.

As for the climate, we simply can't complain. We are the sunniest city in all of Europe. And yet we are in no want of rain, because we have plenty. Every two or three years a smidgeon of snow falls for our young ones to see. When the summer becomes too hot to bear, the landward breeze keeps us cool. The wind *bura* blows to clear the air. We are in no danger of earthquakes for we do not have soil of elastic marl that stretches like rubber, and they can do no more than sway us a little.

Had we entrusted engineers with drawing such an ideal place on the map, we would not have got this for they would have forgotten or missed something. After all, it is not in vain that they say: "*There's no place like Split!*"

And still we complain how expensive everything in Split is! We ought to be happy and keep quiet, for even with no money jingling in our pockets, we are all just by living here - millionaires!

MILJENKO SMOJE

SPLIT October 7, 1964

ISABS Committees

ISABS registration number: 21003655
Date of registration: August 27, 2004

President: **Ivana Erceg-Ivkošić** (General Hospital "Sveti Duh", Zagreb, Croatia)
Vice President: **Ante Ivkošić** (General Hospital "Sveti Duh", Zagreb, Croatia)
Secretary: **Dalibor Marijanović** (Business Innovation Center of Croatia- BICRO, Zagreb, Croatia)

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Stanimir Vuk-Pavlović (Mayo Clinic College of Medicine, Rochester, MN, USA)

Scientific Committee:

Forensic Genetics:

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Zoran Budimlija (Office of Chief Medical Examiner, New York, NY, USA)
Cecelia Crouse (Palm Beach Sheriff's Office, West Palm Beach, FL, USA)
Jürgen Henke (Institut für Blutgruppenforschung, Köln, Germany)
Mitchell Holland (Forensic DNA Consultants, Manassas, VA, USA)
Henry Lee (University of New Haven, West Haven and Connecticut Forensic Science Laboratory, Meriden, CT, USA)
José Lorente (Department of Legal Medicine, University of Granada, Granada, Spain)
Marilyn Menotti-Raymond (National Cancer Institute, Frederick, MD, USA)
Antti Sajantila (Department of Forensic Medicine, University of Helsinki, Helsinki, Finland)

Molecular and Cellular Medicine:
Henry Erlich (Roche Molecular Systems, Inc., Alameda, CA, USA)
Francis Glorieux (Genetics Unit, Shriners Hospital for Children and McGill University, Montreal, QC, Canada)
Robert Huber - Nobel Laureate 1988 (Max Planck Institute for Biochemistry, Martinsried, Germany)
Doron Lancet (Weizmann Institute of Science, Rehovot, Israel)
Pier Franco Pignatti (Institute of Biology and Genetics and Faculty of Medicine and Surgery, University of Verona, Italy)
David I. Smith (Mayo Clinic College of Medicine, Rochester, MN, USA)

Molecular Anthropology:

Pavao Rudan (Institute for Anthropological Research, Zagreb, Croatia)
Peter Underhill (Stanford University Medical Center, Stanford, CA, USA)

Course Committee:

Frederick Bieber (Harvard Medical School and Birgham and Women's Hospital, Boston, MA, USA)
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Thomas Parsons (International Commission on Missing Persons, Sarajevo, B&H)

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Ivana Erceg-Ivkošić (General Hospital "Sveti Duh", Zagreb, Croatia)
Edwin Huffine (Bode Technology Group, Lorton, VA, USA)
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Dalibor Marijanović (Business Innovation Center of Croatia- BICRO, Zagreb, Croatia)

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Petar Projić (Genos, Forensic DNA laboratory, Zagreb, Croatia)
Ivana Šamija Projić (Clinical Hospital Center Zagreb, Zagreb, Croatia)
Vedrana Škaro (Genos, Forensic DNA laboratory, Zagreb, Croatia)

Students Committee:

Ante Vulić (Medical School, University of Zagreb, Zagreb, Croatia)

The Young Investigator Awards

Recipients of the 2001 Young Investigator Awards
Forensic IdentityTesting: Frontiers in Molecular and Cellular Medicine:

- Lucia Cifuentes Ovalle, Chile
- Rima Dada, India
- Katja Drobnič, Slovenia
- Anna Gareeva, Russia
- Nguyen Hoai Giang, Vietnam
- Tomasz Kupiec, Poland

Recipients of the 2003 Young Investigator Awards

- Robert J. Shelton, CO, USA (Forensic Genetics)
- Chiara Magri, Italy (Molecular and Cellular Medicine)

Recipients of the 2005 Young Investigator Awards

- Caroline Round, United Kingdom (Forensic Genetics)
- Tracy Johnson, USA (Forensic Genetics)
- Vedrana Montana, USA (Molecular and Cellular Medicine)
- Mirela Baus Lončar, Germany (Molecular and Cellular Medicine)

Recipients of the 2007 Young Investigator Awards

- Grzegorz Kaczmarczyk, Poland (Forensic Genetics)
- Agnieszka Krzyżańska, Poland (Forensic Genetics)
- Kaye Ballantyne, Australia (Molecular Anthropology)
- Tomislav Domazet-Lošo, Croatia (Molecular Anthropology)
- Coralie Frassati, Switzerland (Molecular Anthropology)
- Taeko Kashima, Japan (Molecular Anthropology)

Recipients of the 2009 Young Investigator Awards

- Chiara Barbieri, Germany (Molecular Anthropology)
- Fernanda Toledo Gonçalves, Brasil (Individualised Medicine)
- Pavlo Feliksovich Tatarskyy, Ukraine (Individualised Medicine)
- Antoinette Westen, Netherlands (Forensic Genetics)

Scientific Program Information

Certificate of Attendance
Confirmations of attendance will be issued at the registration desk.

The Young Investigator Awards
The members of the scientific board will review all submitted abstracts and up to 10 selected authors will receive Young Investigator Award. Recipients of the award will receive 500 € as well as a special certificate.

Credits
The 6th ISABS Conference on Human Genome Project Based Applications in Forensic Science, Anthropology and Individualized Medicine has been approved for 10 (participants) or 15 (lecturers) points by the Croatian Medical Chamber. Credits are intended for medical doctors, members of Croatian medical Chamber, in order to extend their medical doctor's license.

Sponsor Exhibition
Set up: May, 31, 2009, 18:00 to 20:00
Monday, June 1, 2009, 12:30 to 18:00
Tuesday, June 2, 2009, 08:30 to 20:00
Thursday, June 4, 2009, 08:30 to 20:00
Dismantling: Friday, June 5, 2009, 17:30 to 19:00

Poster Setup
Sunday, May 31, 2009, 18:00 – 20:00
Monday, June 1, 2009, 08:00 – 11:00
Poster board numbers can be found in the author's index. The staff at the registration and info desk will help you in finding both the number and location of the board.

Poster Discussion
Tuesday, June 2, 2009, 19:00-20:30 Posters discussion (even numbers)
Thursday, June 4, 2009, 18:15 -19:45 Posters discussion (odd numbers)

If you or a co-author will not be able to be at your board at this time, please leave a note on your poster stating date and time when you will be present.

Wine and cheese meeting with speakers
Tuesday, June 2, 2009, 19:00 - 20:30
Thursday, June 4, 2009, 18:15 - 19:45

In order to make speakers more available to the participants we invite you all to participate in speaker/participant program. A speaker will be assigned a table (tables will be scattered around the various venues) so that the participants can come and talk and move around to various speakers.

Poster Removal
Friday, June 5, 2009, 12:30 – 14:00

Program Changes
The organizers cannot assume liability for any changes in the program due to external or unforeseen circumstances.

Registration Desk Opening Hours
Sunday, May 31, 2009 18:00 – 20:00
Monday, June 1, 2097 08:00 – 20:00
Tuesday, June 2, 2009 08:00 – 16:00
Wednesday, June 3, 2009 08:00 – 16:00
Thursday, June 4, 2009 08:00 – 16:00
Friday, June 5, 2009 08:00 – 16:00

Language
The official language of the conference is English (no simultaneous translation)

Slide and PowerPoint Preview Room
A slide and PowerPoint preview room will be available to all presenters.

Message Center
A Message Center will be available at registration desk.

Service Center
The following services will be available at cost of the Service Center: photocopying, typing, computer printouts.

Smoking Policy
The 6th ISABS Conference on Human Genome Project Based Applications in Forensic Science, Anthropology and Individualized Medicine is officially declared as a “Non-smoking-Conference”.

Special requirements
Registrants with special requirements for physical communication and dietary requirements should contact official service agency of the conference in advance.

Staff
If you should have any questions, the conference staff will be pleased to help you. It will be easy to recognize them by the special name badge they will be wearing.

Podcast
Lectures will be available at www.podcast.isabs.hr

General Information

Badges
Badges will be provided to participants, accompanying persons, exhibitors and press at registration and will be required for admission to all conference facilities and scientific and social events during the Meeting. The badges will be checked by security guards at the conference venue. Any individual who is not wearing an official meeting badge will be directed to the registration desk to register or, if already registered, to purchase a replacement badge. Handling fee for replacement badges is €10.

Bank Services
The official currency in Croatia is the Croatian kuna (HRK). To see current exchange rates provided by Croatian National Bank. The official exchange rates:
1 EUR = 7,37 HRK* (May 18, 2009)
1 USD = 5,47 HRK* (May 18, 2009)
* Please note that exchange rates are variable

Opening hours of official Banks
Banks and post offices are normally opened from 8:00 a.m. to 7:00 p.m., Monday through Friday and from 8:00 a.m. to 12:00 p.m. on Saturdays.

Cash Machines
ATMs accepting all major bank cards and credit cards are located at numerous sites in Split.

Electricity Supply
220-240 V, 50 Hz

Insurance
Participants need to make their own arrangements pertinent to health and travel. By registering for the 6th ISABS Conference on Human Genome Project Based Applications in Forensic Science, Anthropology and Individualized Medicine, participants agree that neither the organizers and its agents nor the sponsors and exhibitors nor the Hotel Le Meridien Lav, Split assume any liability whatsoever.

Restaurants
Most restaurants in Split are opened from 8:00 a.m. – 11:00 p.m. Service charges are included in the price, unless explicitly mentioned otherwise, but an additional tip of 5 to 10 percent is expected. Some restaurants may have a cover charge.

Shops
Shops in Split are usually opened from 8:00 a.m. – 9:00 p.m., Monday to Friday, and from 8:00 a.m. – 3:00 p.m. on Saturdays. Some are opened on Saturdays afternoon. Most shops accept major credit cards.

Taxi
Numerous Taxi stands are located throughout Split city centre and in front of the hotels. All receptionists will be glad to help you.

Hotel Information
At the Hotel Le Méridien Lav, Split a wide choice of accommodation offers luxury and modern comfort. The hotel is perfect choice for both leisure and business travelers. This five star luxury hotel is located at Podstrana on the Adriatic coast, approx 6 km south of historic Diocletian's Palace, the core of the Split and approx 30 mins from Split International Airport (SPU). The hotel is a fully integrated resort destination, unique within the Croatian market. It is the only internationally-affiliated hotel within the area of Split (Croatia's second commercial city and one of the largest ports on the Mediterranean) and it has the largest hotel convention facilities on the Adriatic. The Hotel enjoys a spectacular coastal position overlooking the sea, Split, and surrounding islands.

The highly acclaimed Le Méridien hospitality is reflected in the understated elegance of the 382 well appointed and large (min 32 sq.m.) Rooms and Suites, in 4 interlinked buildings, each of which boasts its own balcony or terrace and over 80% enjoy magnificent views over the sea towards Split and its many islands.

The leisure facilities include a world class Spa and Wellness Centre, with a long list of treatments and massages, the latest Fitness equipment and a circular indoor pool—all of which give an added impetus to the experience of rejuvenation. Other activities include retail therapy at the Shopping Arcade and Promenade, four tennis courts, water sports and scuba diving as well as an extensive animation/activities programme. The children have not been forgotten either as Le Méridien's Penguin Club provides creative activities which will arouse the senses and inventiveness of the Resort's younger guests.

There are three Restaurants and four Bars in the Hotel as well as five Restaurants and four Cafés and Bars overlooking the fascinating yachts in the Resort's very own Marina.

Other facilities: Underground Car Park for 350 cars, Medical Centre, Private Marina for 60 yachts, Non Smoking Rooms, Wheelchair friendly, Transfers from and to airport by Motor Launch, Shuttle Bus Service to Split, Night Club, Casino.

Congress tour
Wednesday, June 3, 2009
A boat trip to Island of Brač
Price per person: EUR 60 (transfer, local drink aboard, lunch)
Duration: half day
Departure by boat from the hotel's marina, private cruising towards Island of Brač. Our English speaking guide will explain you some facts about Croatian Adriatic, Split area and Brač Island. Arrival to Sutivan, small picturesque town on Brač island, short tour. Free time. Lunch on the boat.
Return cruising to the marina of the hotel Lav Le Meridien. Private boat cruising, English speaking licensed guide and lunch are included.

**Please note that congress tour is subject to alteration. Please check at registration desk.*

INVITED SPEAKERS

Melissa Barker (Applied Biosystems, Foster City, CA, USA)

Frederick Bieber (Harvard Medical School and Birgham and Women's Hospital, Boston, MA, USA)

Zoran Budimlija (NYC Office of Chief Medical Examiner, New York, NY, USA)

Cassandra Calloway (Children's Hospital & Research Center Oakland, Oakland, CA, USA)

Theresa Caragine (New York City Office of Chief Medical Examiner (NYC OCME) Department of Forensic Biology)

Michael Coble (Armed Forces DNA Identification Laboratory, Rockville, Maryland, USA)

Henry Erlich (Roche Molecular Systems, Alameda, CA, USA)

Michael F. Hammer (University of Arizona, Tucson, USA)

Eithan Galun (Hebrew University, Jerusalem, Israel)

Mitchell Holland (Forensic Science, Pennsylvania State University, University Park, PA, USA)

Edwin Huffine (Bode Technology Group, Lorton, VA, USA)

Francis Kalush (Rockville, MD,USA)

Sree Kanthaswamy (University of California, Davis, CA, USA)

Jean-Pierre Kocher (Mayo Clinic College of Medicine, Rochester, MN, USA)

Doron Lancet (The Weizmann Institute of Science, Rehovot, Israel)

Henry Lee (University of New Haven, West Haven and Connecticut Forensic Science Laboratory, Meriden, CT, USA)

José A. Lorente (Department of Legal Medicine, University of Granada, Granada, Spain)

Damir Marjanović (Institute for Genetic Engineering and Biotechnology Sarajevo, Sarajevo, B&H and Ruđer Bošković Institute, Zagreb, Croatia)

Adele Mitchell (Office of Chief Medical Examiner of New York City, New York, NY, USA)

Thomas Parsons (International Commission on Missing Persons, Sarajevo, B&H)

Richard J. Roberts (New England Biolabs, Ipswich, MA, USA)

Antti Sajantila (Department of Forensic Medicine, University of Helsinki, Helsinki, Finland)

Aleksandar Sekulic (Scottsdale, AZ, USA)

David I. Smith (Mayo Clinic College of Medicine, Rochester, MN, USA)

Mark Spigelman (Tel Aviv, Israel)

Kári Stefánsson (deCODE Genetics, Reykjavik, Iceland)

Andre Terzic (Mayo Clinic College of Medicine, Rochester, MN, USA)

Daniel Vanek (Forensic DNA Service, Prague, Czech Republic)

George Vasmatzis (Mayo Clinic College of Medicine, Rochester, MN, USA)

Scott A. Waldman (Jefferson Medical College, Thomas Jefferson University, PA, USA)

Elisa Wurmbach (New York City Office of Chief Medical Examiner (NYC OCME) Department of Forensic Biology)

6TH ISABS CONFERENCE ON HUMAN GENOME PROJECT BASED APPLICATIONS IN FORENSIC SCIENCE, ANTHROPOLOGY AND INDIVIDUALIZED MEDICINE

Hotel Le MERIDIEN LAV
Split
Croatia
June 1-5, 2009

SCIENTIFIC PROGRAM

Please note that the programme and speakers are subject to alteration.

All events take place at the Grand Dalmatia Conference Hall except where noted otherwise.

Sunday, May 31, 2009

18:00 -20:00 Registration and Poster Setup (Conference floor, lobby and foyer)

Monday, June 1, 2009

8:00 - 18:00 Registration

8:00 – 11:00 Poster Setup (Conference floor, lobby and foyer)

Perspectives in Genome-Based Science and Applications

8:30 Directors' Introductory Remarks

8:35 **Frederick Bieber** (Boston, MA, USA)
Shaking the family tree: Kinship analysis for forensic identification

9:10 **Michael Coble** (Rockville, MD, USA)
Identification of the two missing Romanoff children by forensic DNA analysis

9:45 Coffee Break

10:00 Inauguration of the Conference

10:30 **Henry Lee** (New Haven CT, USA)
Genetic markers in resolution of cold cases

11:05 **Andre Terzic** (Rochester, MN, USA)
Individualized regenerative medicine

11:40 **Zoran Budimlija** (New York, NY, USA)
Malignant tumors and forensics–dlemmas and proposals

12:15 Discussion

12:30 Opening of Sponsor Exhibits
(Conference floor, lobby and foyer)

Genome-Based Applications in Forensic Science I

15:00 Introduction from the chair (Antti Sajantilla)

15:05 **Sree Kanthaswamy** (Davis, CA, USA)
A validated canine STR reagent kit for use in forensic casework

15:40 **Daniel Vanek** (Prague, Czech Republic)
DNA typing of ancient bone samples

16:15 Young Investigator Award: **Antoinette Westen** (The Hague, Netherlands)
Tri–allelic SNP markers enable analysis of mixed and degraded DNA samples

16:30 Coffee Break

16:45 **Antti Sajantila** (Helsinki, Finland)
Post-mortem pharmacogenetics in medico-legal settings

17:20 **Damir Marjanović** (Zagreb, Croatia and Sarajevo, Bosnia-Herzegovina)
Challenges in identification of WWII human remains by the use of Y-STR and miniSTR

17:55 Discussion

20:00 Welcome Reception
(The Meštrović Gallery, Marjan)

Tuesday, June 2, 2009

Workshop on Low-Copy Number Analysis

8:30 Introduction from the chair (Mitchell Holland)

8:35 **Mitchell Holland** (University Park, PA, USA)
LCN STR analysis–what does it mean?

9:10 **Theresa Caragine** (New York, NY, USA)
Challenges in high-sensitivity DNA testing

9:45 Selected Oral Presentation: **Marie Korabecna** (Pilsen, Czech Republic)
Potential diagnostic use of cell-free DNA circulating in plasma

10:00 Coffee Break

10:15 Selected Oral Presentation: **Reena Roy** (University Park, PA, USA)
Generating DNA profiles from immunochromatographic cards using LCN methodology

10:30 **Mitchell Holland** (University Park, PA, USA)
Working with law enforcement to develop cold hits through LCN STR analysis

11:05 **Michael Coble** (Rockville, MD, USA)
Low template DNA protocols for human identification at AFDIL

11:40 Discussion

12:30-15:00 Poster and exhibit viewing (Conference floor, lobby and foyer)

Anthropology in Individualized Medicine

15:00 Introduction from the chair (Frederick Bieber)

15:05 **Michael Hammer** (University of Arizona,Tucson, AZ, USA)
What genome sequence data teach about human evolution

15:40 **Scott A. Waldman** (Philadelphia, PA, USA)
Molecular diagnostics for staging patients with cancer

16:15 **Frederick Bieber** (Boston, MA, USA)
Clinical utility of aCGH: genome–wide detection of aberrations and copy number changes

16:50 Young Investigator Award: **Pavlo Tatarskyy** (Kiev, Ukraine)
Individual genetic variables in recurrent pregnancy loss

17:05 Coffee Break

17:20 **Elisa Wurmbach** (New York, NY, USA)
Genetic markers in human pigmentation

17:55 **Mark Spigelman** (Tel Aviv, Israel)
Mummies and tuberculosis: Co-evolution of the pathogen and host

18:30 Discussion

19:00 Meet the Professor, poster discussion (even numbers), wine and cheese (Grand Dalmacija terrace)

Wednesday, June 3, 2009

08:30 Half–day Excursion

18:00 General Meeting of the International Society for Applied Biological Sciences

19:00 Special Lecture

20:00 Conference Dinner
Conferring Honorary ISABS Memberships and Young Investigator Awards

Thursday, June 4, 2009

Workshop on Next Generation DNA Sequencing

8:00 Introduction from the chair (David Smith)

8:05 **Doron Lancet** (Rehovot, Israel)
Genome medicine: juggling chips, SNPs and NextGen sequencing

8:40 **Jean-Pierre Kocher** (Rochester, MN, USA)
Analysis of NextGen sequencing data: Opportunities, challenges and potential impact of technology on clinical research

9:15 **George Vasmatzis** (Rochester, MN, USA)
Individualized risk-assessment of prostate and lung cancers

9:50 Coffee Break

10:05 **Aleksandar Sekulic** (Scottsdale, AZ, USA)
From genomics to individualized medicine-the example of malignant melanoma

10:40 **Melissa Barker** (Applied Biosystems, Foster City, CA, USA)
Next Generation sequencing: SOLiD applications

11:15 **David I. Smith** (Rochester, MN, USA)
Direct clinical applications of NextGen DNA sequencing at Mayo Clinic

11:50 Discussion

12:00 **Applied Biosystems Workshop:** The Technology of the SOLiD 3 System and a 360 degree view on Next-Generation Sequencing and Tag Counting Applications **Marco Pirotta and Chiara Reggio**

13:00-15:00 Poster and exhibit viewing (Conference floor, lobby and foyer)

Genome-Based Applications in Forensic Science II

15:00 Introduction from the chair (Edwin Huffine)

15:05 **Edwin Huffine** (Springfield, VA, USA)
Evolving applications of forensic DNA testing

15:40 **Cassandra Calloway** (Oakland CA, USA)
Novel approaches to forensic analysis of mtDNA polymorhpism

16:15 Young Investigator Award: **Chiara Barbieri** (Leipzig, Germany)
mtDNA variability in native Andean populations: the case of Lake Titicaca

16:30 Coffee Break

16:50 **Adele Mitchell** (Office of Chief Medical Examiner of New York City, New York, NY, USA)
Assessing comparisons of known and unknown DNA profiles and complex forensic mixtures based on empirical data

17:25 **Thomas Parsons** (Sarajevo, Bosnia and Herzegovina)
State of the art in complex mass fatality identification

18:00 Discussion

18:15 Meet the Professor, poster discussion (odd numbers), wine and cheese (Grand Dalmacija terrace)

Friday, June 5, 2009

Directors' Closing Symposium: Genes and Medicine

8:00 Directors' Introduction

8:05 **Henry Erlich** (Alameda, CA, USA)
Molecular diagnostics, predisposition and pharmacogenomics

8:40 **Richard Roberts** (Ipswich, MA, USA)
Impact of DNA on research and forensics; a personal perspective

9:15 **José Antonio Lorente** (Granada, Spain)
GENYO–Andalusian Center for Genomics and Oncology: forensic and medical applications of human genetic variability

9:50 Young Investigator Award: **Fernanda Gonçalves** (Sao Paolo, Brasil)
A new polymorphism in microRNA binding site of CDKN2A and XPD in malignant melanoma patients

10:05 Coffee Break

10:20 Selected Oral Presentation: **Adriana Nazarova** (Moscow, Russian Federation)
The relationship of German, Slavic and Finnish–Ugric populations from data on anthropogenetics and archeology

10:55 **Francis Kalush** (Rockville, MD, USA)
Paradigms of development of personalized medicine: A regulatory perspective

11:30 **Eithan Galun** (Hebrew University, Jerusalem, Israel)
Inflammation, regeneration and cancer; a gene and gene therapy story

12:05 **Kári Stefánsson** (Reykjavik, Iceland)
Genetics of common/complex traits as a foundation of individualized medicine

12:40 6th ISABS Conference adjourns. 7th ISABS Conference is announced.

ABSTRACTS – ORAL PRESENTATIONS

INVITED LECTURES

Abstract number: ABS-93-ISABS-2009

NEXT GENERATION SEQUENCING: SOLID™ APPLICATIONS

Barker M[1], Budowle B[2], Cummings C[1], Hyland F[1]

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The introduction of next generation sequencing technologies in recent years has helped redefine the landscape of possibility for the analysis of human variation. The SOLiD™ system from Applied Biosystems uses sequencing by ligation technology to perform massively parallel sequencing, able to produce more than 20 gigabytes of mapped data from a run, with greater than 99.94% accuracy. This technology has opened the door to many applications, including methylation analysis with and without bisulfite conversion, whole transcriptomics, small RNA profiling and discovery, ChIP-seq, targeted resequencing, and analysis of genetic variation through whole genome sequencing. Two applications of this technology will be examined in depth 1) Human genetic variation. Whole genome resequencing data generated as part of the 1000 Genome project will be presented. 2) Guided genome assembly of related diverse bacterial B. anthracis strains, identifying genomic diversity between these multiple related genomes.

Keywords: solid, sequencing, applications, next-gen, DNA

Abstract number: ABS-83-ISABS-2009

SHAKING THE FAMILY TREE: KINSHIP ANALYSIS FOR FORENSIC IDENTIFICATION

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Searching DNA databases for forensic purposes has been successful in identifying criminal suspects in hundreds of unsolved cases. Even more remarkable are cases solved after searches of the DNA database identify a suspect who is not actually in the database, but is closely related to someone who is. Such search successes can occur unexpectedly when close, but not quite identical, DNA matches are observed between crime scene samples and the profiles of known convicted offenders. For example, in North Carolina, retrospective DNA testing of evidence excluded Darryl Hunt who had been convicted of the 1984 murder of Deborah Sykes and had served eighteen years in prison. After Hunt's erroneous conviction was overturned, in 2003, laboratory scientists compared the crime scene DNA profile to the 40,000 offender profiles in the North Carolina state DNA database. While no perfect DNA matches were identified, incidentally a close but not perfect match was noted, leading to the conviction of Willard Brown. In other cases „familial searching“ is performed purposely in an attempt to identify suspects when no perfect DNA matches are found between crime scene samples and known offenders. Familial searching can be performed simply by direct allele count comparisons, searching for rare alleles, or by formal genetic kinship analysis of the entire offender database. This presentation will review the current status of familial searching around the world with specific emphasis on approaches to avoid unnecessary intrusion on privacy of uninvolved parties.

Keywords: forensic DNA, familial searching, CODIS, DNA database, crime

Suggested reading:

1. Bieber FR, Brenner CH, Lazer D. Finding Criminals Through the DNA of Their Relatives. Science 312: 1315-1316, 2006
2. Bieber FR. Shaking the Family Tree, Journal of Law, Medicine and Ethics Summer 2006, 222-233

Abstract number: ABS-82-ISABS-2009

CLINICAL UTILITY OF DNA ARRAYS: GENOME-WIDE DETECTION OF ABERRATIONS AND COPY NUMBER CHANGES

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DNA microarrays are useful in research, laboratory diagnostics and for study of heritable genomic variation. DNA microarrays offer novel possibilities for gene expression studies across the genome through monitoring the gene expression of hundreds of genes simultaneously. When combined with other biological and clinical information, microarray data also provide chances to identify genes associated with disease and to assay for copy number changes or variants (CNVs). This presentation will provide an overview of DNA arrays for use in medical genetics. Issues of reliability and informatics will be discussed, as will applications such as SNP genotyping, bioinformatics, and applications to forensics and human identification.

Keywords: DNA arrays, genomics, medical genetics, copy number changes, genetic disease

Suggested reading:

1. Bengtsson H, Ray A, Spellman P, Speed TP. A single-sample method for normalizing and combining full-resolution copy numbers from multiple platforms, labs and analysis methods
2. Carter NP. Methods and strategies for analyzing copy number variation using DNA microarrays. Nature Genetics 39, S16 - S21, 2007
3. Perry GH, Ben-Dor A, Tsalenko A, et al. The fine-scale and complex architecture of human copy number variation. Am J Hum Genet 82:685-695, 2008

Abstract number: ABS-75-ISABS-2009

MALIGNANT TUMORS AND FORENSICS – DILEMMAS AND PROPOSALS

Budimlija Z[1], Lu C[1], Axler-DiPerte G[1], Seifarth J[1,2], Popiolek D[3], Fogt F[4], Prinz M[1]

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Genetic instability manifests as expansion, contraction or loss of microsatellite DNA repetitive sequences. The aim of this study was to evaluate whether biological variability of archived histology samples influenced the validity of human identity testing, and assess its effect on the statistical significance required for human identification when these samples were used as exemplars. 228 slides of archival pathology tissues from 13 different types of malignant tumors were processed, analyzed and compared to healthy tissues from the same individuals. Analysis of nuclear DNA was performed using standard validated techniques for forensic STR analysis, with two platforms: PowerPlex16 (Promega) and Identifiler (ABI). The extent of genetic instability was assessed by comparing reference tissues to pathologically altered tissues derived from the same individual. Loss of Heterozygosity (LOH), defined by a ≥50% reduction in HR between healthy and diseased samples, and Microsatellite Instability (MSI), defined as the presence of an additional allele in the sample not present in reference tissue, were assessed. Expressed mathematically LOH ratios were calculated according to the formula [A1/A2]diseased/[A1/A2]healthy, where a ratio between 0.51 and 1 indicates no change from the reference tissue. Ranges between 0.0-0.5 and ≥2 indicated LOH. Comparisons were made with respect to the intensity of the signal peak and the size of the fragments, as well as to peak balance/imbalance. This allowed us to establish firm criteria to distinguish effects of tissue degradation vs. genetic instability. Using this information we were able to recommend rules for interpretation of these potentially problematic samples.

Keywords: Forensic STR typing, Reference samples, Malignant tumors, Genetic instability, interpretation issues

Abstract number: ABS-85-ISABS-2009

NOVEL APPROACHES TO FORENSIC ANALYSIS OF MITOCHONDRIAL DNA POLYMORPHISM

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The hypervariable regions I/II (HVI/II) of the mitochondrial genome are routinely targeted by forensic DNA laboratories for the analysis of limited and/or degraded samples. However, there are limitations to targeting only the hypervariable regions I/II independent of the method of analysis. The power of discrimination is limited for all population groups as a result of a few common HVI/II sequences. Most notably, seven percent of Caucasians share the same common HVI/II sequence (differing from the rCRS at 263G). To increase the informativeness of mtDNA analysis, additional sequence polymorphisms outside the HVI/II regions need to be targeted. A highly sensitive, easy to use 5-plex and 10-plex PCR and linear array assay was developed for analysis of polymorphic regions distributed throughout the mitochondrial genome. This assay targets 61 polymorphic sites using 15 primer pairs and a total of 105 sequence specific oligonucleotide probes. Population and validation data are presented here to illustrate the increased discrimination power as well as the ease of use of this assay. These data show that the discrimination power was greatly increased for all populations by targeting an additional 43 polymorphic sites beyond that of the HVI/II linear array assay (18 sites). The application of Next-Generation sequencing (454 GS FLX) to mtDNA analysis will also be discussed.

Keywords: mitochondrial DNA, LINEAR ARRAY, Next Generation DNA Sequencing, HVI/HVII Regions, Coding Region

Suggested reading:

1. Gabriel, Matthew N., Cassandra D. Calloway, Rebecca L. Reynolds, Simun Andelinovic, and Dragan Primorac. (2001) Population Variation of Human Mitochondrial DNA Hypervariable Regions I and II in 105 Croatian Individuals Demonstrated by Immobilized Sequence-Specific Oligonucleotide Probe Analysis. Croat Med J 42 (3):328-335
2. Gabriel, Matthew N., Cassandra D. Calloway, Rebecca L. Reynolds, Simun Andelinovic, and Dragan Primorac. (2003) Identification of human remains by immobilized sequence-specific oligonucleotide probe analysis of mtDNA hypervariable regions I and II. Croat Med J, 2003. 44(3): p. 293-8
3. Divne, Anna-Maria, Martina Nilsson, Cassandra Calloway, Rebecca Reynolds, Henry Erlich and Marie Allen. (2005). Forensic Casework mtDNA analysis using a Reverse HVI-HVII Sequence-Specific Oligonucleotide Probe Assay. J. Forensic Sci. 50(3): 548-554
4. Kline, Margaret C., Peter M. Vallone, Janette W. Redman, David L. Duewer, Cassandra D. Calloway, and John M. Butler. (2005). Mitochondrial DNA Typing Screens with Control Region and Coding Region SNPs. J. Forensic Sci 50(2): 1-9
5. Florence Mauger, Keith Bauer, Cassandra D. Calloway, Jérémy Semhoun, Tetsuya Nishimoto, Thomas W. Myers, David H. Gelfand and Ivo G. Gut. (2007). DNA sequencing by MALDI-TOF MS using alkali cleavage of RNA/DNA chimeras. Nucleic Acids Res 35(8):e62

Abstract number: ABS-77-ISABS-2009

ADDRESSING CHALLENGES TO LOW TEMPLATE DNA ANALYSIS

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The analysis of Low Template DNA for forensic purposes presents several technical and legal challenges such as evaluating the weight and the probative nature of the DNA results. The protocols and the analytical tools currently used to meet these challenges will be addressed. Determining the DNA profiles of the individual contributors to a mixture may not always be feasible rather some mixtures may only be suitable for comparison. Since some DNA alleles may not be detected, a suspect's alleles, for example, may be present at all loci with the exception of one or two alleles. Similarly, there may be alleles that that are present that cannot be attributed to known DNA sources. Our laboratory is developing formulae and a software program that will give a statistical weight to this comparison while considering these stochastic events based on empirical data. Until this program is validated, one must be careful in reporting DNA results such that the consequence of these phenomena is properly conveyed. Furthermore, the significance of detecting a person's DNA on a handled item depends upon the circumstances of the case. The relevant issue is often whether one would expect that the person in question touched an item previously. Regarding how DNA is deposited on an item, studies from our laboratory will be discussed that show that tertiary transfer was not detected. In other words, if person A touched object 1, then person B touched object 1 followed by object 2, person A's DNA was not detected on object 2.

Keywords: Low Template DNA, Allelic dropout, Allelic drop-in, Tertiary transfer, Secondary transfer

Suggested reading:

1. Gill P. Application of Low Copy Number DNA Profiling. Croat Med J. 2001 Jun;42(3):229-32. Review
2. Gill P, Curran J, Neumann C, Kirkham A, Clayton T, Whitaker J, and J Lambert. 2008. Interpretation of complex DNA profiles using empirical models and a method to measure their robustness. Forensic Sci Int Genet. Mar 2 (2):91-103
3. Gill P, Brenner CH, Buckleton JS, Carracedo A, Krawczak M, Mayr WR, Morling N, Prinz M, Schneider PM, and BS Weir; DNA commission of the International Society of Forensic Genetics. Recommendations on the interpretations of mixtures. Forensic Sci Int. 2006 Jul 13;160(2-3):90-10
4. Lowe A, Murray C, Whittaker J, Tully G, and P Gill. The propensity of individuals to deposit DNA and secondary transfer of low level DNA from individuals to inert surfaces. Forensic Sci Int. Sep 10;129(1):25-34
5. Phipps M and'sPetricevic. 2007. The tendency of individuals to transfer DNA to handled items. For Sci Int. May 24;168(2-3):162-8

Abstract number: ABS-88-ISABS-2009

THE IDENTIFICATION OF THE TWO MISSING ROMANOV CHILDREN USING DNA ANALYSIS

Coble MD[1], Loreille OM[1], Wadhams MJ[1], Edson SM[1], Maynard K[1], Meyer CE[1], Niederstätter H[2], Berger C[2], Berger B[2], Falsetti AB[3], Gill P[4,5], Parson W[2], Finelli LN[1]

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For over 300 years, the Romanov Dynasty ruled the country of Russia. In 1917 following the Bolshevik revolution, the last Russian Tsar, Nicholas II, abdicated his throne and was eventually exiled to Yekaterinburg with his wife, Tsarina Alexandra, and their five children: Olga, Tatiana, Maria, Anastasia, and the Tsarevich Alexei. Also present with the royal family were four loyal servants: Dr. Botkin, the family physician; Mr. Trupp, valet to the Tsar; Ms. Demidova, maid to the Tsarina; and Mr. Kharitonov, the family cook. In July of 1918, the Bolsheviks feared an attempt to rescue the Tsar and his family by the White Russian Army. A decision was made by the Bolsheviks to execute the entire family, with the hope that upon hearing of the Tsar's death the will of the people loyal to the Tsar would be broken. In the early morning hours of July 17, 1918 the royal family and their servants were led to the basement of the Ipatiev house where they were being held and were executed. In the late 1970s, a local geologist discovered the mass grave containing most of the royal family and their servants, and following the fall of the Soviet Union in 1991, an official recovery was conducted. Forensic DNA testing of the remains recovered in 1991 was conducted by Dr. Peter Gill, formerly of the Forensic Science Service and Dr. Pavel Ivanov, a Russian geneticist. Nuclear STR testing of five loci confirmed the sex of the skeletons and established a familial relationship among the remains of the Tsar, the Tsarina and three of their daughters recovered from the same grave. Mitochondrial DNA testing confirmed a maternal relationship between HRH Prince Philip, the Duke of Edinburgh, and the Tsarina (and her daughters). The Duke of Fife and Princess Xenia were used to match the putative remains of the Tsar. A single point heteroplasmy at position 16169 (C/T) was observed in the mtDNA sequence of the Tsar, whereas his maternal relatives were fixed for 16169 T. In testing conducted at the Armed Forces DNA Identification Laboratory (AFDIL), the identity of the Tsar was further confirmed by the mtDNA heteroplasmy shared with Grand Duke Georgij Romanov, brother of Tsar Nicholas II. Despite the overwhelming forensic evidence, doubts about the authenticity of the remains persisted. Skeptics often referenced the two children missing from the mass grave - Alexei and one of his sisters, either Anastasia or Maria. The missing remains also encouraged the beliefs held by some that these two children had somehow miraculously escaped the bullets of the executioners and made their way out of Russia. The most

famous case was Anna Anderson, who claimed to be the Grand Duchess Anastasia. Forensic DNA testing eventually disproved her claim. After the discovery of the „first“ mass grave, several attempts were made in the following years to find the „second“ grave containing the two missing children, which was believed to be relatively nearby. In the summer of 2007, a group of amateur archeologists discovered a set of 44 bone fragments and teeth approximately 70 meters from the „first“ grave. In late 2007, the Russian government invited a team of scientists to conduct an independent forensic DNA testing of the remains from the „second“ grave. We will present results from mtDNA, nuclear STR, and Y-STR testing of these remains. DNA testing on the skeletal remains from the „first“ grave that conclusively link the two graves will also be presented. The results from the DNA analysis of all three genetic systems confirms that the samples tested from the second grave are one female and one male child of Tsar Nicholas II and Tsarina Alexandra, and resolves the mystery of the missing Romanov children.

Keywords: Romanov Family, Ancient DNA, LCN Typing, mtDNA and Y-STRs, Forensic DNA

Suggested reading:

1. Gill P, Ivanov PL, Kimpton C, Piercy R, Benson N, Tully G, Evett I, Hagelberg E, Sullivan K. (1994) Identification of the remains of the Romanov family by DNA analysis. Nat Genet. 6(2): 130-135
2. Ivanov PL, Wadhams MJ, Roby RK, Holland MM, Weedn VW, Parsons TJ. (1996) Mitochondrial DNA sequence heteroplasmy in the Grand Duke of Russia Georgij Romanov establishes the authenticity of the remains of Tsar Nicholas II. Nat Genet. 12(4): 417-420
3. Gill P, Kimpton C, Aliston-Greiner R, Sullivan K, Stoneking M, Melton T, Nott J, Barritt S, Roby R, Holland M, Weedn, V. (1995) Establishing the identity of Anna Anderson Manahan. Nat Genet. 9(1): 9-10
4. Zhivotovsky LA (1999) Recognition of the remains of Tsar Nicholas II and his family: a case of premature identification? Ann Hum Biol 26: 569-77
5. Coble MD, Loreille OM, Wadhams MJ, Edson SM, Maynard K, et al. (2009) Mystery Solved: The Identification of the Two Missing Romanov Children Using DNA Analysis. PLoS ONE 4(3): e4838.

Abstract number: ABS-87-ISABS-2009

EVALUATION OF A MODIFIED Y-FILER AMPLIFICATION STRATEGY FOR COMPRIMISED SAMPLES

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To further characterize the data produced using a modified amplification protocol for the Yfiler™ amplification kit and further explore the potential of Y-STR recovery from severely degraded skeletal remains encountered at the Armed Forces DNA Identification Laboratory (AFDIL). Experiments were performed using two sets of Yfiler™ amplification parameters. One set of parameters reflected the manufacturer's recommendations. The second set of parameters included twice the recommended Taq concentration and six additional cycles. Recovery of authentic alleles and the incidence of drop-in alleles were assessed for three data sets: dilute pristine DNA samples, artificially-degraded samples and non-probative case samples. Samples tested with both protocols from all three data sets yielded twice as many authentic alleles under the modified parameters than under the standard parameters (62% versus 31%, respectively), with only a nominal associated increase in the occurrence of non-authentic alleles (1.36% of all alleles detected). When applied to a range of representative casework samples, the modified protocol leveraged 9 or more reproducible alleles from over half of the specimens tested. Reproducible and informative Y-STR profiles can be recovered from a broad range of degraded and inhibited skeletal remains extracts when a commercially available kit is employed under modified amplification parameters.

Keywords: Degraded DNA, LCN Typing, Y-STR Analysis, Y-Filer, Forensic DNA

Suggested reading:

1. Gill P, Whitaker J, Flaxman C, Brown N, Buckleton J. An investigation of the rigor of interpretation rules for STRs derived from less than 100 pg of DNA. Forensic Sci Int. 2000; 112: 17-40
2. Gill P. Application of low copy number DNA profiling. Croat Med J. 2001; 42: 229-32
3. Taberlet P, Griffin S, Goossens B, Questiau S, Manceau V, Escaravage N, et al. Reliable genotyping of samples with very low DNA quantities using PCR. Nucleic Acids Res. 1996

Abstract number: ABS-64-ISABS-2009

MOLECULAR DIAGNOSTICS, PREDISPOSITION, AND PHARMACOGENETICS

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Based on extensive genetic association studies, molecular diagnostic genotyping tests can now identify individuals with a high risk for a specific disease or for a specific response to a particular drug. The HLA class I and class II genes, the most polymorphic genes in the human genome, influence specific immune responses and have been highly associated with predisposition to a variety of autoimmune diseases as well as to allergic hypersensitive responses to certain drugs. For example, the HLA-B*5701 allele is highly predictive of a potentially fatal allergic hypersensitive response to the HIV drug, abacavir (Mallal et al, 2008). In the management of HIV patients, individuals with this allele would be treated with HIV drugs other than abacavir. We have developed a B*5701- specific real-time PCR assay on the Cobas AmpliPrep/Cobas Taqman instrument, the same platform used to measure HIV viral load. Specific HLA alleles are also highly associated with type 1 diabetes (T1D) Data from the Type 1 Diabetes Genetics Consortium (T1DGC) (Rich et al, 2006), an international consortium that has collected thousands of simplex and multiplex families, will be presented and discussed. Highly susceptible as well as highly protective DRB1-DQA1-DQB1 haplotypes have been identified; a specific genotype, DRB1*0301-DQA1-*0501-DQB1*0201/DRB1*0405-DQA1*0301-DQB1*0302 has an OR of around 40 (Erlich et al, 2008). In addition, alleles at the HLA-A and B loci as well as DPA1-DPB1 haplotypes also contribute to T1D risk. Pharmacogenetic and predisposition tests, such as those discussed above, promise to usher in a new era of personalized medicine in which individual patients are treated based on their genotypes at specific clinically informative genes.

Keywords: HLA, Type 1 Diabetes, Abacavir, prediction, genetic association

Suggested reading:

1. Mallal S, Phillips E, Carosi G, Molina JM, Workman C, Tomazic J, Jägel-Guedes E, Rugina S, Kozyrev O, Cid JF, Hay P, Nolan D, Hughes S, Hughes A, Ryan S, Fitch, N, Thorborn D, Benbow A; PREDICT-1 Study Team. HLA-B*5701 screening for hypersensitivity to abacavir. N Engl J Med. 2008 Feb 7;358(6):568-79.
2. Rich SS, Concannon P, Erlich H, Julier C, Morahan G, Nerup J, Pociot F, Todd JA: The Type 1 Diabetes Genetics Consortium. Ann N Y Acad Sci 1079:1-8, 2006
3. Erlich H, Valdes AM, Noble J, Carlson JA, Varney M, Concannon P, Mychaleckyj JC, Todd JA, Bonella P, Fear AL, Lavant E, Louey A, Moonsamy P; Type 1 Diabetes Genetics Consortium. HLA DR-DQ haplotypes and genotypes and type 1 diabetes risk: analysis of the type1 diabetes genetics consortium families. Diabetes. 2008 Apr;57(4):1084-92

Abstract number: ABS-106-ISABS-2009

SEX-BIASED EVOLUTIONARY FORCES SHAPE GENOMIC PATTERNS OF HUMAN

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Like many primate species, the mating system of humans is considered to be moderately polygynous (i.e., males exhibit a higher variance in reproductive success than females). As a consequence, males are expected to have a lower effective population size (Ne) than females, and the proportion of neutral genetic variation on the X chromosome (relative to the autosomes) should be higher than expected under the assumption of strict neutrality and an equal breeding sex ratio. We test for the effects of polygyny by measuring levels of neutral polymorphism at 30 independent loci on the X chromosome and 61 autosomal loci in six human populations. To correct for mutation rate heterogeneity among loci, we divide our diversity estimates within human populations by divergence with orangutan at each locus. Consistent with expectations under a model of polygyny, we find elevated levels of X-linked versus autosomal diversity. While it is possible that multiple demographic processes may contribute to the observed patterns of genomic diversity (i.e., background selection, changes in population size, and sex-specific migration), we conclude that an historical excess of breeding females over the number of breeding males can by itself explain most of the observed increase in effective population size of the X chromosome.

Keywords: Genomic Patterns

Abstract number: ABS-107-ISABS-2009

FROM INFLAMMATION THROUGH REGENERATION TO CARCINOGENESIS

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Chronic inflammation is considered as one of the major causes of cancer, accounting for nearly 20% of human cancers. Hepatocellular carcinoma (HCC) is the third leading cause of cancer mortality worldwide and considered to be the outcome of chronic liver inflammation. Surgical resection is the preferred treatment for HCC; however, survival rates are suboptimal partially due to tumor recurrence. Our objective was to understand the molecular mechanisms linking liver regeneration under chronic-inflammation to tumorigenesis. Mdr2-knockout mice, a model of inflammation-associated cancer, had undergone partial-hepatectomy, and experienced enhanced hepatocarcinogenesis. Yet, liver regeneration in these mice was severely attenuated. The inflamed livers had elevated levels of double stranded DNA breaks and a genomic-instability signature resulting in hepatocyte apoptosis and cell-cycle arrest. We propose that under the regenerative proliferative stress, the genomic-unstable hepatocytes escape apoptosis and reenter the cell cycle, causing the enhanced tumorigenesis induced by liver resection.

Keywords: inflmmation, cancer, regeneration, hepatocarcinogenesis, MRI

Suggested reading:

1. Toll-like receptor 3 signaling attenuates liver regeneration. Zorde-Khvalevsky E, et al Hepatology 2009
2. HCV tumor promoting effect is dependent on host genetic background.Klopstock N. PLoS One 2009
3. Functional magnetic resonance imaging monitoring of pathological changes in rodent livers during hyperoxia and hypercapnia. Barash H. Hepatology 2008
4. Molecular mechanisms of liver carcinogenesis in the mdr2-knockout mice. Katzenellenbogen M. Mol Cancer Res 2007
5. The H19 non-coding RNA is essential for human tumor growth. PLoS One 2007

Abstract number: ABS-95-ISABS-2009

LCN STR ANALYSIS: WHAT DOES IT MEAN?

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At what point does STR analysis enter a low copy number (LCN) realm? The ideal target for most STR multiplex systems is 0.5-2 ngs of starting template DNA. However, analyses of far lower quantities of DNA are routinely conducted in crime laboratories. In many instances, the low end of the range will approach 100 pgs of starting template. At this level, and assuming an expected 6-6.6 pgs of DNA per cell, a scientist is sampling 15-16 cells worth of DNA in an extract volume of 5-10 uL being added to the PCR reaction. The concentration of DNA in this volume of liquid would need to be approximately 10-20 pgs/uL in order to reach the target of 100 pgs. This is below the standard range of quantification assays, so in many cases, the amount of input DNA is lower than the expected 100 pgs. Given this knowledge, and assuming that standard PCR conditions are being run, should this be considered LCN STR analysis? Most laboratories do not claim to be doing LCN analysis unless the PCR conditions are altered (e.g., increased PCR cycle numbers) or the approach to the analysis process has changed (e.g., altered extraction methods). As forensic scientists, we need to be careful of how we classify LCN STR analysis. The influence of stochastic sampling from extracts containing low quantities of DNA have been well documented, and will have an impact on the way profile data is interpreted. As a result, guidelines need to be adjusted to maintain the reliability and integrity of the reported profile information. This becomes especially important when conclusions are being drawn regarding matches or with the appearance of potential minor contributors of unknown origin. These and other issues will be discussed during this presentation.

Keywords: STR, Low Copy Number, Interpretation, Guidelines, Admissibility

Suggested reading:

1. Gill P (2001) Application of Low Copy Number DNA Profiling, CMJ 42(3), p. 229-32
2. Gill P, Kirkham A, Curran J (2007) LoComatioN: A software tool for the analysis of low copy, FSI 166, p. 128-38

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WORKING WITH LAW ENFORCEMENT TO DEVELOP COLD HITS THROUGH LCN STR ANALYSIS

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The value of CODIS and international offender databases has been clearly illustrated for more than a decade. Comparison of offender DNA profiles to scene profiles continues to serve as a central means for identify potential perpetrators across State or Country lines, helping to solve cold cases that would otherwise remain unsolved. However, the majority of crime occurs locally, and involves local offenders. In addition, most of the DNA analysis performed in crime laboratories focuses on violent crime. When considering property crime, not only are the offenders primarily local, but the cases tend to be low priority and may never be sent to the laboratory for analysis. However, it has also been clearly illustrated that petty thieves commit serious felonies when the opportunity presents itself; for example, committing an assault, rape or murder when caught in the act of a robbery. Numerous studies and projects have been conducted between laboratory personnel and law enforcement to assess touch evidence found at crime scenes involving property and robbery-related offenses. A U.S. Department of Justice report from April of 2008 demonstrated that the use of DNA analysis in property crime cases identified twice as many suspects, resulted in twice as many arrests, and led to twice as many cases being accepted for prosecution. While Great Britain has been using this approach since 2001, the United States has been slow to follow. Nonetheless, one of the missing components of the current approach has been the delivery of a database searching tool directly into the hands of law enforcement. LODIS™ (Local DNA Index System) is an investigative software tool that allows the status of submitted samples and the results of DNA hits to be downloaded directly to police agencies through a secure internet connection. This eliminates the need to go through a CODIS laboratory to perform the DNA analysis, the database searches, and the release of hit information on local crimes. While the data is not compared to an offender database, it can be used to link cases with local offenders and can be used to identify potential perpetrators from identified suspects. The challenges surrounding the implementation of LODIS, including sample collection and assessment of laboratory techniques for processing high volumes of touch evidence containing low quantities of DNA, will be discussed during this presentation.

Keywords: Police, Software, Searching, DNA, Local

Suggested reading:

1. Roman JK, Reid S, Reid J, Chalfin A, Adams W, Knight C (2008) The DNA Field Experiment: Cost-Effectiveness Analysis of the Use of DNA in the Investigation of High-Volume Crimes, NCJ 222318
2. Phipps M, Petricevic's(2007) The tendency of individuals to transfer DNA to handled items, FSI 168, p. 162-68

Abstract number: ABS-103-ISABS-2009

EVOLVING APPLICATIONS OF FORENSIC DNA TESTING

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As greater experience in DNA testing continues to develop and the results provided by DNA testing increase, a better understanding of how such testing can be used to combat various types of crimes and violent acts is established. This understanding has led to improved methodologies in the testing process as well as a greater comprehension of what information is contained within the DNA data. Not only is information about the individual owner of biological material present in DNA data, but patterns associated with organized criminal behavior may also be revealed. In this manner, organized criminal and violent activity may provide patterns that can be determined by DNA testing. For example, if government organized and sponsored rape is allegedly occurring, DNA testing would show if the same set of male profiles is associated with multiple victims over a widely dispersed region. By evaluating if that particular area is undergoing significant upheavals and/or is experiencing conditions that make travel hazardous, questions can then be asked about how these males maintain mobility. In addition, patterns may exist in conjunction with human trafficking and sex slavery. Therefore, once the existence of these patterns has been established through the use of DNA testing, the question of why these patterns are present can then be answered. In this manner, both the individuals who left biological samples at the crime scene and those who helped organize such activities may one day be held accountable.

Keywords: Human Trafficking, Government Sponsored Rape, Sex Slavery, Judicial, Criminal

Suggested reading:

1. Developing Role of Forensics in Deterring Violence and Genocide. Croat Med J. 2007; 48:431-6
2. Edwin Huffine, John Crews, Jon Davoren;International Impact of Forensic DNA Testing, Forensic Magazine, Oct - Nov 2008, 23 - 29
3. Ed Huffine;Latin America Turns to DNA Tests to Solve War Crimes, Reuters, December 14th, 2005, Mica Rosenberg
4. Stringing Together the Clues of DNA, The Washington Post, Sep 12, 2008, Michael Laris

Abstract number: ABS-80-ISABS-2009

PARADIGMS IN THE DEVELOPMENT OF PERSONALIZED MEDICINE: REGULATORY PERSPECTIVE

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A regulatory perspective in the paradigms for personalized medicine development and recent FDA initiatives to facilitate the integration of pharmacogenomics into drug development will be discussed. Major challenges such as development of strong scientific evidence, evolving regulatory models and understanding clinical utility are essential to bring these tests into routine clinical practice. Regulatory principles for personalized medicine and co development of a companion drug-diagnostics in oncology will be presented using colorectal, breast and lung cancer examples. For colorectal cancer, changes in scientific knowledge for EGFR and KRAS in targeted therapy subsequently changed clinical practice and raised new regulatory challenges.

Keywords: personalized medicine, pharmacogenomics, companion drug-diagnostics, co-development, regulatory perspective

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A CANINE STR REAGENT KIT FOR USE IN FORENSIC CASEWORK

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Canine DNA evidence remains largely untapped in forensic investigations and this is partially attributed to the lack of well-defined forensic STRs, and the lack of validated canine forensic PCR/STR reagent kits, poorly developed nomenclature and no allelic ladders also contribute to this under-utilization. The low likelihood of obtaining informative STR profiles from shed hair evidence further compound this indifference among the human forensic community regarding the value of non-human DNA evidence. Canine databases thus far are predominated by purebred dogs registered with kennel clubs and were originally established via routine parentage and pedigree assessment or for other non-forensic objectives. Therefore there is scant information on the genetic structure of outbred or mixed breed dogs. We have developed and validated a canine-specific 5-flurorescence dye-based 19-plex including gender typing markers, that is robust, reliable and informative for regionally representative dogs including mixed and purebred dogs. Development validation studies to determine the robustness and reliability in forensic DNA typing of this multiplex assay include sensitivity testing, reproducibility studies, intra- and inter-locus color balance studies, annealing temperature and cycle number studies, peak height ratio determination, characterization of artifacts such as stutter percentages and dye blobs, mixture analyses, species-specificity, case type samples analyses and population studies. The reagent kit robustly amplifies domesticated dog samples and consistently generates full 19-locus profiles from as little as 125 pg of dog DNA. In addition, wolf DNA samples can be analyzed with our kit. We have developed the components needed for broader use of the canine STR typing by the forensic community including allelic nomenclature, and a regional database.

Keywords: Domesticated dog, breed and geographic sampling, population genetics, mtDNA, non-human forensics

Suggested reading:

1. Smalling, B.B., Satkoski, J.A., Tom, B.K., Szeto, W.Y., Erickson, B.J-A., Spear, T.F., Smith, D.G., Budowle, B., Webb, K.M., Allard, M. and Sreetharan Kanthaswamy (submitted). The significance of regional and mixed breed canine mtDNA databases in forensic science. Journal of Forensic Science
2. Tom, B.K., Koskinen, M.T., Dayton, M.R., Mattila, A-M., Johnston, E., Fantin, D., DeNise, S., Spear, T., Smith, D.G., Satkoski, J., Budowle, B., Sreetharan Kanthaswamy (submitted). Development of a Nomenclature System for a Canine STR Multiplex Reagent Kit. Journal of Forensic Science
3. Sreetharan Kanthaswamy, Tom, B.K., Mattila, A-M., Johnston, E., Dayton, M., Kinaga, J., Erickson, B., J-A., Halverson, J., Fantin, D., DeNise, S., Kou, A., Malladi, V., Satkoski, J., Budowle, B., Smith, D.G., Koskinen, M.T. (in press). Canine Population Data Generated from a Multi-Plex STR Kit for Use in Forensic Casework. Journal of Forensic Science
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Abstract number: ABS-92-ISABS-2009

ANALYSIS OF NEXT GENERATION SEQUENCING DATA. OPPORTUNITIES, CHALLENGES AND POTENTIAL IMPACT OF THIS TECHNOLOGY ON CLINICAL RESEARCH.

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The recent development of a new generation of high-throughput, high-coverage genomic sequencing platforms will enable, in the near future, the cost effective sequencing of complete individual human genomes. Mayo Clinic has recently acquired 2 Illumina GS2 platforms and is in the process of acquiring a long read Roche-454 GS/FLX sequencer. The Bioinformatics Core has been working in collaboration with investigators to validate the platforms. This presentation summarizes some of the work done, discuss analytical and IT infrastructure challenges and summarized advantages and limitations of NextGen technology.

Keywords: Genomics, Bioinformatics, Next generation sequencing, Data Management, Data Analysis

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GENOME MEDICINE: JUGGLING CHIPS, SNPS AND NEXTGEN SEQUENCING

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Genome medicine is now witnessing a true revolution. This is brought about an avalanche of novel technologies, all centered on a capacity to compare human genomes in exquisite detail. Such revolution was initiated some years ago by expression microarrays, and is now continuing with the advent of high throughput single nucleotide (SNP) and copy number variation (CNV) microarrays. The most exciting development relates to next generation (next-gen or deep) DNA sequencing, a set of related technologies that afford the sequencing of several gigabases of DNA in a one-week experiment for a few thousand dollars. When put together, all these DNA sequence-related methods allow one to obtain, in unprecedented accuracy, a complete genome variation picture for numerous human individuals. In the realm of monogenic diseases, affordable whole-exome sequencing will soon make it possible to discover rare mutations in diseases for which only very few affected individuals are available. We are currently generating a consortium in Israel to employ this approach, and plan to join forces with similar efforts elsewhere. In parallel, we are using the human olfactory sub-genome, encompassing 500 olfactory receptor (OR) genes and segregating pseudogenes (loci for which only some subjects an intact open reading frame) as a testbed for genome variation technology innovations. We are striving for a complete OR variation picture, including deleterious SNPs and small indels, as well as null alleles for entire genes in the realm of CNVs. Such a project, addressing about 0.1% of the extent of the human genome, can teach us important lessons relevant to polygenic diseases and pharmacogenetics.

Keywords: next-generation sequencing, Single nucleotide polymorphism, copy number variation, genetic disease, olfaction

Suggested reading:

1. Hasin, Y*., Olender, T*., Khen, M., Gonzaga-Jauregui C., M. Kim, P., Eckehart Urban, A., Hasin, Y., Lancet, D. and Olender, T., Human olfaction: from genomic variation to phenotypic diversity, Trends Genet. 25:178-184 (2009)
2. Menashe, I., Man, O., Lancet, D. and Gilad, Y. Different noses for different people. Nature Genetics. 34(2): 143-144 (2003)
3. Grossman, I., Avidan, N., Singer. C., Goldstaub, D., Hayardeny, L., Eyal, E., Ben-Asher, E., Paperna, T., Lancet, D., Beckmann, J.S. and Miller, A. Pharmacogenetics of Glatiramer Acetate therapy for Multiple Sclerosis reveals drug-response markers. Pharmacogenetics and Genomics 17:657-666 (2007)
4. Yanai, I., Benjamin, H., Shmoish, M., Chalifa-Caspi, V., Shklar, M., Ophir, R., Bar-Even, A., Horn-Saban, S., Safran, M., Domany, E., Lancet, D. and Shmueli, O. Genome-wide midrange transcription profiles reveal expression level relationships in human tissue specification. Bioinformatics 21(5):650-659 (2005)

Abstract number: ABS-60-ISABS-2009

THE UTILIZATION OF FORENSIC EVIDENCE

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Recognition of Forensic evidence and laboratory analysis of physical evidence can be helpful in directing an investigation along a productive path. Not all types of physical evidence will be directly linked to or can identify a suspect. In fact, most common use of physical evidence found at crime scenes is to identify the substance or chemical present in the question sample. However, physical evidence could provide indirect investigative information or leads to the solution of the crime. This is the most important and significant use of physical evidence collected from crime scenes. Not every crime scene will have a smoking gun or an eyewitness, but the scene will hold physical evidence that can provide help to the investigating officers. For example, in a hit-and-run investigation, a seven-layer paint chip from the victim's clothing can be used to narrow down the number and kinds of cars that could have been involved in the accident. The size of a shoeprint found at the scene can help the investigator to eliminate or include a suspect; the DNA profiles from the semen on a victim's rape kits can lead to a potential suspect; The number of different types of spent casings could indicate the number and types of weapon used in a crime; the locations of the blood spatters and the fingerprint impressions could yield information about a possible sequence of events at the scene, and the condition of the pattern evidence could also help identify the activity of the scene. Following are the objectives of utilization of forensic evidence found at a crime scene in any investigations: 1. Information on the corpus delicti, 2. Information on the modus operandi, 3. Linkage of persons to other persons, objects, or scenes, 4. Linkage of evidence to persons, objects or locations, 5. Determining or eliminating the events and actions that occurred, 6. Disproving or supporting witness statements or testimony, 7. Identification or Elimination of a suspect, 8. Identification of unknown substance, 9. Reconstruction of a crime, 10. Providing investigative leads. Case examples will be used to illustrate the applications of forensic evidence in criminal and civil cases.

Keywords: Corpus Delicti, Links, Events & Actions, Testimony, Identifications

Suggested reading:

1. Henry Lee's Crime Scene Handbook
2. Forensic Science Today
3. Advances in Fingerprint Technology
4. Dr. Henry Lee's Forensic Files
5. Cracking Cases

Abstract number: ABS-71-ISABS-2009

GENYO – ANDALUSIAN CENTER FOR GENOMICS AND ONCOLOGY: FORENSICS AND MEDICAL APPLICATIONS OF HUMAN GENETIC VARIABILITY

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Next April 2010, the Pfizer – University of Granada – Junta de Andalucia Center for Genomics and Oncology (GENYO) will be inaugurated in a whole new building now under construction. Meanwhile, last June 2008, the GENYO started its activities in the University of Granada Biomedical Research Center facilities. The GENYO will host the Andalusian DNA & Biomolecules Bank and will focuse its research in 3 main areas: human genetic variability (GV), oncology (ON), and farmacogenomics (FG). At the GV area we are currently working on auto-immune pathologies, sudden cardiac death of genetic origin, and genetics of depression. At the ON area research is focused on genes related to tumor angiogenesis and on detection and genetic identification of metastatic circulating cells from solid tumors (breast and colon cancers). At the FG areas research is focused on new targets for cytostatic medication that could be used in prostate, kidney and lung cancer. Finally, it should be mentioned that GENYO will be the scientific headquarter of the DNA-PROKIDS program, an international database designed to identify missing children trying to avoid children exploitation and trafficking. GENYO want to become a reference in research in the above mentioned areas, and we are open to scientist willing to either work or collaborate with us.

Keywords: GENYO, genetic variability, oncology, databases, DNA biobank

Suggested reading:

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2. J.C. Alvarez et al., Leg Med. 9, 293 (2007)
3. J.J. Mulero et al., J Forens Sci 51, 64 (2006)
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5. P.J. Collins et al ., J Forens Sci 49, 1265 (2004)

Abstract number: ABS-62-ISABS-2009

CHALLENGES IN THE IDENTIFICATION OF WWII HUMAN REMAINS: USAGE OF Y-STR AND MINISTR APPROACH

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The identification of human remains found in mass graves always employs different methods: identification by a living person, fingerprint analysis, dentition analysis, identification of special features, recognition of clothing and belongings, autopsy findings, the analysis by forensic anthropologists to estimate the species of the remains, sex, age, race, reconstruction of facial features from skulls, hair comparisons and DNA analysis. Since 60 years long time period from the end of the WWII, DNA analysis became the only solution in identification of victims\' remains from that time. During the last few years, international scientific team was working on the challenging topic: DNA identification of the skeletal remains from the two WWII mass graves from Slovenia. Initially, PowerPlex 16 was successfully used for obtaining this goal. Additional analysis of Y-STRs markers was performed in the second phase of the project. Using this method, some of previously obtained lower matchings were confirmed and some of them were rejected. But in some cases both of those kits could not provide us any useful information. In those cases, we have performed analysis using two different miniSTR kits: PowerPlex S5® system and AB Minifiler. In some cases this approach gave us sufficient results for the strong, final conclusion about identity of processed human remains and proves it that the concept of miniSTR kits will certainly upgrade the analysis of DNA from old bones and teeth.

Keywords: human remains, WWII, DNA identification, Y-STR, miniSTR

Suggested reading:

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2. Anđelinović Š et al. Twelve-year Experience in Identification of Skeletal Remains from Mass Graves. Croat Med J 2005;46:530-9
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Abstract number: ABS-79-ISABS-2009

ASSESSING COMPARISONS BETWEEN KNOWN AND UNKNOWN DNA PROFILES AND COMPLEX FORENSIC MIXTURES BASED ON EMPIRICAL DATA

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The generation of short tandem repeat (STR) DNA profiles from small amounts of skin cells was historically not feasible. However, with the advent of more sensitive molecular technologies, it is now possible to obtain genotypes from these samples. While these advances have expanded the range of case types for which DNA evidence is useful, they have also introduced new analytic challenges. The comparison of known DNA profiles to evidence samples containing small amounts of DNA or degraded DNA can be challenging, as many of the results produce mixtures and/or partial DNA profiles. Alleles from known contributors may be absent or, conversely, extraneous alleles that cannot be attributed to known contributors may be present. These phenomena are known as allelic drop-out or drop-in, respectively. The probability of drop-out and drop-in must be included in any statistical analysis of profiles produced from small or degraded evidentiary samples or from plentifu! l samples in which there is very little DNA from a minor contributor. Here, we present results from a comprehensive cataloging of drop-out and drop-in rates, as a function of starting quantity of DNA, STR locus, and genotype, in low copy number DNA single source samples and in high and low copy number DNA mixtures. These rates will be incorporated into a likelihood ratio method for estimating the weight of evidence for these types of samples.

Keywords: low copy number DNA, statistical analysis, empirical data, DNA profiles, likelihood ratio

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2. Gill P, et al. (2000) Forensic Sci Int 112:17-40
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INTEGRATED FORENSIC SCIENCES IN HIGH THROUGHPUT MISSING PERSONS IDENTIFICATION

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Specialized, high-throughput DNA typing has in recent years revolutionized the ability to identify large numbers of persons missing from such events as armed conflict and crimes against humanity, terrorist attacks, transportation accidents, and natural disasters. The International Commission on Missing Persons (ICMP) has played a formative role in the development of these capabilities, for example, in generating DNA matches on over 14,500 individuals killed in the conflict in the former Yugoslavia. The presentation will highlight the components required for successful large scale identification efforts, focusing on the integration of forensic evidence needed to identify individuals recovered from mass graves. Large scale DNA matching of victim and family reference profiles is the primary driver of the identification process, but the final outcome is also dependent on integration with forensic archaeology, anthropology, and pathology. Likewise, informatics plays a critical role. The talk will address future prospects for increasing the accessibility of DNA identification worldwide, and will discuss the important challenge of data protection in international identification efforts.

Keywords: ICMP, mass graves, DVI, DNA identification, forensic anthropology

Suggested reading:

1. Loreille OM, Diegoli TM, Irwin JA, Coble MD, Parsons, TJ. (2007). “High efficiency extraction of DNA from bone by total demineralization.” FSI: Genetics. 1: 191-195
2. Parsons TJ, Huel R, Davoren J, Katzmarzyk C, Miloš A, Selmanović A, Smajlović L. (2007) “Application of novel ‘mini-amplicon’ STR multiplexes to high volume casework on degraded skeletal remains.” FSI:Genetics 1:175-179
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LESSONS FROM THE EARLY DAYS OF DNA FORENSICS IN THE USA

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When forensic DNA evidence was first being introduced in the US there were many trials that examined in detail its validity. Was it reliable? Just how certain could one be that the evidence was of sufficient quality to present to a jury. I was involved in many of these cases testifying for the prosecution and had a close-up view of both the US court system and the quality of the early forensic work. I will describe some of these cases and the lessons learned. One case in particular, the Castro case in New York, was very informative and is now taught in some law schools. It is very instructive to examine the interface of science and law and to consider alternative ways of presenting such evidence.

Keywords: DNA forensics, forensic work, Castro case, interface of science and law, alternative ways

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POST-MORTEM PHARMACOGENETICS IN MEDICO-LEGAL SETTINGS

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Pharmacogenetics studies genetically determined variation in drug response, and its ultimate goal is individually tailored drug therapy. The CYP2D6, CYP2C9, and CYP2C19 enzymes affect the metabolism of about 20-30% of clinically used drugs. The genes coding for these enzymes show high genetic variation in the human populations, being therefore of major interest in human evolution, population genetic and pharmacogenetic studies. Recently, also the application of pharmacogenetics in post mortem medico-legal setting has been evaluated. We have developed genotyping methods for CYP2D6, CYP2C9, and CYP2C19 that would cover the most important genetic variants altering the enzyme activity. By using this method we have, for the first time, described the distribution of genetic variation at these loci on a global scale. The population genetic study consisted of 55 population samples for CYP2D6, 129 for CYP2C9, and 146 for CYP2C19 distributed world-wide. In addition, we have applied this methodology to post-mortem forensic setting in order to elucidate the role of genetic variation in drug intoxications. We have focused mainly on cases related to tricyclic antidepressants, which are commonly causing fatal drug poisonings in Finland and elsewhere in Scandinavia. Also, over 200 post-mortem forensic cases were examined with respect to drug and metabolite concentrations and genotypic variation at CYP2D6 and CYP2C19.

Keywords: pharmacogenetics, post mortem, genetic variation, population genetics, CYP genes

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FROM GENOMICS TO INDIVIDUALIZED MEDICINE-THE EXAMPLE OF MALIGNANT MELANOMA

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Rapid advances in genetic and genomic technologies over the recent years have fueled an accelerated phase of discovery that is beginning to shed light on the molecular landscape of melanoma and starting to bring within reach an opportunity for development of targeted, individualized therapies in this disease. Alterations in gene copy numbers and DNA sequence, along with changes in gene expression profiling patterns are intricately associated with onset and progression of melanoma. Significant progress achieved by genome-wide studies of gene copy number alterations in melanoma, has set the stage for disease classification and identification of patterns of molecular changes that highlight importance of individual signaling pathways contributing to melanoma biology, such as MAPK pathway and PI3K pathway. Such gene copy number changes combined with sequencing and gene expression data has provided the initial identification of potential points of tumor vulnerability that can be identified and targeted in individualized fashion by both existing and developmental therapeutics. Several such molecular changes recently identified in melanoma will be reviewed and their practical impact on management of patients with melanoma will be examined. In addition, innovative approaches for identification of potentially targetable molecular aberrations in melanoma will be discussed.

Keywords: Melanoma, Genomics, individualized medicine, therapy, gene copy number

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2. Curtin, J.A., et al., Distinct sets of genetic alterations in melanoma. N Engl J Med, 2005. 353(20): p. 2135-47
3. Curtin, J.A., et al., Somatic activation of KIT in distinct subtypes of melanoma. J Clin Oncol, 2006. 24(26): p. 4340-6
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CANCER GENOMICS BASED UPON NEXT GENERATION DNA SEQUENCING

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It is becoming increasing clear that there are many more alterations in each cancer genome than previously anticipated. There are also multiple different types of alterations present in each cancer genome. This includes both mutations in protein coding genes and also changes in the copy number of different regions of the genome. In addition, there are multiple insertions, deletions and novel translocations present in each cancer. In order to better understand cancer it becomes important to more fully characterize the changes that have occurred during cancer development. Only then can more focused therapies be developed to specifically target each specific cancer. The classical technologies for doing this type of analysis have included microarrays to measure changes in gene expression, array CGH to characterize alterations in copy number, and then exon sequencing to analyze mutations. The new technologies of Next Generation DNA sequencing offer powerful alternatives to these classical technologies that provide much greater detailed information about the alterations that have occurred during cancer development. We have initiated a project with our colleagues at AB/Life Technologies to begin to characterize the changes that have occurred in three cancers of the oral tongue. We have utilized whole transcriptome sequencing to compare the transcriptome of these oral tongue cancers to matched normal tissue from the same patient. The protocol utilized for the sequencing of the transcriptome preserves the strandedness of the transcripts which provides much more information about changes that occur throughout the transcriptome. In addition to determining information about allele-specific expression much of the transcriptome can also be searched for mutations that have occurred during cancer development. To complement the full transcriptome analysis we also did mate-pair sequencing of the DNA from the same samples. This technology enables us to characterize deletions, insertions and changes in copy number throughout the genome and this information complements the transcriptome sequencing data. We will describe our results using these technologies and show how this new technology will rapidly replace older technologies to characterize cancers. In addition, Next Generation DNA sequencing promises a new world in cancer diagnostics and therapeutics based upon a more detailed characterization of the alterations that have occurred during cancer development.

Keywords: cancer genetics, Next Generation DNA sequencing, sequenced based transcriptomics, oral cancer, copy number changes

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Abstract number: ABS-81-ISABS-2009

MUMMIES AND TUBERCULOSIS: CO-EVOLUTION OF PATHOGEN AND HOST

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The molecular identification of human pathogens in ancient human remains has recently opened new scientific fields that provide considerable insight into the history and evolution of both the host, the pathogen and their interaction. This allows us to track the changes in the bacillus as it becomes more and more exposed to the environment and to the immune system of its human host. Conversely we can track changes in the genes of the human population which confer resistance or susceptibility to disease over time. We are studying 2 large mummy collections for both the presence of TB DNA and changes in the host genome as it relates to suspected host susceptibility/resistance genes and their changes over time. The collections come from mummies from 18th century Hungary and 5-15 Cent Sudan. The Hungarian collection is the pivotal one as we have full church records from a middle class population enjoying a good diet and standard of housing during a period of peace in this region, 63% of the population have TB DNA found in their tissues. Three genes are being studied and our preliminary results show interesting and important variations when the affected mummies are divided into those who died of Tb, those who had a ghon lesion that healed and those who had TB but survived and died of other causes as well we compare the uninfected population. Genetic results to be discussed include the The KIR locus and NRAMP1 (now SLC11A1 gene).

Keywords: TB, DNA, PCR, Mummies, susceptibility/resistance

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GENETICS OF COMMON/COMPLEX TRAITS AS A FOUNDATION OF INDIVIDUALIZED MEDICINE

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Abstract not provided

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INDIVIDUALIZED REGENERATIVE MEDICINE

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Personalization of medical therapy through molecular technologies has the potential of transforming current practice of medicine by applying the most appropriate therapy to each individual patient depending on unique profiles. One area of particular interest is stem cell-based regenerative medicine. The pandemic of chronic degenerative diseases mandates development of effective approaches for tissue repair. As stem cells contribute to innate healing, the capacity for de novo tissue reconstruction harbors a promising role for regenerative medicine. Indeed, a spectrum of natural stem cell sources ranging from embryonic to adult progenitors has been identified with unique characteristics for regeneration. The accessibility and applicability of the regenerative armamentarium has been further expanded with stem cells engineered by nuclear reprogramming. Through strategies of replacement to implant functional tissues, regeneration to transplant progenitor cells or rejuvenation to activate endogenous self-repair mechanisms, the overarching goal of regenerative medicine is to translate stem cell platforms into practice and achieve cures for diseases limited to palliative interventions. Harnessing the full potential of each platform will optimize matching stem cell-based biologics with the disease-specific niche environment of individual patients to maximize the quality of long-term management. Emerging discovery science with feedback from clinical translation is therefore poised to transform medicine offering safe and effective stem cell biotherapeutics to enable personalized solutions for a broad spectrum of diseases.

Keywords: regenerative medicine, stem cells, induced pluripotent stem cells, biotherapeutics, molecular technologies

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DNA TYPING OF ANCIENT BONE SAMPLES - TRANSFER OF EXPERIENCE TO THE DAILY FORENSIC WORK

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Bone samples belong to the group of the most challenging samples we can face during our forensic practise. Criminal cases involving up to 20-years old skeletons are not rare and having a robust and reliable DNA extraction and STR typing method is a must. Work with the ostheological specimen that is several hundred years old is even more challenging and the chance of false negative or false positive identification results is increasing with the longer post-mortem interval and bad storage conditions. The author of this talk will demonstrate how can be the knowledge gained on the ancient material used during the processing of standard criminal cases involving bone samples.

Keywords: archaeogenetics, mini-STR, forensic, degraded DNA, inhibition

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INDIVIDUALIZED RISK-ASSESSMENT OF PROSTATE AND LUNG CANCERS

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An integrated approach, combining medical information, genomic technologies, bioinformatics methodologies, and superbly annotated sample sets applied to improve management of cancer will be presented. Two ongoing projects will serve as examples to demonstrate the power of applying genomics towards individualizing medicine.
Prostate caner: Two major challenges in the management of prostate cancer patients are: (1) the identification of men with GS≥7 who are at the greatest risk for metastasis after surgery or radiation therapy, and who are likely to get the most benefit from adjuvant systemic treatment and (2) stratification of men with clinically insignificant prostate cancer who can avoid the expense and morbidity of treatment from men with more aggressive prostate cancer requiring treatment. Biomarker panels predictive of prostate cancer behavior that extend beyond the predictive power of GS and other conventional prognostic factors are likely to play an essential role in the separation of clinically insignificant from significant GS6 prostate cancer and aggressive from non-aggressive GS≥7 prostate cancer. Such panels would be a key prerequisite for a more individualized approach to therapy for these patients including active surveillance for the low-risk prostate cancers. We have generated transcriptomic and epigenomic datasets from more that 200 patients by utilizing sophisticated cell capture techniques to isolate cancer cells and for many of them adjacent normal epithelial cells. This database is used as the first filter to sort out markers and find those that are truly associated with caner progression. We then use our patient registry (Mayo Clinic Prostatectomy Database) to test and validate these markers and develop prognostic models. The registry follows more than 15,000 RP prostate cancer patients treated at Mayo Clinic and extensive presurgical, surgical and postsurgical data are maintained. We have recently shown that simple multi-variable models using just a few molecular markers has significant predictive accuracy (AUC = 0.79) beyond clinical and pathologic variables when applied specifically to the high-risk patient population in a case-control setting where all clinically available prognostic measures including tumor state, lymph node involvement, and adjuvant therapy were either matched or balanced in a case-control study design. Furthermore, we examined protein levels for selected markers on the tissues by immunohistochemistry (IHC). Even though expression and methylation assays accurately quantify levels of markers in isolated DNA and RNA from a collection of cells, specific expression changes in subsets of cells will be obfuscated in this process because the morphologic features are not retained. We have found that at least for TOP2A, these changes can be more informative than qRTPCR for stratifying GS≥7 cancers for aggressiveness.
Lung Cancer: The objective of the lung cancer project is to develop and validate an assay that will assist in the histologic differentiation of lung carcinomas.

Currently, lung cancer is the leading cause of death worldwide and in the US and the survival rate has remained unchanged over the last 50 years. Treatment strategies are predominantly guided by staging and separating lung carcinomas in small cell carcinomas (SCLC) and non-small cell carcinomas (NSCLC). Furthermore, NSCLC represent a heterogeneous group of carcinomas with the main histologic subtypes including adenocarcinomas, squamous cell carcinomas and large cell carcinomas. Although, for treatment purposes, all NSCLC subtypes are grouped together, patients' response to therapy is quite variable, probably because of cancer heterogeneity. This heterogeneity is observed at the molecular level as different subtypes of NSCLC exhibit different gene expression signatures. Our data derived from Laser Capture Microdissected (LCM) tumors and other public lung cancer expression profiles show high degree of heterogeneity in these tumors. Because of variability in therapy response, more targeted therapies are being developed specific to lung cancer subtypes. Developing a panel of genes that could distinguish SCLC from NSCLC and squamous cell from non- squamous cell carcinomas, in poorly differentiated tumors or in small biopsy specimens, would be helpful in the management of patients with lung cancer.
This presentation will also include unpublished NextGen Sequencing analysis of cancer samples. Recently, chromosomal translocations, deletions, and amplifications have been described in hematological malignancies as well as in solid tumors. Such modifications often result in gene fusions with abnormal functional properties and altered control. In a pilot project we attempted to use Next Gen paired-end sequencing technology to discover novel translocations in cancer. Two lung cancer samples and one prostate cell-line (VCaP) were used in this experiment. DNA was isolated, fragmented and processed according to the pair-end protocol. Mapped data were analyzed for known and novel translocations, amplifications, and deletions. Results from this pilot project will be presented, as well as potential problems associated with the technology.

Keywords: Diagnosis, Prognosis, Predictive modeling, Biomarkers, Biomarkers

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MOLECULAR DIAGNOSTICS FOR STAGING PATIENTS WITH CANCER

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Patients with pN0 colorectal cancer have a ~25% risk of disease recurrence reflecting, in part, under-diagnosis of lymph node metastases at staging. Improved methods that predict recurrence would identify patients who could benefit from adjuvant chemotherapy. GUCY2C, expressed selectively by intestinal cells and universally in colorectal tumors, is a marker whose detection in lymph nodes could enhance staging. At staging, 273 patients with pN0 colorectal cancer from 9 hospitals were enrolled. Fresh lymph nodes >5 mm were bisected for histopathology and GUCY2C qRT-PCR. Tissues from 257 patients provided sufficient mRNA for analysis. GUCY2C expression was estimated in 2,570 lymph nodes from these patients, who were followed to assess time to recurrence. Median follow-up of patients was 24 months (range 2-63 months). Lymph nodes from 32 (12.5%) patients were free of occult metastases by GUCY2C qRT-PCR and all but 2 (6.3%) remained free of disease. Conversely, 47 (20.9%) patients with lymph nodes containing occult metastases by GUCY2C qRT-PCR developed recurrent disease (p=0.006). In multivariable Cox models, controlling for T stage, tumor location, lymphovascular invasion, and tumor differentiation, occult metastases in lymph nodes by GUCY2C qRT-PCR was the most powerful independent predictor of recurrence (adjusted Hazard Ratio=4.66, p=0.039, 95%CI=1.11, 19.57). GUCY2C qRT-PCR identifies occult metastases in lymph nodes that independently predict time to recurrence in pN0 colorectal cancer patients. Thus, GUCY2C may serve as a prognostic and predictive marker, identifying pN0 patients at minimum risk for disease recurrence and, conversely, who might benefit from adjuvant chemotherapy, respectively.

Keywords: Molecular diagnostics, GUCY2C, colorectal cancer, staging, lymph nodes

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GENETIC MARKERS FOR HUMAN PIGMENTATION

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An essential component in the identification of human remains is documenting the decedent's visible characteristics, such as eye, hair and skin color. However, if a decedent is decomposed or only skeletal remains are found, critical, usually externally visible information is lost. It is presently not possible to use genetic information to reveal such visible characteristics. The objective of our study is to identify genetic markers which reveal eye, hair and skin color of an individual and thus can be used to confirm or predict such traits. The variety of phenotypes is caused by multiple polymorphisms in genes of which some are involved in the pigmentation process. The simplest kind of polymorphism is the single nucleotide polymorphism (SNP). Since there are thousands of SNPs, it is extremely challenging to find those few which correlate with a person's eye, hair and skin color. Association studies, mostly performed in European descendants, including genome-wide SNP-scans, point to a few genes relevant for eye, hair, and skin pigmentation. Currently we are testing candidate SNPs in these genes in different populations. The previously identified SNP rs12913832 for its correlation with the brown and blue eye color in Europeans shows also a good correlation in other and mixed populations.

Keywords: pigmentation, SNP, identification, eye color, correlation

Suggested reading:

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SELECTED LECTURES

Presentation number: FG 1 Abstract number: ABS-51-ISABS-2009

THE POTENTIONAL DIAGNOSTIC USE OF CELL-FREE DNA CIRCULATING IN PLASMA

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Apoptosis and active release of cell-free DNA (cfDNA) by cells are thought to be the main source of plasma cfDNA, but its dynamics and clearance under various pathological conditions are to be clarified with respect to the interpretation of changes in cfDNA levels in clinical applications. We focused on patients with pregnancy related disorders and patients with renal failure. Real-Time PCR method based on amplification of GADPH gene sequences was employed for quantification of total cfDNA in plasma. We examined samples from 86 physiological pregnancies bearing single male fetuses in the third trimester and compared them with samples from pregnant women with long-term tocolysis (n=15), pre-term delivery (n=13), preeclampsia (n=21) and gestational diabetes (n=5). In second part of our study, we focused on patients with renal impairment. We compared the values of plasma cfDNA in healthy volunteers (n=20) and hemodialysed patients (n=17) and patients on peritoneal dialysis (PD, n=18). In all examined pregnancy-related disorders, we found significant elevations of plasma cfDNA concentration in comparison with physiological controls. In hemodialysed patients, we revealed non-significantly elevated concentrations of plasma cfDNA in interdialytic interval. In PD patients, we found negative correlation of cfDNA levels in overnight effluent with the duration of the PD treatment. Concentrations of total cfDNA in plasma could be used as an interesting marker of the pathological changes in organism. Further studies are needed to standardize the analytical methods. Supported by the Ministry of Education of the Czech Republic, grants no. MSM 0021620819 and MSM 0021620807.

Keywords: cell-free DNA, Real-Time PCR, gynecology, hemodialysis, peritoneal dialysis

Presentation number: FG 2 Abstract number: ABS-15-ISABS-2009

THE RELATIONSHIP OF GERMAN, SLAVIC AND FINNISH-UGRIC POPULATIONS FROM DATA OF ANTHROPOGENETICS AND ARCHEOLOGY

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The calculation of genetic distances of 55 human populations belonging to four great human races considering loci of proteins, enzymes and blood groups, and construction the dendrogram of those populations distinguished some relationship of German, Slavic and Finnish-Ugric populations. So, Russians are in one subcluster with Poles, Iranians, Komi, Chuvashes, Udmurtians, Nentses and Ossetians. Germans are in one subcluster with Serbs, Moldavians, Hungarians, Croatians and Czechs. There were common migrations of this populations from places of first differentiation in Asia. In Europe German populations were migrated by another way than ancestors of Russians, which were migrated in Europe across North of Siberia. The ancestors of Germans probably migrated by the same way as Hunnu. Now are investigated settlements of ancient Caucasoids in Central Asia. The calculation of genetic distances of 35 Slavic, German and Finnish-Ugric populations and construction of dendrogram of those populations confirmed our conclusion about relationship of those populations. The studing of mitochondrial DNA of rural Russian population in Yaroslavsky region discovered all haplogroups of Russians and even Caucasoids (H, W, I, U, X, T1). The last decoding of petrogliphs in Baical region (Kifishin et al., 2005) discovered the presence of ancestors of Shumers and Japans in Siberia in paleolithic. The ancestors of Russians were inhabitating in whole Eurasia were having the ancient inscription “runitsa” (Chudinov, 2006) in paleolithic.

Keywords: Caucasoids, Genetic Distances, Dendrodram, Relationship, Differentiation

Presentation number: FG 3 Abstract number: ABS-13-ISABS-2009

GENERATING DNA PROFILES FROM IMMUNOCHROMATOGRAPHIC CARDS USING AN LCN METHODOLOGY

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The aim of this research was to obtain DNA profiles from immunochromatographic test devices which have already yielded positive or negative results with body fluids such as blood and saliva. The present research involved body fluid samples from several male and female donors. Each body fluid was detected using the appropriate immunochromatographic card. The used cards were kept at room temperature for various lengths of time. The membranes were removed at the end of the designated times and the entire strip was extracted using a low copy number (LCN) extraction procedure. This included cell lysis in a buffer containing 0.01% SDS, and Proteinase K. The extracted DNA was purified and concentrated using a Microcon® 100 device, and quantified using the Applied Biosystems (AB) Quantifiler™ kit on the AB 7500 Real Time PCR System. The extracted DNA was amplified using a reduced amplification volume and higher PCR cycle numbers for both the AB AmpFlSTR® Identifiler™ and AmpFlSTR® Yfiler™ kits. While the best results were obtained when membranes were extracted at the end of one week, it was possible to obtain complete STR DNA profiles from some of the cards which were stored at room temperature for almost three months. Given these results, when evidence samples are limited in size, an analyst may not have to extract DNA without confirming the identity of the body fluid to determine if the samples are of human origin. Therefore, the above procedure allows the analyst to identify the body fluid as well as its donor.

Keywords: Low Copy Numbers, STR DNA Typing, PCR, AmFlSTR Identifiler, AmFlSTR Yfiler

YIA

Presentation number: FG 4 Abstract number: ABS-42-ISABS-2009

MTDNA VARIABILITY IN NATIVE ANDEAN POPULATIONS: THE CASE OF LAKE TITICACA

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Genetic diversity in South America makes for an informative case-study for investigating past and present human population dynamics. Present-day genetic structure has been shaped by two major drivers: a succession of expansive complex societies, and a range of eco-geographical pressures. The Andean region, characterized by its high-altitude environment, witnessed several waves of cultural expansions, culminating with the short-lived Inca Empire and then European conquest. Lake Titicaca, a strategic region which saw the rise and fall of a number of these societies, is still inhabited by three native groups, to judge by linguistic (and some ethnic) criteria: Uro, Aymara and Quechua-speakers. This study seeks to contribute to the reconstruction of the pre-history of the Titicaca region, delineating a novel molecular-genetic landscape. During field survey, we collected 83 samples from Uro, Aymara and Quechua-speaking populations on the Peruvian shore of Lake Titicaca. In this report we present mitochondrial DNA HVSI sequences for these subjects, which include the first representative data for an Aymara-speaking population. We combine these data with an extensive database of 49 native Amerindian populations assembled from previously published works, so as to further clarify the genetic structure of the wider region and the place of our Titicaca sample within it. Our results uncover an interesting pattern in which the distinctiveness of the Aymara-speakers within the Andean context suggests the persistence of an original genetic component. In contrast, all the various Quechua-speaking samples, spread across great expanses of Peru and Bolivia, are characterized by their clear homogeneity.

Keywords: mtDNA, Titicaca, Aymara, Quechua, Andes

Presentation number: IM 1 Abstract number: ABS-40-ISABS-2009

A NEW POLYMORPHISM IN MICRORNA-BINDING SITE OF *CDKN2A* AND *XPD* IN MALIGNANT MELANOMA PATIENTS

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The strongest risk factors for Cutaneous Malignant Melanoma (CMM), a high case-fatality rate, are family history for melanoma, multiple benign or atypical nevi, previous melanoma, sun sensitivity and mainly ultraviolet radiation exposure. DNA damage by direct (pyrimidine dimmers) and indirect effects (oxidative stress) are expected results. Both types of DNA damage lead to diverse cellular responses in melanocytes, including cell cycle arrest triggered by p16 gene (CDKN2A locus) and DNA repair. A hospital-based case-control study was conducted in Sao Paulo, Brazil, to evaluate CDKN2A microRNA-binding region and DNA repair gene XPD/PstI polymorphisms in 193 patients with confirmed CMM and 208 cancer free controls. The frequency of CDKN2A and XPD/PstI polymorphisms observed in the patients (5.8% and 15.2% respectively) was higher than that observed in the control group (3.4 and 12.7% respectively) but the difference was not considered statistically significant for CDKN2A (OR = 2.10; 95% CI, 0.73 – 6.05) or XPD/PstI (OR = 1.33; 95% CI, 0.71 – 2.52) mutated genotypes. The negative results for the association between melanoma and the polymorphism in microRNA binding site of CDKN2A seams to indicate no interference in cell cycle regulation in the patients. To our knowledge, this is the first report that evaluated this polymorphism in patients with CMM and the preliminary results suggest the evaluation of a large population. The negative association of XPD/PstI variant genotype and CMM in our population seems to be in accordance with other data in the literature but we are increasing the sample size for statistical confirmation. (FAPESP/CNPq/LIM40/LIM-24).

Keywords: CDKN2A, XPD, Melanoma, Polymorphism, Case-Control

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INDIVIDUAL GENETIC VARIABLES IN RECURRENT PREGNANCY LOSS

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Recurrent Pregnancy Loss (RPL) represents an intriguing problem in obstetric practice in which genetic factors play a role. Enzymes such as P4501A1 (CYP1A1) metabolize organic compounds to reactive compounds which damage cells and DNA. N-acetyltransferase 2 (NAT2) is involved in the biotransformation metabolism of aromatic amines. Glutathione S-transferase (GST) catalyze the binding of a large variety of electrophils to the sulphydryl group of glutathione. During pregnancy, changes in blood coagulation may play a role in the occurrence of abortion. Factor V Leiden (FVL) gene, is associated with a hypercoagulable state and increased susceptibility for venous thrombosis. Factor II (prothrombin) gene is associated with higher plasma protrombin concentrations. Aim of this study was to investigate the possible role of I and II stage detoxification and coagulation systems genes polymorphisms in the pathogenesis of RPL. The polymorphic variants of those genes were analyzed in 24 women (case group) with RPL and in 171 women (control group) with the uncomplicated obstetric history. The frequency (80%) of NAT2 gene SS genotype in case group was significantly ($p<0.05$) higher than in control group (57%). Frequencies of GSTM1, GSTT1, CYP1A1, FII and FVL polymorphic variants were practically similar in both analyzed groups. It had been shown that NAT2 S/S genotype really can be involved in the process of RPL, which may be associated with changes in steroid hormones level. From our data the identification of NAT2 S/S genotype can be used as a marker for high risk recurrent pregnancy loss prediction in genetic testing family programs.

Keywords: Recurrent Pregnancy Loss, Polymorphism, Gene, Detoxification, Thrombophilia

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TRI-ALLELIC SNP MARKERS ENABLE ANALYSIS OF MIXED AND DEGRADED DNA SAMPLES

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For the analysis of degraded DNA in disaster victim identification (DVI) and criminal investigations, single nucleotide polymorphisms (SNPs) have been recognized as promising markers mainly because they can be analyzed in short sized amplicons. Most SNPs are bi-allelic and are thereby ineffective to detect mixtures, which may lead to incorrect genotyping. We developed an algorithm to find non-binary (i.e. tri-allelic or tetra-allelic) SNPs in the NCBI dbSNP database. We selected 31 potential tri-allelic SNPs with a minor allele frequency of at least 10%. The tri-allelic nature was confirmed for 15 SNPs residing on 14 different chromosomes. Multiplex SNaPshot™ assays were developed, and the allele frequencies of 16 SNPs were determined among 153 Dutch and 111 Netherlands Antilles reference samples. Using these multiplex SNP assays, the presence of a mixture of two DNA samples in a ratio up to 1:8 could be recognized reliably. Furthermore, we compared the genotyping efficiency of the tri-allelic SNP markers and short tandem repeat (STR) markers by analyzing artificially degraded DNA and DNA from 30 approximately 500-year-old bone and molar samples. In both types of degraded DNA samples, the larger sized STR amplicons failed to amplify whereas the tri-allelic SNP markers still provided valuable information. In conclusion, tri-allelic SNP markers are suited for the analysis of degraded DNA and enable the detection of a second DNA source in a sample.

Keywords: tri-allelic SNP, human identification, degraded DNA, mixtures, forensic genetics

ABSTRACTS – POSTER PRESENTATIONS

POSTER PRESENTATIONS

Forensic Genetics

Presentation number: FG 6 Abstract number: ABS-65-ISABS-2009

COMPARATIVE ANALYSIS OF SALTING OUT AND QIAGEN DNA EXTRACTION PROCEDURES FROM BUCCAL SWABS AND CHEWING GUMS

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First and the most important step in the forensic DNA analysis of the collected specimens is the extraction of the nucleic acids (DNA). The main goal of this study was optimization of the salting-out DNA extraction protocol, (Miller et al.) from the forensic specimens of buccal swabs and chewing gum and its comparison with standard Qiagen DNA extraction protocols. Sampling was carried out at the Institute of Genetic Engineering and Biotechnology, Sarajevo, BIH. Each of volunteers donated two specimens. One of the collected specimens was subject to the optimized salting out protocol for isolating buccal cell genomic DNA and other was processed by Qiagen DNA extraction method. Preliminary verification of the acquired extraction results was realized by using horizontal gel electrophoresis on 1,5% agarous gel. Further treatment of extracted DNA understood polymerized chain reaction (PCR) with PowerPlexTM16 Kit. Detection of the amplified STR loci was carried out by standard procedure of capillary electrophoresis on ABI PRISM 310 genetic analyzer. Obtained results indicate advantages of salting out procedure, in terms of abundant gDNA yield and substantial costs reduction, but on the other hand some disadvantages, since it has shown to be a time consuming procedure in comparison with standard DNA extraction protocols.

Keywords: DNA extraction, salting out, buccal swabs, chewing gum sample, DNA analysis

Presentation number: FG 7 Abstract number: ABS-17-ISABS-2009

UNUSUALLY LARGE VARIANT ALLELES OBSERVED IN A PHILIPPINE POPULATION

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The International Commission on Missing Persons (ICMP) was founded in 1996 to address the issue of persons missing as a result of the conflicts that occurred during the breakup of the former Yugoslavia during the 1990's. Since its assistance to authorities in Thailand in the wake of the tsunami in 2004 the ICMP has increased its role to include disaster victim identification (DVI) as a result of natural disasters. In June 2008, as a result of the sinking of the ferry MV Princess of the Stars off the coast of Sibuyan Island, the ICMP assisted the International Criminal Police Organization (INTERPOL) and the Philippine authorities with DNA typing both reference samples from family members of the missing and victim samples. During the typing of family reference samples a number of unusually large alleles were observed in PentaE and FGA. We will present genotype and sequence information, and subsequent structure of the unusual variants, to confirm their designation.

Keywords: Off-ladder alleles, Variant alleles, Penta E, FGA, STR, Missing persons

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IMPLEMENTING MALE DNA SCREENING INTO SEXUAL ASSAULT CASE PROCESSING

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As Y-chromosome screening tools become more widely available, they can easily be implemented into the process flow of forensic DNA sexual assault cases. For laboratories with large sexual assault backlogs, these screens can quickly identify positive cases, and isolate the most positive/probative sample(s) for STR analysis. Some jurisdictions find these male DNA screens can even replace conventional serological identification of semen in the majority of their cases. Even when conventional serology is still required, it can now be performed on the back-end exclusively on the samples processed for STR, so that only confirmation of positive samples is needed in most cases. This greatly reduces the serology bottleneck that negative cases often cause. In cooperation with our clients, Bode Technology has been successfully implementing such Y-chromosome screens into sexual assault case flows for the past eight years. Starting with an in-house Y Marker Screen, then implementing Quantifiler Y, and now with the advent of Quantifiler Duo, we have shown these tools to be highly beneficial for both efficiency and quality assurance in sexual assault case processing.

Keywords: Forensic Science, Sexual Assault, Quantifiler, Male DNA, Y-Chromosome

Presentation number: FG 9 Abstract number: ABS-67-ISABS-2009

Y STRs IN PROCESS OF DNA IDENTIFICATION OF WWII SKELETAL REMAINS: CASE STUDY

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DNA analysis became almost the only solution in identification of victims\' remains from WWII. In this case study, PowerPlex 16 kit was used initially for obtaining this goal. Male victim's profile positively matched to certain male referent sample with lower probability. Since it was presumptive son-father matching case, additional analysis of Y-STRs markers was performed in the second phase of the project. Extraction of genomic DNA was performed according to the modified Qiagen protocol. QuantifilerTM Human DNA Quantification kit was used for quantifying human DNA. PowerPlex® Y System (Promega Corp., Medison, WI) kit was used for the amplification and detection of Y-STR loci. The detection of the results was completed on AB310 genetic analyzer. In this particular case study, usage of Y STR method helped in confirmation of previously obtained lower match.

Keywords: DNA analysis, Y chromosome, Y-STR, WWII, skeletal remains

Presentation number: FG 10 Abstract number: ABS-98-ISABS-2009

NON-HUMAN ERRORS ARE THE MAIN SOURCE OF FALSELY DETERMINED ALLELES IN DNA DATABASES

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Aiming to estimate frequency of various types of errors that may have occurred during the process of identification of victims of war in Croatia we compared genotypes of 911 parent - child pairs in the database of nearly 3500 relatives of missing people. By repeated analysis of mismatched genotypes we identified seven errors in the database. Out of these seven errors, falsely genotypes alleles were caused by human error, while the remaining five errors were caused by allelic dropout or electrophoretic aberrations. An important observation is that all three observed allelic dropouts occurred at D2S1338 locus which is the largest fragment amplified by the AmpFlSTR Identifiler kit. Larger alleles at this locus frequently amplify with lower efficiency, sometimes not reaching the detection level indicating that additional proofreading procedures should be performed when homozygous D2S1338 locus is being reported.

Keywords: DNA typing, Human identification, STR loci, DNA database, Quality control

Presentation number: FG 11 Abstract number: ABS-72-ISABS-2009

RATIO OF „NON-PATERNITY OCCURRENCE“ IN PATERNITY TESTING IN BOSNIA AND HERZEGOVINA

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A maternity or paternity identification test is conducted to establish whether a person is the biological mother (maternity test), or biological father (paternity test) of a certain individual. Paternity tests are more common than maternity tests, and Bosnia and Herzegovina is not exception for that. In this presentation we have presented analysis of some of the paternity tests made in B&H, performed by the Laboratory for forensic genetics of the Institute for Genetic Engineering and Biotechnology in Sarajevo (INGEB). Main goal of this preliminary study was to answer of the frequently asked question: what is the ratio of the „non-paternity occurrence“ in our country. Non-paternity occurs when a child is found to have DNA that is not in his (her) alleged father and is not found in his (her) mother. We have analyzed results only of the analysis that were asked from Bosnian citizens. Consequently, 131 tests of disputable paternity were included in our study. We observed „mother-present“ and „mother-less“ tests. „Mother-present“ tests include the witnessing of the mother, her presence and also her profiling, unlike „mother-less“ tests, where the test is performed without the mother's assistance. These tests where performed upon court or private request. The greatest shares of these analyses are by court requests and included mother presence. Final result was that 25 tests (of total 131 that where done) were negative (that represents 19,084% of total cases), and 106 were positive (80,916%).

Keywords: paternity tests, mother test, non-mother test, non-paternity occurrence, Bosnia-Herzegovina

Presentation number: FG 12 Abstract number: ABS-19-ISABS-2009

FORENSIC MOLECULAR PHOTOFITTING: THE USE OF mtDNA IS FEASIBLE IN MIXED POPULATION SUCH AS IN BRAZIL?

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Forensic Molecular Photofitting has been emerging as a new field where the main goal is to get from DNA profiles information such as skin color and facial features to obtain a probable phenotype of the suspect and/or the victim, nowadays using genetic markers of ancestry and pigmentation genes. In order to do a preliminary evaluation if mtDNA haplogroups classification could be used to infer the skin color in Brazil we analyzed 102 unrelated individuals living in São Paulo city (79.2% born in the Southeast region and 20.8% born in Northeast). The samples were sequenced for HVI/HVII, haplogroups were defined and compared with individual skin color information. A total of 95 different haplotypes were identified. The observed haplotypes were distributed in 38.2% of Amerindians, 34.3% of Africans and 27.5% of Euro-Asiatics haplogroups. From the individuals with Amerindian haplotypes, 60.5% was White, 36.9% was „mulatto“ (mix of Black and White) and 2.6% was Black; from the Euro-Asiatic haplogroups, 82.1% was White, 10.7% of mulatto and 3.6% of each, Black and Asiatic; from the African haplogroup 34.4% was White, 56.2% was mulatto and 9.4% was Black. These results are in agreement with the historical data of Brazil colonization. When European and African males migrated and mixed with the Brazilian Amerindian females, the resulted phenotype do not necessarily reflected the haplogroup which their belong to. The use of Forensic Molecular Photofitting in Brazil should be done carefully since it is a typical multiethnic population with notable heterogeneity of phenotypic features. Support: FAPESP; LIM-HC/FMUSP

Keywords: mtDNA, Brazilian population, human identification, HVI/HVII, haplogroups

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POLYMORPHISMS IN ALCOHOL METABOLIZING GENES IN A BRAZILIAN POPULATION: CLINICAL AND LEGAL IMPORTANCE

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Variability in the rate and extent of absorption, distribution and elimination of ethanol has important ramifications in clinical and legal medicine. Alcohol absorption and elimination vary amongst individuals, and are influenced by a variety of factors including the gene polymorphism of alcohol dehydrogenase (ADH), aldehyde dehydrogenase (ALDH), and CYP2E1. The mutant genotypes and haplotypes results in enzymes that have 70-80 fold higher turnover rate that modifies acetaldehyde (cancer risk) and alcohol concentration (forensic impact). A hospital-based case-control study was conducted to evaluate allele frequency and genetic risks associated to the polymorphisms of ADH1C Ile350Val, ADH1B Arg48His, ADH1B Arg370Cys, and CYP2E1 PstI in 207 histophatologically confirmed head and neck cancer (HNC) patients and 244 cancer free controls. The chronic and intense consume of alcoholic beverages was reported by 93% of HNC patients and 43% of controls. The mutant genotype ADH1B Arg48His was detected in 12,7% of controls and in 5,8% of HNC patients conferring protection for the disease (OR=0.42; 95% CI; 0.21-0.85). Similar results were observed for individuals with ADH1B*2 (OR=0.41; 95% CI; 0.20-0.82) or ADH1B*2/ADH1C*1 (OR=0.32; 95% CI; 0.13-0.79) mutated haplotypes. Individuals ADH1B Arg48His that consumes alcohol higher than 30 g/l/day increases more than four times the HNC risk (OR= 4.42; 95% CI, 1.21-16.11). Alcohol metabolizing enzymes displays polymorphisms, which accounts not only for racial and ethnic variations but also depends on the frequency and intensity of alcohol consume. These variables should be taken in account in forensic determination of admitted alcohol concentration in different countries. FAPESP/LIM40

Keywords: ADH1B polymorphisms, ADH1C polymorphisms, CYP2E1 polymorphisms, head and neck cancer risk, forensic use

Presentation number: FG 14 Abstract number: ABS-41-ISABS-2009

Y-CHROMOSOME STR HAPLOTYPES IN A POPULATION SAMPLE FROM EASTERN CROATIA

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A population genetic analysis of the 17 Y-chromosome short tandem repeats (STR) loci in the Eastern Croatia region. A total of two hundred and twenty unrelated healthy men from the Eastern Croatia were included in the study. Genomic DNA was extracted using Chelex procedure from FTA cards. Y-chromosomal STRs were determined using the AmpFISTR Yfiler PCR amplification kit that coamplifies 17 Y-STRs (DYS19, DYS389I, DYS389II, DYS390, DYS391, DYS392, DYS393, DYS385, DYS437, DYS438, DYS439, DYS448, DYS456, DYS458, DYS635 and GATAH4). The haplotype frequencies were determined by direct counting and analyzed using Arlequin 3.1. A total of 207 haplotypes were recorded, 197 of which were unique (89.55%). Haplotype diversity was 0.9993, with the commonest recorded haplotype being shared by only four recruits. Locus diversity varied from 0.256 for DYS392 to 0.780 for DYS458. Average locus diversity was 0.600. This is the first attempt to describe the genetic structure of a sample of the inhabitants of Eastern parts of Croatia, which may serve as the standard for various genetic epidemiology and forensic studies. Further studies are needed to characterize the genetic structure of the entire Croatian population in order to create an authoritative overview of the modern Croatian population. The results reported herein are of great importance for paternity testing, forensic casework on sexual assault evidence as well as individual identification.

Keywords: Y chromosome, short tandem repeats, population genetics, haplotypes, Eastern Croatia

Presentation number: FG 15 Abstract number: ABS-78-ISABS-2009

ASSESSMENT OF DNA DEGRADATION AND THE GENOTYPING SUCCESS OF HIGHLY DEGRADED SAMPLES

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In the case of mass disasters (eg. tsunamis, earthquakes, terrorist attacks, military conflicts, plane crashes) and some forensic casework, it is common to encounter highly degraded biological samples. Where conventional methods of victim identification such as fingerprint, visual and dental comparisons are unable to be applied, DNA genotyping of Short Tandem Repeats (STR) becomes the principle means of identification. DNA becomes progressively more fragmented as biological tissue degrades, and this results in a decreasing ability to gain an accurate DNA profile. Often the successful identification of samples exhibiting very high levels of DNA degradation are further complicated by also presenting in very low quantities. Such highly degraded samples often produce incomplete or no STR profiles. Much focus has been placed on designing reduced amplicon STR multiplexes (mini-STRs) which have proven to be more successful in identifying degraded samples. The most degraded of samples, namely very old skeletal material, commonly produce no STR or mini-STR profiles and therefore the less informative mitochondrial DNA is genotyped. A diagnostic tool which can simultaneously quantify total human DNA and the extent of DNA degradation in these precious samples would prove extremely valuable in choosing which of the DNA typing systems available will prove to be the most informative. This current study presents both a quantitative PCR and capillary electrophoretic method of assessing DNA degradation in highly degraded samples and their ability to predict the success rate of genotyping such samples using industry standard STR and mini-STR systems.

Keywords: Degraded DNA, DNA Quantitation, STR, mini-STR, Quantitative PCR

Presentation number: FG 16 Abstract number: ABS-101-ISABS-2009

VARIABILITY, HERITABILITY AND ENVIRONMENTAL DETERMINANTS OF HUMAN PLASMA N-GLYCOME

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Plasma glycans were analyzed in 1008 individuals to evaluate variability and heritability, as well as the main environmental determinants that affect glycan structures. By combining HPLC analysis of fluorescently labeled glycans with sialidase digestion, glycans were separated into 33 chromatographic peaks and quantified. A high level of variability was observed with the median ratio of minimal to maximal values of 6.17 and significant age- and gender-specific differences. Heritability estimates for individual glycans varied widely, ranging from very low to very high. Glycome-wide environmental determinants were also detected with statistically significant effects of different variables including diet, smoking and cholesterol levels.

Keywords: Human plasma glycome, N-glycosylation, Variability of glycans, Heritability of glycans, Age dependent changes

Presentation number: FG 17 Abstract number: ABS-49-ISABS-2009

A NOVEL REAL-TIME PCR STRATEGY FOR THE QUANTITATION OF TOTAL HUMAN AND MALE DNA

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Heavily multiplexed Short Tandem Repeat (STR) analysis requires a defined range of template quantity to produce optimal results. Additionally, quantification of DNA helps saving lab resources. A multiplex assay, Plexor® HY, has been developed for the simultaneous quantitation of total human DNA and human male DNA. The IPC target is a synthetic sequence included in all wells to monitor inhibition. The assay uses three dyes to detect amplification and a fourth dye as a passive reference. Both, the autosomal and the Y-chromosomal target are a multicopy targets. The IPC target is a synthetic sequence added to all wells. Associated analysis software has been developed to visualize amplification data from multiple instrument platforms, plot standard curves and calculate DNA concentrations. A normalization module has been built in to the software that, with simple user inputs, allows the software to compute all necessary dilutions of DNA template samples. Quality control checks are incorporated in to the system as well. Support documentation has been developed specifically for the Applied Biosystems 7500, Stratagene Mx3000P® and Mx3005P® and Bio-Rad iQTM5 with support of more platforms planned. In addition to analysis software, automated methods for qPCR set-up, DNA normalization and STR amplification set-up are in development. Data will be presented demonstrating the performance of this assay and the interface of the analysis software.

Keywords: Forensic Science, DNA Quantitation, Real-Time PCR, Plexor, software

Presentation number: FG 18 Abstract number: ABS-34-ISABS-2009

FOUR SPERMS ENOUGH FOR IDENTIFICATION OF A RAPIST? INTRODUCTION OF LM IN FORENSIC PRACTISE

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Laser microdissection is a new technique used in forensic DNA analysis that enables precise separation of target cells from mixed forensic samples. This method is non-contact and contamination-free. The obtained cells can be used for a subsequent genetic analysis with the aim to determine single DNA profile via STR analysis that leads to individual identification of contributors to the mixed sample. The goal of our project is to optimize methods of cell separation from mixed forensic samples such as vaginal smears after rape (epithelial cells, blood and sperm) and placental tissue obtained from abortion material (maternal decidua and fetal chorionic villi). We have tested and compared several DNA extraction methods from the mentioned samples as well as post-PCR purification. For now we are able to get relevant DNA profil, i.e. DNA profil enabling individual idetification up to four dissected sperms. We plan to utilize this technique for recovery of fetal cells from placental tissue after abortion in the near future.

Keywords: sperm, laser microdissection, vaginal smear, DNA exctraction, DNA profile

Presentation number: FG 19 Abstract number: ABS-24-ISABS-2009

WORLDWIDE HUMAN POPULATION STRUCTURE AND RECENT SELECTION: EVIDENCE FROM NEARLY 1 MILLION SNPs

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Genome-wide scans of hundreds of thousands of single-nucleotide polymorphisms (SNPs) have resulted in the identification of new susceptibility variants to common diseases and are providing new insights into the structure and relationships of human populations. In the present study, we report the results of genotyping approximately 500,000 SNPs (using Affymetrix GeneChip Human Mapping 500K Array Set) in 255 individuals (5 individuals from each of 51 worldwide populations) from the Human Genome Diversity Panel (HGDP-CEPH). When merged with non-overlapping SNPs typed previously in 250 of these same individuals (using Illumina HumanHap650K Beadchips, data publicly available), the resulting dataset consists of over 950,000 SNPs, providing the most detailed characterization of worldwide human genetic diversity to date. Our analyses both confirm and extend previous studies; in particular, we highlight the impact of various dispersals, and the role of substructure in Africa, on human genetic diversity. We also provide a worldwide context for patterns of genetic diversity among the HapMap3 population samples, and we utilize a modified lnRsb approach for contrasting extended haplotype homozygosity (EHH) profiles in detecting signals of local selection in genome-wide data. Our analysis revealed wide-spread signals of recent positive selection both at the continental level and from specific populations.

Keywords: genotyping, SNP, HGDP-CEPH, genetic diversity, selection

Presentation number: FG 20 Abstract number: ABS-16-ISABS-2009

MUTATION FREQUENCIES OF STR LOCI OBSERVED IN A LARGE NUMBER OF KINSHIP CALCULATIONS

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The International Commission on Missing Persons (ICMP) was founded in 1996 to address the issue of persons missing as a result of the conflicts that occurred during the breakup of the former Yugoslavia during the 1990's. The ICMP employs a DNA-led approach to assist authorities identify the large number of missing persons. This approach matches both the DNA profiles from the family members of the missing and the DNA profiles obtained from samples of bone. To date more than 500 instances of mutations have been observed in kinship analysis performed as part of our routine casework. We will present the mutation frequencies observed at the various loci of the Promega PowerPlex16 STR kit, whether the mutation is paternally or maternally inherited, and the rates of stepwise increase/decrease of mutations.

Keywords: Mutation frequencies, Kinship calculations, Inheritance patterns, STR, Missing persons

Presentation number: FG 21 Abstract number: ABS-22-ISABS-2009

SELECTION OF MULTIALLELIC SNP POLYMORPHISMS AND ALLELE FREQUENCY ASSESSMENT IN LOWER SILESIAN POPULATION

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Single nucleotide polymorphisms (SNPs) are being considered for a potentially useful role in forensic human identification. The advantages of SNP typing in forensic genetics are well know and include a wider choice of high-throughput platforms, lower mutation rates, lower amplicon size and improved analysis of degraded samples. The aim was to test whether SNP typing is realistic supplement to the current suite of assays available to the forensic investigator. The NCBI dbSNP was searched, and out of 19 markers selected, six proved of both nonbinary polymorphism and expected allele distribution in Lower Silesian population. The SNP heksaplex has been developed to analyse highly degraded DNA, archaeological samples and paternity testing. DNA fragments were amplificated in one multiplex PCR reaction and SNPs were identifited by minisequencing method. The amplicon size were beetwen 43-119 bp. The power of exclusion for trios was PEtrio=0,87612 and PEduo=0,65294 for cases without a mother, which makes the heksaplex not sufficient yet for routine paternity investigation. However since the mutation rate of SNPs has been estimated to be lower then that of STRs, present SNP multiplex system seems to be useful in paternity testing with hereditary discrepancy caused by mutation in STR locus. The combined power of discrimination was PD=0,99965, which makes the heksaplex useful for forensic applications. The SNP multiplex panel is a good alternative when STRs fail to give results for challenging samples such as bones, teeth and highly degraded tissues commonly encountered in mass-disasters.

Keywords: SNP, minisequencing, forensic human identification, degraded DNA, paternity testing

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HOW DID WAR LIFE CONDITIONS IN BOSNIA AND HERZEGOVINA INFLUENCE ON EXPRESSION OF INTERNAL FETAL GROWTH AND DEVELOPMENT FACTORS?

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War and war life conditions (WLC) are complex of factors influencing on fetal growth and development (FgD). Aims were to estimate war multifactor influence on mean number of newborns per year (MNpY), mean body length(MBL) and mean body mass of newborns at birth(MBW) as parameters of FgD in prewar(PWp), war(Wp)and after war period(AWp)and related to gender(RtG). We used The Book of Evidence of Deliveries in Maternity hospital in city of Kakanj in Central Bosnia (CB), for collecting data. Official beginning and the end of the war in Bosnia and Herzegovina were taken from „Sluzbene novine“. We compared our results with results of similar researches done in city of Sarajevo. Statistically, we used X2 and T-test. We found statistically significant(SS) decrease in MNpY in Wp($p<0.05$) and highSS difference in MBL RtG in favour of M in all periods($p<0.001$).Comparing to PWp, there was SS decrease in MBL in Wp in both-F($p<0.01$) and M($0.01<0.05$)and in AWp in F($p<0.05$).We found SS increase in MBL in F($0.01<0.05$)and M($p<0.001$) in AWp comparing toWp. We found SS difference in MBW RtG in all periods in favour of M newborns ($p< 0.001$). There weren't SS difference in MBW between PWp and Wp and between PWp and AWp RtG but there was SS difference between Wp and AWp in F newborns ($p<0.05$)with decreased in MBW in Wp. This pointed negative war influence is long-lasting and it needs time to attenuate. Comparing to researches done in Sarajevo we've got the similar results what could point to similar WLC in all CB.

Keywords: war conditions, birth body weigh and length, fetal growth factors, fetal development factors, Bosnia and Herzegovina

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D2S1338 RARE ALLELE IDENTIFICATION AND CONFIRMATION BY DIRECT SEQUENCING

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An out of locus allele was observed while analyzing the sample data generated using the AmpFlSTR® Identifiler™ PCR amplification kit. Since both loci adjacent to the observed allele, D16S539 and D2S1338, showed a single-peak homozygous pattern, it was neccessary to confirm the origin of the allele by direct sequencing. Locus D2S1338 was amplified using the specific primers, the PCR products were purified and cloned into pSC-B-amp/kan plasmid vectors. The clones with an insert of suitable length were identified and sequenced using the M13 universal primers. The sequence analysis and comparison with the reference sequence obtained from the NCBI GenBank revealed that the allele indeed belongs to the D2S1338 locus and that it is consistent with (TGCC)6 (TTCC)7 repeat pattern. In this way a possible misinterpretation was avoided and it is a recommended procedure when a rare allele like this one is encountered.

Keywords: DNA typing, STR loci, Alelle variant, DNA sequencing, Croatian population

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ROUTES OF INTRODUCTION OF SICKLE CELL ANEMIA IN PORTUGAL: INSIGHTS FROM MITOCHONDRIAL DNA AND Y CHROMOSOME DIVERSITY

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High frequency of sickle cell anemia (HBB*S) is correlated with malaria endemicity. In Portugal, the prevalence of HBB*S has a clinal distribution with frequencies ranging from virtually 0% in the North to 1% in the South. Here, foci of high prevalence can reach 5-6%, namely in Coruche, Alcácer do Sal and Serpa. Molecular epidemiological data indicate that the introduction of HBB*S in Portugal was due to migration routes that varied geographically and timewise. The aim of this work is to understand the extent at which population history played a role in determining hot spots of high prevalence of hereditary anemias in restricted geographical regions where malaria was endemic. Mitochondrial DNA and Y-chromosome were analysed since they provide reliable clues on female and male demographic histories in populations. Results reveal that Y-chromosome diversity is similar to that previously reported for other Portuguese regions. Considering mtDNA, Serpa has higher frequencies of haplogroups I, J and T, which shows a stronger Mediterranean influence. The absence of sequences from North Africa suggests that this influence may not have resulted from the Islamic occupation but from contacts with ancient Mediterranean populations. In Alcácer do Sal the levels of haplogroup L (22%), typical of sub-Saharan populations, are the highest ever reported in Portugal. Here, the high incidence of HBB*S may be in part explained by the influx of African slaves between the 15th and 19th centuries. In Coruche, the genetic profile has not shown any clue about the possible introduction of HBB*S.

Keywords: HBB*S, mtDNA diversity, Y chromosome diversity, anemia prevalence, Iberia

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Y CHROMOSOMAL SHORT TANDEM REPEATS (Y-STRS) AND IT'S ASSOCIATION WITH AZOOSPERMIA FACTORS' (AZF) MICRODELETIONS OF INFERTILE MALES

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This capability of Y chromosome is important in situations where a small amount of male DNA may be recovered. Molecular techniques, typing for a length variation in the X-Y homologous amelogenin genes, are used for accurate gender assignation and are crucial in forensic investigations. The aims of the present study were to perform paternity and identification tests using 17 Y-STRs loci and to determine the size of the amelogenin (AMELY and AMELX) genes. 702 unrelated males were analyzed in VTMEC laboratory, and combination of different molecular approaches was used: AmpFlSTR® IdentifilerTM, AmpFlSTR® SGMPlusTM (Applied Biosystems, USA), Promega GenePrint® STR Systems, detection kit on AMELY and AMELX genes, and PowerPlex Y System (Promega, USA). Microdeletions in AZF region were determined by two multiplex PCR amplifications using ten primer pairs. Using AmpFlSTR® IdentifilerTM one sample has shown the absent of 112 bp fragment of AMELY gene (Y:p11.2). Performing the analysis with AmpFlSTR® SGMPlusTM kit, a 109-bp fragment of AMELY gene has been revealed. Height of the109-bp fragment - peak in comparison with AMELX (X:p22.1-22.3) was in ratio 1:17 (usually +/- 1:1). We have also observed microdeletions in three AZF regions. The analysis of 17 Y-STRs allows us to detect only two microsatellites. From medical consultation is known that DNA donor has azoospermia manifestation. In order to identify persons and to determine a deletion of AMELY gene in forensic caseworks the use of one PCR-specific kit is not sufficient, therefore, several molecular approaches should be applied.

Keywords: Y chromosome, forensic investigations, Y-STRs, Amelogenin genes, azoospermia

Presentation number: FG 26 Abstract number: ABS-102-ISABS-2009

STABILITY OF N-GLYCAN PROFILES IN HUMAN PLASMA

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Almost all plasma proteins are glycosylated and their glycan parts can exist in various structural forms, resulting in different glycoforms of the same molecule. Glycan heterogeneity was shown to be connected to many diseases and glycosylation holds an unbelievable diagnostic potential due to main biological features and structural characteristics of glycans. Recently we observed high biological variability of human plasma N-glycome at population level. Thus, it was of great importance to standardize analytical methods and examine the temporal constancy of N-glycome in human individuals before routine implementation of techniques that determine glycosylation changes in diagnostic laboratories. Plasma samples were taken from 12 healthy individuals. The blood was drawn on seven occasions during five days. N-linked glycans, released from plasma proteins, were separated using hydrophilic interaction high performance liquid chromatography into 16 groups (GP1-GP16) and quantified. The results showed very small variation in all glycan groups, indicating very good temporal stability of N-glycome in individual. Coefficients of variation from 1.6% for GP8 to 11.4% for GP1, with average of 5.6%, were obtained. These variations were comparable to those due to limitations in the experimental methods when analytical procedure was tested for its precision. We conclude that plasma N-glycome in each individual has very good stability which implies that it is under genetic regulation. Changes occurring in glycan profiles are consequence of environmental influences and physiologic responses and therefore carry good potential diagnostic value.

Keywords: Human plasma glycom, N-glycosylation, Variability of glycans, Stability of N-glycan profile, HPLC

Presentation number: FG 27 Abstract number: ABS-4-ISABS-2009

MULTIPLEX PCR ANALYSIS OF PARAFFIN EMBEDDED TISSUE JUSTIFIED THE VARIATION BETWEEN PRE AND POST SURGICAL REPORTS OF A CANCER PATIENT

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A patient was diagnosed with high-grade breast carcinoma by all the pre-surgery clinical evidences (clinical examination, mammography and FNAC) of malignancy. Later, the histopathological reports did not reveal any tumor residue in post surgical tissue block which raised the suspicion either of block exchange, labeling error or the technical error during gross examination of the tissue. Due to acute shortage of space at histopathology lab, the mastectomy residue was unavailable to sort out the problem at their level. So, two doubtful paraffin blocks processed on same day, were sent to DNA fingerprinting laboratory. DNA extracted from paraffin fixed tissue samples were subjected to multiplex DNA short tandem repeat analysis. The partial DNA profiles (8-9 loci/15) of these samples were obtained which could be due to the low and degraded DNA. The random matching probability for both the paraffin blocks and the patient's blood were found to be 1 in 3.97E8, 1 in 3.36E10 and 1 in 5.04E11 respectively. Therefore, multiplex short tandem repeat analysis applied in this case determined that exact cause of absence of tumor was the error in gross examination of post surgical sample. No effect of LOH and MSI was observed in this case. Moreover, it helped in justifying the therapy given to the patient.

Keywords: breast, carcinoma, paraffin, STR, DNA

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LOW TEMPLATE DNA: TECHNIQUES TO INCREASE SUCCESS RATES AND ASSESSMENT OF THE CONSENSUS APPROACH IN FORENSIC CASEWORK.

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Many DNA extracts obtained from forensic samples contain concentrations of DNA that are sub-optimal for PCR amplification using commercially available STR kits. In order to increase SGM Plus® profiling success from these samples, a combination of increasing the number of thermocycles performed during PCR and increasing the amount of PCR product injected during capillary electrophoresis (Enhancement) has been used to develop a flexible, staged approach for processing these samples. After DNA quantification, the samples are amplified using either 28 or 30 thermocycle PCR and then subsequent to reviewing the profiles, two stages of Enhancement can be used to detect very small quantities of PCR product. This process results in a substantial increase in the number of scorable peaks over 28 thermocycle PCR alone. However, as with all process involving samples containing very low quantities of DNA, distinguishing allelic drop-in from alleles contained within the sample can be problematic. A common practice for distinguishing between allelic drop-in and a “real” allele is to perform duplicate amplifications and then generate a consensus profile only from alleles observed in both profiles. Experiments have been carried out to quantify the occurrence of allelic drop-in. This data has been used to determine whether duplicate amplifications are sufficient for excluding drop-in alleles from consensus profiles and to provide a basis for a database of the frequency of drop-in for each allele at all of the SGM Plus® loci.

Keywords: forensic, low template DNA, Enhancement, SGM Plus®, consensus profile

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VALIDATION OF 4N6 DNA SWABS FOR FORENSIC SAMPLING

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The aim of this presentation is to inform the forensic community about the results of validation studies performed on the novel sample collection system designed especially for the forensic use. Sample collection capacity, assay sensitivity, DNase-free, RNase-free, Human DNA-free and PCR-inhibitor free status and a suitability for automated DNA extraction are the core features that have been tested and compared with “traditional” cotton, dacron or ryon swabs. 4N6 DNA swabs can be used not only for reference sampling (mouth swabs) but due to its sampling capacity and especially the efficiency of sample release from the swab matrix are extremely suitable for crime scene sampling. The key factor influencing the suitability for CS sampling is the ~100% release rate of sample from the swab.

Keywords: sampling, swab, forensic, DNA analysis, automation

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ESTIMATION OF FINE-SCALE RECOMBINATION RATES IN HUMAN GENOME

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The rate of meiotic recombination (i.e. cross over) in humans varies on different physical scales. While broad-scale rates are relatively similar across populations and possibly across species, on a finer –scale situation is different: most of cross over events happen to be concentrated into 1-2 kb regions named “recombination hotspots”. The goal of this study was to obtain fine-scale cross over events in 4 Encode regions located on chromosome 11using single sperm-typing approach in a sample of 1000 sperm cells and to compare the results with available broad-scale recombination maps. Our sperm-typing screen revealed reduced amount (compared to expected) of cross over (3) and, surprisingly, higher rate of homologous gene conversion events (6). Our data supports current hypothesis of gene conversions “clustering” near coding sequence, but rejects presence of correlation between conversion rate and cross over hotspot activity. Distinct distribution of these events can be determined by necessity to maintain coding sequence conservation.

Keywords: gene conversion, cross over, hotspot, fine-scale, sperm-typing

Presentation number: FG 31 Abstract number: ABS-33-ISABS-2009

COULD GENETIC ANALYSIS REVEAL THE MEN'S SURNAME FROM THE BIOLOGICAL EVIDENCE IN THE FUTURE? STUDY OF GENETIC AND GENEALOGICAL RELATIONSHIP IN THE CZECH REPUBLIC.

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Implication of paternally inherited genetic markers (Y-STR,Y-SNP) with surnames distributions in Czech male population and development of methodology for presumption of geographic origin of males in biological evidence The Y chromosome like the most male surnames in Europe is paternaly inherited and this fact supports theory of sharing the similar Y chromosomes by men sharing the same surname. Such a relationship could take an advantage of prediction surname from crime scene evidence despite of several limitatations. Another implication of link between men surnames and Y haplotypes lies in their common geographical origin whereby is possible with definite likelihood ratio to predict population, etnic or national classification for forensically useful conclusions.

Keywords: DNA, Y-chromosome, surname, geographical origin, haplotype

Presentation number: FG 32 Abstract number: ABS-23-ISABS-2009

EVOLUTION AND PHYLOGEOGRAPHY OF HUMAN Y-CHROMOSOMAL LINEAGES IN NORTH EURASIA

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Phylogenetic and phylogeographic research of human Y-chromosomal lineages in population of North Eurasia has been conducted. Composition and frequencies of Y-chromosomal haplogroups in 72 populations belonging to 30 ethnic groups of Eastern and South-Eastern Europe, Central Asia, Siberia and North-East Asia were determined. The data obtained witness the substantial Y-chromosomal genetic diversity of North Eurasian population and the high level of between-population differences which are much higher than those for autosomal markers and for mitochondrial DNA haplotypes. Detailed phylogenetic analysis of the major Y-chromosomal haplogroups (in particular, C3, N1b (N2), N1c1 (N3a), R1a1) by means of the analysis of microsatellite haplotypes based on 17 YSTRs reveals the molecular structure and the age of the most common Y-chromosomal lineages in the modern Eurasian populations. It was sown that haplogroup N2, represents the marker of pre-historic connections between ancient Siberian and Proto-Uralic populations. It was revealed that haplogroup N3a originated in upper Paleolithic in the Eastern Europe – Fore-Ural region and dispersed through Siberia and North-East Asia 8 – 12 ky ago. The age and geographic pattern of the founder haplotype of R1a1 haplogroup testifies its Paleolithic Eastern European origin. However much lower estimates of European and Asian populations divergence (9 -11 ky) corresponds to its post-glacial expansion from west to east of Eurasia. This work was supported by the grants from the Russian Foundation for Basic research ## 06-04-48274 and 07-04-01629.

Keywords: Y chromosome, phylogeography, YSTR, human genetic diversity, population genetics

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COMPARATIVE STUDY ABOUT DIGIT RATIO IN TWO FEMININE POPULATIONS OF BIHOR COUNTY (FROM ORADEA AND ŞTEI LOCALITIES)

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This paper is about the differences of digit ratio in two human populations from two localities. These localities are: Oradea and Ştei, from Bihor county. Oradea is a locality with over two hundred thousands of inhabitants, which means the variability of some phenotipical features must be a large one. Ştei is a smaller locality (has under fifty thousands inhabitants), which means the variability of some phenotipical features is lower than in Oradea. We investigated 100 females in each locality. It were measured the lenghts of the digits 2, 3 and 4, and then we made the digit ratio. The results are important: the digit lenghts are very different in the two localities; the 2D:4D digit ratio, too. We observed in general the decreased variability of all digit ratio in Oradea locality. The observation is justified for all digit ratio, for both hands. Comparing the two hands, we didn't noticed significant differences in the cases of these two ratio in right hand. The difference was observed in the case of 2D:3D digit ratio. In the cases of left hands, the results are different. The F distribution shows that the data proceed from a very different populations in the cases of 3D:4D digit ratio. But, the z test in the case of this digit ratio didn't show a significant difference between the the populations averages. The differences are significant in the cases of the 2D:4D and 3D:4D digit ratio.

Keywords: digit ratio, feminine populations, Oradea, Ştei, genetic variability

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CONTRIBUTIONS ABOUT THE COMPARATIVE DIGITAL MEASUREMENTS IN TWO MASCULINE POPULATIONS OF BIHOR COUNTY

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Our study is about the differences of digit ratio in two human populations of localities. These localities are: Oradea and Pietroasa, in Bihor county. Oradea is a locality with over two hundred thousands of inhabitants, which means the variability of some phenotipical features must be a large one. Pietroasa is a smaller locality (has under ten thousands inhabitants), which means the variability of some phenotipical features is lower than in Oradea. This fact is showed in our study. We investigated 100 males from each locality. It were measured the lenghts of the digits 2, 3 and 4, and then we made the digit ratio. The results are important: the digit lenghts are very different in the two localities; the 2D:4D digit ratio, too. We may conclude the following: low variability of all fingers lengths in male population of Oradea, for both hands; we noticed that the averages are not significant different; we can notice also the low variability of finger lengths in male population of Pietroasa; we noticed that there are no significant differences between the two hands. The exception consists in the ring finger of left hands. In the case of comparison of the two localities averages, the situation is very different than in each population, separately. After z-test calculation, we noticed that the two studied populations are very different, in all cases the obtained values exceeding the 2.58 value which coresponding to p=0.01.

Keywords: digital measurements, digit ratio, masculine population, Oradea, Pietroasa

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EFFECT OF DACTYLOSCOPIC REAGENTS ON DNA AMPLIFICATION

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The purpose of this study was to investigate the effect of fingerprint-enhancement metods on quantification and amplification of DNA. Defined amounts of blood (1, 5 and 10μL) were deposited with fingerprint marks on different surfaces (treated wood, raw wood, plastic, glass, metal and paper). Three defined amounts of blood were applied onto different surfaces three times because the purpose was to determine the influence of time exposure (1, 7 and 14 days) to dactyloscopic reagents. Visualization of bloody fingerprints was performed by using six different dactyloscopic reagents (Amido Black, DFO, Ninhydrin, Cyanoacrilate, Black Magnetic powder and Silver Special powder). As negative control, same defined amounts of blood (1, 5 and 10μL) were deposited with fingerprint marks onto the same surfaces with the same time exposure, but those fingerprints were not treated with dactyloscopic reagents. The results were as follows: no inhibition was detected during quantification of DNA using Real-Time PCR method. Considerable loss of biological material was observed in bloody fingerprints that were treated with Amido Black and Silver Special powder. Longer exposure to dactyloscopic reagents resulted in lower DNA concentration. Untreated fingerprints did not show decrease in DNA concentration. Caution is therefore recommended in situations where bloody fingerprints are very scarce, the loss of blood cells during enhancement may result in insufficient amounts of DNA, which, in turn would jeopardize the DNA analysis in sense of partial DNA profile, or no profile at all.

Keywords: dactyloscopic reagents, bloody fingerprints, DNA, RT-PCR, PCR

Presentation number: FG 36 Abstract number: ABS-73-ISABS-2009

THE PORTUGUESE GYPSY COMMUNITY: A GENETIC APPROACH TO THE DEMOGRAPHIC HISTORY PROVIDED BY THE ANALYSIS OF AUTOSOMAL MARKERS

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The main purpose of this study was to assess to the genetic history of the Portuguese Roma through the analysis of 15 autosomal microsatellites in a sample of 123 unrelated individuals. Average gene diversity for this battery of STRs was lower than the observed for the non-Gypsy Portuguese population showing the reduced genetic variability which characterises the Gypsy people. This feature results from random drift experienced during their diaspora as well from high levels of endogamy. Comparisons between Roma and corresponding host populations denoted that diversity reduction within Roma compared to the non-Roma followed a gradient of decrease according to a geographical direction quite similar to the route of migration and dispersion of Gypsy groups across Europe. On one hand, when genetic distances were calculated high heterogeneity among the Roma groups was revealed, by greater genetic differentiation between Gypsy groups then between non-Gypsies populations, which can be explained again by the strong action of genetic drift and limited inter-group flow. Despite that, all Gypsy populations clustered together when genetic relationships were addressed by Principal Component Analysis, clearly evidencing they share a common origin. Admixture analysis was also conducted revealing a substantial European contribution to the current gene pool of all Roma groups, whereas the component ascribed to the ancestral origin in India comparatively appeared to be more diluted. Thus, it seems more likely that the incorporation of the Indian fraction autosomal genome stems primarily then European genetic contribution from contemporary times.

Keywords: autosomal STRs, Roma, Portugal, genetic diversity, admixture

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DEVELOPMENT OF A NEW STR SYSTEM TO MEET THE CHANGING NEEDS OF THE EUROPEAN DNA-TYPING COMMUNITY

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The Treaty of Prüm encourages cross-border data sharing and cooperation. With over 6 million profiles currently stored in European databases, and the number expected to increase, the likelihood of random matches will undoubtedly increase as well. To improve the overall power of discrimination as well as provide standardization across Europe, the ENFSI and EDNAP committees have made a recommendation to extend the current European Standard Set (ESS) for STR systems. We will discuss the PowerPlex® European Systems, which comply with the new recommendation. The kits are based on five-color-technology and allow co-amplification and detection of the current commonly tested loci, plus the 5 new recommended loci. These kits will be offered in multiple formats, including the option to detect SE33, to accommodate various requirements and/or preferences. Additionally, the kits have increased tolerance to common inhibitors and increased sensitivity to obtain! full profiles from low-level DNA and are robust enough to genotype degraded DNA samples through the use of mini STR loci. In this presentation we will present the design of these systems and data on overall performance, including sensitivity and resistance to inhibitors. The PowerPlex® European Systems will be a useful tool in database sharing and standardization throughout Europe.

Keywords: STR, European Standard Set (ESS), PowerPlex, mini STR, inhibitors

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DEVELOPMENT OF THE POWERPLEX® 16 HS SYSTEM

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Short tandem repeat (STR) analysis remains the primary method for human identification. Forensic typing, criminal databasing and relationship testing laboratories in the US and many other regions of the world use a standard set of 13 STR markers selected by the US Federal Bureau of Investigation for the Combined DNA Indexing System (CODIS). The PowerPlex® 16 HS System co-amplifies these 13 loci (D18S51, D21S11, THO1, D3S1358, FGA, TPOX, D8S1179, vWA, CSF1PO, D16S539, D7S820, D13S317 and D5S818) plus the low-stutter Penta E and Penta D markers and the gender-determining Amelogenin locus. One primer for each of these loci are labeled with fluorescein, carboxy-tetramethylrhoamine (TMR) or 6-carboxy-4',5'-dichloro-2',7'-dimethoxy-fluorescein (JOE). Amplicon size is determined by comparison with the Internal Lane Standard 600 (ILS 600) labeled with carboxy-X-rhodamine (CXR). This four-color chemistry can be analyzed on the ABI PRISM® 310, 3100 and 3100-Avant Genetic Analyzers and Applied Biosystems 3130 and 3130xl Genetic Analyzers using existing dye matrix standards. The PowerPlex® 16 HS System provides a hot-start Taq DNA polymerase in a modified master mix to provide increased ease-of-use and performance over previous PowerPlex® systems. This assay has increased tolerance to common forensic sample inhibitors known to reduce genotyping success rates. The presentation will share results from sensitivity and inhibitor studies along with developmental validation results.

Keywords: STR, forensics, CODIS, PowerPlex®

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DEVELOPMENT OF A FORENSIC SCREENING TOOL: THE POWERPLEX® S5 SYSTEM

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Multiplexed Short Tandem Repeat (STR) analysis has become the dominant technology in DNA-based human identification. As the number of samples typed per case increases, especially in complex homicide or sexual assault cases, the need for less expensive methods for screening these multiple samples becomes apparent. By using a simple yet extremely sensitive STR system, the forensic DNA laboratory can quickly discriminate between the limited number of donors present in a given case. In addition, large pools of suspects can be mass-screened inexpensively at a level of discrimination sufficient to identify only a very small number of possible matches. Following this, the laboratory can then select the most probative DNA samples to continue with a full compliment of STR testing. The PowerPlex® S5 System has been developed for the co-amplification and two-color-detection of 4 STR loci: (D18S51, D8S1179, TH01 and FGA) and Amelogenin. The amplicon lengths of the largest loci have been significantly shortened so that all amplicons are less than 260bp. The robust and careful design of the PowerPlex® S5 System provides maximum sensitivity with low quantities of DNA (less than 100pg). This makes the system ideal for use with low copy numbers samples including touch samples. The reduced number of loci in the PowerPlex® S5 System provides enough data for screening purposes at an economical price point. Sensitivity testing and inhibitor testing data will be shown.

Keywords: Forensic DNA, STR, Screening, PowerPlex, inhibitors

Presentation number: FG 40 Abstract number: ABS-68-ISABS-2009

CHALLENGES IN STATISTICAL PRESENTATION OF PATERNITY TESTING RESULTS

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Over the last decades the analysis of autosomal STR (Short Tandem Repeats) loci has become almost ultimate tool for paternity testing as in trios, mother, child and putative father, also in duos, putative father and child. This presentation will provide an overview of current efficiency and statistical challenges of motherless paternity testing and specific paternity testing results. DNA analysis was performed four children, two sons and two daughters, also putative father. Buccal swabs were collected from all children and putative father. DNA extraction was done using commercial Qiagen protocol. Promega PowerPlex 16 kit was employed for simultaneous amplification of 15 STR loci and amelogenin. Electrophoresis of the amplification products was performed on ABI PRISM 310 genetic analyzer. Paternity was statistically positive for two children (PP>99,99%), but for the other two children PP was under that desired value, including even one mutation at D18S51 for one child (first female child PP was 99.85734%, and for second one was 99.98716%). Therefore it was recommended mother's sample to be processed. This is another proof that motherless paternity testing sometimes could vary in its statistically significance even between putative father and child in paternity testing cases.

Keywords: matherless paternity testing, buccal swabs, statistics, DNA analysis, results presentation

Presentation number: FG 41 Abstract number: ABS-38-ISABS-2009

HIGHER CAPILLARY ELECTROPHORESIS INJECTION SETTINGS AS AN EFFICIENT APPROACH TO INCREASE THE SENSITIVITY OF STR TYPING

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Evidentiary traces may contain low quantities of DNA, and regularly incomplete short tandem repeat (STR) profiles are obtained. In this study, higher capillary electrophoresis injection settings were used to efficiently improve incomplete STR profiles generated from low-level DNA samples under standard PCR conditions. The method involves capillary electrophoresis with higher injection voltage and extended injection time. STR peak heights increased six-fold. Inherent to the analysis of low-level DNA samples, we observed stochastic amplification artifacts, mainly in the form of allele dropout and heterozygous peak imbalance. Increased stutter ratios and allele drop-in were rarely seen. Upon STR typing of 10:1 admixed samples, the profile of the major component did not become overloaded when using higher injection settings as was observed upon elevated cycling. Thereby an improved profile of the minor component was obtained. For low-level DNA casework samples, we adhere to independent replication of the PCR amplification and boosted capillary electrophoresis.

Keywords: forensic science, DNA-typing, low copy number, mixed samples, capillary electrophoresis

POSTER PRESENTATIONS

Molecular Anthropology

Presentation number: MA 1 Abstract number: ABS-6-ISABS-2009

GENETIC ASPECTS OF MALE INFERTILITY IN AZERBAIJAN

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Male infertility is the consequence of complex pathologic influence on male reproductive system. The share of male infertility comprises not less than half of all the reasons of their infertility while married. Alongside with that the reason of 30% of male infertility is still not identified. At the same time with anatomic, inflectional, endocrynal, immunologic causes of infertility professionals pay more and more attention to genetic factor studies. They define gene, chromosome and genome mutations. 80 male patients with diagnosis: infertility - were studied in IVF program as well as 60 male patients with diagnosis: infertility in the consultancy office called “Marriage and family”. The control group was 30 healthy men with normal reproductive activity. Genetic methods were as chromosome analysis, PCR technology, and genealogical analysis. Laboratory methods were as blood hormones identification as well as infections and sperm gram. Genetic causes after infections and hormone defects take the 3rd place: around the same 6,7% in IVF program patients and 6,6% in “Marriage and family” consultancy patients’ group. To genetic abnormalities we relate as follows Kleinfelter syndrome with chromosome set of 47XXY, 46XY/47XXY, 46XY\\48XXXY; Poli-Y syndrome with genotype of 47XYY; Shereshevski-Terner syndrome with genotype of 46XY\\45X0; 46 XY\\t(7;16)(p21q22), 46XU\\ t(3;5)\\(qter1q15), Lawrence-Moon-Barde-Biddle. Cryptorchism and hypospodia were classified as inherited abnormalities. Chromosomal, gene and genome defects in the genetic structure causes of male infertility were observed among men in Baku city. The frequency of genetic causes and inherited development abnormalities in the male infertility structure is 13,3%.

Keywords: infertility, chromosomes, syndromes, reproductive, activity

Presentation number: MA 2 Abstract number: ABS-14-ISABS-2009

SEX DETERMINATION IN CHILDREN AND UNDETERMINABLE SKELETAL REMAINS FROM BURIAL SITE POHANSKO NEAR BRECLAV

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The archaeological area Pohansko is situated in the south-east area of the Czech Republic, near the town Breclav. The South Outer Precinct is the second largest burial site that was discovered at Pohansko and it is dated within the end of 8th century and the beginning of 10th century. Bone material was excavated during a rescue archaeological research in the period of 1975 – 1979. The skeletal remains from The South Outer Precinct are badly preserved, the bones are fragmentary and in most cases unidentifiable. Of the 190 skeletons, only 27 were determined as male, 40 as female and 87 as children. The sex of the remaining 36 skeletons was impossible to define by standard methods. The aim of this study was to determine the sex of children's and undeterminable skeletons using two sex markers – the amelogenin gene and the SRY gene. The amelogenin gene shows size differences between the X and the Y human chromosome. We amplified short fragments of the amelogenin gene, 106 bp of the X chromosome and 112 bp of the Y chromosome. A 93 bp fragment of the male specific SRY gene was used as the second marker. The results are important for demography of the burial site.

Keywords: sex determination, amelogenin gene, SRY gene, skeletal remains, Pohansko

Presentation number: MA 3 Abstract number: ABS-3-ISABS-2009

GENETIC STRUCTURE OF KABARDINIANS AND BALKARS OF THE NORTH CAUCASUS BASED ON 15 ALU INSERTIONS

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Study of 15 Alu insertion loci (Ya5NBC27, Ya5NBC51, Ya5NBC102, Ya5NBC123, Ya5NBC148, Ya5NBC182, ACE, APO, B65, PV92, TPA25, Ya5NBC171, Ya5NBC242, Yb8NBC480, Yb8NBC485) have been implemented in two populations of the North Caucasus: Kabardinians (n=58) and Balkars (n=89). The highest frequency of alleles has been observed on ApoA1 locus in Kabardinians (up to 0.95), the lowest frequency has been observed on Ya5NBC174 locus in Balkars. Population comparison revealed statistically significant differences between the two populations basing on 15 alu insertions the loci ($\chi 2=53.2$, df=32, p=0.01). The value of expected heterozygosity on 15 Alu insertions is 0.358 in Kabardinians and 0.397 in Balkars. Gst for the two populations on 15 Alu insertions was 0.001 what is quite low value. For example Gst in European and southeast Asian populations are 0.004 and 0.026 respectively for the same Alu insertions dataset (Watkins et al., 2003). It needs to be stressed here that frequency of PV92 (which frequency is highest in southeastern Asia populations) locus in Balkars is almost two times higher than in Kabardinians (0.32 vs 0.17), though its value fits the range of European populations. Moreover the frequency of Yb8NBC480 and Yb8NBC485 loci which demonstrate clinal longitudinal changes alongside Eurasian continent show insertion frequency pattern like European populations. Principal component analysis revealed that Kabardinians and Balkars are close to European populations forming a distinct cluster with Europeans.

Keywords: Alu insertions, population genetics, Caucasus

Presentation number: MA 4 Abstract number: ABS-32-ISABS-2009

NON-DESTRUCTIVE DNA ELUTION FROM BLOOD STAIN PAPER - "EAT CAKE AND STILL HAVE CAKE"

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The starting inspiration to our work was a hearing about trouble of our colleagues from Cracov Institute of Forensic Research. They try to identify of Nicolaus Copernicus putative scull, exhumed some years ago in Frombork. The best reference material seemed the blood stain on Copernicus calendar, probably effect of inadvertent sharpening the goose feather, but curators of these valuable documents definitively not agreed for destroying paper by cutting a fragment of stain for DNA preparation using routine forensic science techniques. We decided try to develop the quite new, non-destructive technique of elution DNA from paper surface. To reach of our aim, we must overcome three technical problems: 1.Construction of special “elutor” prototype (the small, but heavy apparatus which is placed on stained paper surface, with small sucker, tightly putted into stain). The photograph of these apparatus will presented to all interested in. 2. Composition of elution fluid, aggressive, suitable to permanent old blood stains, but safe for paper and not too excessive infiltrating into background. Finally, the fluid contains water, hydrolised starch, glycerol, sodium dodecyl sulphate, triton X100, proteinase K and EDTA. All details will be revealed during congress presentation. 3. Fine tuning the time of elution, suitable temperature and right fluid flow parameters, details will accessible as above. Using of this new method, we successfully eluted DNA suitable to PCR test from blood stains on paper aged as follow: fresh (experimental and from crime scene) stains 1, 2,5, 11, 47 and 57 years old. In the moment, we already have no access to sure dated, older blood stains on paper, but we are open to cooperation with all interested researchers.

Keywords: Ancient DNA, Non-destructive elution, Elution from paper, Blood stain, Isolation DNA

Presentation number: MA 5 Abstract number: ABS-36-ISABS-2009

SEQUENCE ANALYSIS OF NEOLITHIC AND MUMMIFIED HUMAN REMAINS

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One working with ancient DNA faces the challenges of amplification of low copy number DNA templates. To get reliable sequence data of an aDNA sample, the independent reproducibility is also criteria. That requires careful experimental strategy throughout the whole multi-step processes that are employed to successfully extract the low concentrations of DNA present in ancient remains, their amplification via PCR, and even postPCR modification of amplicons and their sequencing. Primer walking strategy was used to map through the hypervariable region of human mitochondrial DNA to identify specific polymorphic sequence in 7-5000 year old Neolithic remains. This technique was developed on an almost recent mummy collection. Amplifiable fragments were isolated and their sequences were determined via direct sequencing of PCR products of interest. The spectra of the amplification product were found 80-455 bp, but this efficiency was only achievable when we applied DNA purification step in the prePCR protocol. In our Neolithic aDNA preparation, the efficiency was poor without this purification. DNA sequence analysis showed that certain parts of the mitochondrial DNA contain point mutations specifically bound to the aDNA of the Neolithic remains. These polymorphisms were trapped through the Neolithic remain collection, and checked with amplification experiments using polymorphism specific primers. Their distribution is under survey. This analysis will be extended on other Neolithic sites in Europe, in order to add data to the mtDNA polymorphism pattern of Neolithic people. This study was supported by The Wenner-Gren Foundation (grant No. 7610) and Hungarian Scientific Research Fund (OTKA, grant No. 61155).

Keywords: mitochondrial DNA, Neolithic, polymorphism, ancient DNA, sequence comparision

Presentation number: MA 6 Abstract number: ABS-5-ISABS-2009

GENETIC SCREENING ON INHERITED HEMOGLOBINOPATHIES IN GABALA DISTRICT OF AZERBAIJAN REPUBLIC

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Population genetic researches in the population of Azerbaijan Republic have demonstrated high genetic heterogeneity of inherited hemoglobinopathies. Alpha- and beta-thalassemias, abnormal hemoglobins as HbS, HbD, HbE and HbC were observed. In our population studies we decided to identify genetic heterogeneity and frequencies of inherited hemoglobinopathies in the population of Gabala district of Azerbaijan. For genetic screening of inherited hemoglobinopathies there were used: test on erythrocytes osmotic resistance, method of hemolysate isoelectrofocusing in polyacrylamid-ampholine plates with pH 3,5-9,5 and pH 5,5-9,5, test for sickle-cells in erythrocytes and test for hemoglobin solubility. Genetic screening of inherited hemoglobinopathies has revealed in 2 cases sickle-cell anemia (HbSS), in 8 heterozygotes with HbS, in 2 cases compounds (phenotype - β+-HbS), 18 cases with heterozygous β-thalassemia, 13 cases with homozygous β-thalassemia (β0- и β+ -phenotypes), 2 cases with HbH with HbBart's traits in patients from district hospital. Testing mutations in patients with β-thalassemia allowed us to identify 2 mutation types: microdeletion of two nucleotides adenine in codon 8 of the first exon of β-globin gene (β-codon 8 -AA) and nucleotide substitution of guanine by adenine in 110 position of the first intron of β-globin gene (β-IVS-1-110,G-A). Taking into account high frequencies of inherited hemoglobinopathies in Gabala district of the Republic, genetic screening among marriage couples is recommended, and in case of genetic risk revealing the fetus prenatal diagnostics should be carried out.

Keywords: sickle-cell, anemia, thalassemias, mutation, screening

Presentation number: MA 7 Abstract number: ABS-20-ISABS-2009

ANCIENT DNA EXTRACTION FROM BONE & TOOTH WITH EFFICIENCY OF TAQ POLYMERASE INCREMENT IN PREVENTING INHIBITION BY HUMIC ACID

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The forensic application of DNA-typing for the identification of old bone and tooth provides objective evidence in the characterisation of traces found at crime scenes. However, DNA-typing from samples of old bone and tooth is often problematic in forensic science. Old bone and tooth contains very small quantities of DNA or bad quality. Here we describe an experimental study about Ancient DNA Extraction from Bone & Tooth with Efficiency of Taq polymerase increment in preventing inhibition by Humic Acid. Characteristic features of humic substances are their structural heterogeneity, their property to bind metal ions by complex formation, and their property to interact with a variety of organic compounds. Humic substances are ubiquitous in soil and water and can contaminate any material exposed to those environments, which causes false negative results. Real-time detection is a very fast and accurate technology that does not require post-PCR processing, since detection is done during each PCR cycle. QRT-PCR methods have the ability to quantitative trace amounts of human DNA isolated from old bone samples. To enhance the PCR efficiency in samples containing inhibitors, example HA or other humic substances, by 2-4U extra Taq DNA polymerases were included in the reactions. Altered amplification plots were observed during the analysis of old bones and teeth to the presence of inhibitors. The addition extra Taq DNA polymerases amounts has been proven efficient in overcoming the effects of inhibitors.

Keywords: Ancient Bone, Ancient Tooth, DNA Extraction, Taq Polymerase, Humic Acid (HA)

Presentation number: MA 8 Abstract number: ABS-28-ISABS-2009

THE USE OF NOVEL Y-CHROMOSOME MINI-STR PENTAPLEXES FOR THE ANCIENT DNA ANALYSIS AND GENETIC GENEALOGY

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Commercially available Y-chromosomal short tandem repeat (Y-STR) multiplexes that incorporate 12-17 loci have only moderate discrimination potential compared to the available scale of autosomal STR markers. Hence we developed 2 new Y-chromosome mini-STR pentaplex systems for new Y-STR loci (DYS426, DYS459ab, DYS449, DYS447, DYS388, DYS444, DYS446, and DYS481) to supplement the 17-loci from the Y-filer kit (Applied Biosystems) and to enlarge the number of tested loci to 26. In addition, the selected amplicons were designed as short as possible in order to find applications also in analysis of degraded DNA samples. The suitability of those mini-STR multiplexes for the prediction of Y-chromosome haplogroup will also be discussed.

Keywords: Y-chromosome, mini-STR, degraded DNA, forensic, haplogroup

Presentation number: MA 9 Abstract number: ABS-30-ISABS-2009

RT-PCR QUANTITATION OF FORENSIC SAMPLES AND THE DETERMINATION OF THE LEVEL OF DNA DEGRADATION USING THE 4N6QUANT SYSTEM

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The authors present the results of the validation study performed on the system for RT-PCR quantitation of forensic samples. The novel 4N6Quant system enables not only to precisely quantify the minute amounts of degraded DNA but this system can also be used for the determination of the level of DNA degradation. The target sequences of this SYBR-Green based RT-PCR system are placed to ALU non-autonomous mobile elements. The human genome contains more than 1million of these ALU repeats and therefore 4N6Quant offers the sensitivity of at least 1pg DNA/ul. The size of PCR amplicons (229 bp and 140 bp) employed in 4N6Quant system reflects the size of commercial STR kits and therefore the quantitation results are more precise when compared to the commercial qPCR systems with amplicons bellow 100 bp. An added value is the possibility to check the DNA quality (level of degradation).

Keywords: ALU, quantitation, forensic, degraded DNA, RT-PCR

Presentation number: MA 10 Abstract number: ABS-31-ISABS-2009

DNA ANALYSIS OF THE 7TH CENTURY HUMAN REMAINS FROM THE BURIAL SITE IN ERGOLDING, GERMANY

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The main goals of this study were to develop novel DNA extraction and typing procedure that would enable to perform DNA identification of 7th century human remains, to set the familiar relationship between the individuals, to estimate the Y-chromosome haplogroup and to compare the Y-chromosome haplotype with the contemporary populations. Early-medieval burial-place in Ergolding (Bavaria, Germany) was archaeologically examined in years 1997-2002 by the Bavarian State Department of Monuments and Sights, Germany and they recovered more than 440 graves. The human remains of six early adult males examined using DNA analysis in this study were found in the central grave number 244. We clearly demonstrated that the modern methods and procedures of forensic DNA analysis can be successfully used also in the area of archaeogenetics to determine not only the familiar relationship but also to predict the place of the geographic origin of the unknown skeletal remains. Application of forensic genetics into the archaeology can bring new information and help in interpreting of the findings. The number of successfully typed autosomal and Y-STR loci from ancient specimen is one of the most complex published so far for aged samples.

Keywords: archaeogenetics, degraded DNA, Y-chromosome, mini-STR, skeleton

Presentation number: MA 11 Abstract number: ABS-45-ISABS-2009

HUMAN SKULL DIMENSIONS FROM ANTIQUE TO LATE MEDIEVAL IN CONTINENTAL CROATIA

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Human evolution, mixing of nations during population movements, diseases and dietary pattern can induce changes of bone dimensions. Aim is to evaluate changes in skull dimensions during the period from antique (A) and early medieval (EM) to late medieval (LM). Six standard cephalometric dimensions were measured on 255 adult skulls from continental Croatia. LM males showed statistically significant higher values of transverse (Euryon-Euryon: A 138.7±6.0 mm, EM 137.6±5.2 mm, LM 149.6±6.6 mm) and vertical (Nasion-Prosthion: A 68.0±2.0 mm, EM 70.5±4.0 mm, LM 71.8±4.4 mm and Nasion-Gnathion: A 107.5±15.4 mm, EM 117.9±6.0 mm, LM 120.1±10.1 mm) diameter of the skull. The mid-sagittal diameter (Opisthocranion-Glabella) was statistically significant lower in LM than in the A and EM sample (A 181.0±7.0 mm, EM 183.5±4.8 mm, LM 175.3±6.6 mm). LM females showed statistically significant higher values of transverse diameter of the skull (Euryon-Euryon: A 133.5±5.4 mm, EM 129.6±6.5 mm, LM 142.5±3.9 mm) and lower the mid-sagittal diameter (Opisthocranion-Glabella: A 178.9±5.4 mm, EM 178.9±6.8 mm, LM 168.7±6.0 mm). Males from the LM period showed significant lower values of Gonion-Gonion distance (A 107.5±7.1 mm, EM 103.1±6.2 mm, LM 101.6±6.8 mm). Changes of skull dimensions can be explained by population movement during the wars in the late antique – early medieval transition period. In this period new nations from the northern parts of Europe came in the continental Croatia and mixed with native people from antique times. Lower values of Gonion-Gonion distance in LM sample could indicate changes in dietary pattern.

Keywords: Paleodontology, Skull dimension, Antique, Medieval, Croatia

POSTER PRESENTATIONS

Individualized Medicine

Presentation number: IM 3 Abstract number: ABS-100-ISABS-2009

EXPRESSION OF GLYCOSILATION-RELATED GENES IN PATIENTS WITH POSTTRAUMATIC STRESS DISORDER

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Glycosylation is the most important post-translational modification of proteins and lipids. Glycan structures play numerous roles, including protein folding, targeting, recognition and adhesion. Transcriptional regulation of the enzymes involved in glycan synthesis and catabolism is one of the major modes of regulation of cellular glycosilation. Aim of this study is to unravel possible chronic changes of expression of a selected group of 22 glycosilation-related genes (10 fucosyltransferases and 12 sialyltransferases) in diseases characterized with chronic dysregulation of hypothalamus pituitary adrenal (HPA) axis. Our assumption was that dysregulated HPA axis inevitably leads to changes of expression of glycosilation-related genes, resulting in different glycan profile on immune cells (leukocytes/lymphocytes) of control subjects and patients with chronic posttraumatic stress disorder (PTSD), as one disease characterized with chronic dysregulation of HPA axis. Total RNA was isolated from blood of 153 patients with combat-acquired PTSD and 42 psychically healthy war veterans, as controls. Relative quantification of gene expression (real-time PCR) was performed using SYBR Green method and t-test for analysis of significance. Part of the samples has been analyzed; 88 out of 153 patients and 27 out of 42 controls. Preliminary data show that there is no statistically significant difference in expression of selected glycosilation-related genes, although differences in expression levels of fucosyltransferase 7 approach to significance threshold of p=0, 05.

Keywords: gene expression, glycosylation, posttraumatic stress disorder, war veterans, glycosilation-related genes

Presentation number: IM 4 Abstract number: ABS-58-ISABS-2009

ANALYSIS OF THE CORRELATION BETWEEN AUTISM AND *(GATA)$_n$* MICROSATELLITE ON THE 5'FLANKING REGION OF THE AVPR1A GENE

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The neuron-anatomic distribution of the arginine-vasopressin receptor 1A and the subsequent amount of arginine-vasopressin influences attachment and social behavior, thereby demanding research on the correlation between AVPR1A gene and autism spectrum disorders (ASD). ASD seriously impair intellectual development, bring about behavioral imbalances and often overlap with mental retardation. The study was case-control type and involved three groups: 32 patients diagnosed with mental retardation (MR), 19 patients suffering from ASD and 196 subjects with normally developed intellects as a control group. DNA was isolated from white blood cells, under informed consent from authorized caretakers. The (GATA)n microsatellite, located on the 5'UTR of the AVPR1A gene, was analyzed by PCR - PAGE technique, and the results were interrogated using population genetic specific programs. 9 alleles associated to the microsatellite sequence previously amplified and designated A to I were identified. The allele frequencies calculated for each group shown that allele A is missing on ASD patients (f(A)=0)), comparing with MR patients and control (f(A)=0.031 and 0,013 respectively) Also, the frequency of allele D is higher on ASD and MR group (0,368 and 0,328) comparative with the control group (0,281). Concerning the genotype frequencies, the homozygous genotypes EE and HH are well represented in controls, but are absent in both patient groups. The observed and expected data match in a satisfactory manner, and suggest that all three groups are in a state of genetic balance.

Keywords: autism, microsatellites, AVPR1A, arginine vasopressin, social behavior

Presentation number: IM 5 Abstract number: ABS-10-ISABS-2009

GENETIC RESEARCHES IN TWO DISTRICTS OF AZERBAIJAN REPUBLIC

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Results of genetic researches of inherited diseases in Guba and Khachmas districts of the Republic are brought to attention. Registration of phenotypicaly easiest diagnosed forms of inherited diseases have been carried out, and summary frequency was averagely 0,0614% and 0,0850%, respectively. Genetic diseases have been found in Guba district and according to inheritance types were divided as follows: multifactoral - 44,94%, autosome-recessive - 22,47%, autosome-dominant - 10,11%, X-linked recessive - 12,35% and chromosomal diseases - 10,11%. In Khachmas district in boys with hemizygous genotype we managed to differentiate two phenotypes: total G6PD “0-phenotype” and partial deficiency of G6PD enzyme “+-phenotype”. Using complex of DNA diagnostics methods three mutation types of β-thalassemia were identified: 1. Substitution of guanine nucleotide by adenine in position 110 of the first intron of β -globin gene with β +- thalassemia phenotype, 2. Deletion of two adenine nucleotides in codon 8 of the first exon of β -globin gene with phenotype of β - thalassemia and 3. Substitution of guanine by adenine in position 1 of the second intron of globin gene with phenotype ofoβ - thalassemia. The ways of prophylaxis of genetic abnormalities in the population of those two districts are being discussed.

Keywords: mutation, chromosomal disease, inherited disease, intron, exon, G6PD deficiency

Presentation number: IM 6 Abstract number: ABS-12-ISABS-2009

THE STUDY OF AR GENE CAG-POLYMORPHISM IN PATIENTS WITH AZOOSPERMIA AND OLIGOZOOSPERMIA FROM UKRAINE

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Androgens are the male sex hormones that belong to the steroid hormone family. They are required for male sex determination, development and spermatogenesis. They exert this effect through the androgen receptor encoded by the androgen receptor gene (AR), which located on chromosome Xq11-12 and has a repetitive DNA sequence in exon 1 that encodes a polyglutamine tract. Within the normal polymorphic range this (CAG)n tract length is inversely related to the transcriptional activity of the androgen receptor. The AR gene exon 1 CAG-repeats number was determined in group of 228 infertile males (68 – azoospermia, 160 – oligozoospermia) and in 124 fertile controls by fluorescent polymerase chain reaction followed by fragment analysis on automated fluorescent analyzer "A.L.F.-express". The frequency ($p<0.01$) of AR gene alleles with ≤18 CAG -repeats was significantly higher in group of patients with azoospermia (17.7%) comparing with control group (2.4%). The similar difference ($p<0.01$) was found between group of patients with oligozoospermia (12.5%) and control group (2.4%). Our data confirm the hypothesis that reduces of the CAG-repeats number is closely related to impaired sperm production in infertile males. The frequency ($p<0.01$) of alleles with≥28 CAG -repeats was significantly differed ($p<0.01$) between group of patients with oligozoospermia (12.5%) and control group (2.4%). Our data is an according to results of other authors that enlargement of the polyglutamine tract ≥28 glutamine residues in infertile males is associated with a 4-fold increased risk of infertility. Obtained data are the evidence of association between CAG-repeats number and impaired spermatogenesis in infertile males.

Keywords: spermatogenesis, androgen receptor, azoospermia, oligozoospermia, CAG-repeats

Presentation number: IM 7 Abstract number: ABS-40-ISABS-2009

A NEW POLYMORPHISM IN MICRORNA-BINDING SITE OF *CDKN2A* AND *XPD* IN MALIGNANT MELANOMA PATIENTS

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The strongest risk factors for Cutaneous Malignant Melanoma (CMM), a high case-fatality rate, are family history for melanoma, multiple benign or atypical nevi, previous melanoma, sun sensitivity and mainly ultraviolet radiation exposure. DNA damage by direct (pyrimidine dimmers) and indirect effects (oxidative stress) are expected results. Both types of DNA damage lead to diverse cellular responses in melanocytes, including cell cycle arrest triggered by p16 gene (CDKN2A locus) and DNA repair. A hospital-based case-control study was conducted in Sao Paulo, Brazil, to evaluate CDKN2A microRNA-binding region and DNA repair gene XPD/PstI polymorphisms in 193 patients with confirmed CMM and 208 cancer free controls. The frequency of CDKN2A and XPD/PstI polymorphisms observed in the patients (5.8% and 15.2% respectively) was higher than that observed in the control group (3.4 and 12.7% respectively) but the difference was not considered statistically significant for CDKN2A (OR = 2.10; 95% CI, 0.73 – 6.05) or XPD/PstI (OR = 1.33; 95% CI, 0.71 – 2.52) mutated genotypes. The negative results for the association between melanoma and the polymorphism in microRNA binding site of CDKN2A seams to indicate no interference in cell cycle regulation in the patients. To our knowledge, this is the first report that evaluated this polymorphism in patients with CMM and the preliminary results suggest the evaluation of a large population. The negative association of XPD/PstI variant genotype and CMM in our population seems to be in accordance with other data in the literature but we are increasing the sample size for statistical confirmation.
(FAPESP/CNPq/LIM40/LIM-24).

Keywords: CDKN2A, XPD, Melanoma, Polymorphism, Case-Control

Presentation number: IM 8 Abstract number: ABS-43-ISABS-2009

FREQUENCY OF POLYMORPHISMS C677T MTHFR AND A66G MTRR OF FOLATE CYCLE GENES IN EARSTERN UKRAINE

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The pivotal role of folate cycle genes in a wide spectrum of clinical pathology is under the focus of intense research. According to the pilot study by Matalon and colleagues, (2007), the Ukrainian population may have a higher frequency (0.57) of allele 66G MTRR, which has been associated with the neural tube defects. To better characterize this putative association, we investigated incidence of C677T MTHFR and A66G MTRR polymorphisms and in more extensive group of patients (1238) with deficiency of the folate cycle. The SNPs in MTHFR and MTRR were screened by using the PCR test-systems. The gene fragments were visualized in 3% agarose gel. The genotypes and allele frequencies of C677T MTHFR and A66G MTRR were calculated. Heterozygous genotype CT was present in 539 patients (43.5%), homozygous genotype TT MTHFR in 104 (8.4%), and CC in 595 (48.1%). The frequency of 677T allele was 0.30. According to earlier studies, the allelic frequency for healthy populations in Europe varied: France - 0.41; Italy – 0.47; Russia – 0.28. For MTRR polymorphism, the genotype AG – 512 (41.4%), GG was present in 450 patients (36.3%), AA – 276 (22.3%). The frequency of 66G MTRR allele was 0.57 (European population – 0.54). These data emphasize the necessity of screening the polymorphic genes in a group of high risk, which associated with deficiency of folate cycle: families with chromosomal anomalies, oncogenetic pathology, reproductive disorders.

Keywords: polymorphism, MTHFR 677T, MTRR 66G, Ukrainian population, folate cycle

Presentation number: IM 9 Abstract number: ABS-18-ISABS-2009

AN ULTRASTRUCTURAL STEREOLOGIC ANALYSIS OF THE FEMALE BREAST PARENCHYMAL CELLS IN DIFFERENT PHYSIOLOGICAL STATES

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Parenchymal cells of premenopausal and postmenopausal female breast ductules were studied to determine the limits of normal ultrastructural variability by using stereologic analysis as an objective method of determining morphological characteristics. Different physiological states also have been compared in pre- and postovulatory period of premenopausal breasts. The relative volumes of epithelial and myoepithelial cells in examined material were obtained by the stereologic method of point counting. Stereologically were examined and compared numerical densities (NV) of epithelial and myoepithelial cells and the volume density (VV), surface density (SV) and specific surface density (SV/VV) of the epithelial cells nuclei and cytoplasm. Stereologic parameters have been evaluated statistically by applying Student's t-test. In all examined states numerical density of epithelial cells were much greater than numerical density of myoepithelial cells which slightly decreased in postovulatory and postmenopausal period. Postovulatory, the volume density and surface density of nuclei as well as specific surface density of epithelial cells cytoplasm were much less, while a volume density of epithelial cells cytoplasm were greater. Postmenopausally, a slight decrease of stereologic parameters of epithelial cells nuclei was noted, while epithelial cells cytoplasm parameters were slightly increased. The fact that these quantitative differences of epithelial cells were not statistically significant leads to conclusion that the ultrastructural characteristics of the epithelial cells after menopause do not undergo essential changes.

Keywords: female breast, parenchymal cells, ultrastructure, stereology, physiological states

Presentation number: IM 10 Abstract number: ABS-1-ISABS-2009

PREOPERATIVE DIAGNOSTICS OF THYROID NODULES BY MOLECULAR ANALYSIS OF FNAB MATERIALS

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Molecular markers of papillary thyroid carcinoma (PTC) including the BRAFT1799A mutation, RET/PTC1,3 rearrangements and differentially expressed SFTPB (up-regulated) and TFF3 (down-regulated) genes were prospectively assessed in FNAB (fine needle aspiration biopsy) material from thyroid nodules. Totally 109 FNAB samples in 107 patients (23 males, 84 females aged 19.1-65.4 years) were analyzed. Cytological examination revealed PTC in 57 cases, non-malignant disease in 50 and it was non-informative in 2 cases. Concordantly with cytology, molecular diagnosis of PTC by SFTPB and TFF3 expression levels was confirmed in 56/57 cases (98.2%); in them 28/57 (49.1%) had mutant BRAF and 11/57 (19.3%) had RET/PTC. For non-PTC nodules, concordance was observed in 43/50 (86.0%) cases. Among 7 patients with discordant molecular and cytological diagnoses, 5 were examined repeatedly. Two of them were diagnosed for PTC (both BRAFT1799A-positive) about 1 year, nodule growth was documented in 1 patient (with BRAFA1801G mutation) and in 2 cases diagnosis remains unchanged so far. Overall, the findings indicate that molecular analysis is an informative adjunctive means of preoperative evaluation of thyroid nodules. Given its high sensitivity and specificity, molecular testing may identify patients with possible PTC before other diagnostically meaningful changes take place.

Keywords: papillary, thyroid, carcinoma, molecular, markers

Presentation number: IM 11 Abstract number: ABS-44-ISABS-2009

PHYSICAL-CHEMICAL AFFECT POISONS IN SHAKSPEARE'S TRAGEDIES

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In this paper definition poisons with medical aspect like no poisons in one dose and like poisons in another dose. The aim of the paper was about poisons from aspect physical-chemistry to make a connection with medical aspect like medicine. In more new, studies, publish in Honkong, in publicity not long ago appear news to Chinese doctors successful and safe cured pacients falsick of leukemia and cancer marrow with combination arsenious and vitamine A. The same poisons with he poisoned a king Dona and himself. So, arsenious - poison and medicine. Even in XVIII century composition of arsenious were used like medicine. American Ministry of health made approval to use arsenious for cure a pacients with cancer marrow and leukemia 2000 year. It was a big meaning of Shakspeare's work of art on expansion general and health culture in all the world. World is early discovered for wisdom in Shakspeare's work of art. About that witness and example little country Montenegro. In library, Petar I“, in Njegoshe’s library we can find Shakspeare’s work of art, made on English language in Leipsic (printed for ernst pleischer) 1824 year. With consideration poisons from aspect toxical and medicial articulated multioccupational approach in problems like inseparable connection between sciences.

Keywords: poisons, dose, medical, arsenious, toxical

Presentation number: IM 12 Abstract number: ABS-8-ISABS-2009

FACTOR V LEIDEN MUTATION AND THR312ALA POLYMORPHISMS AS RISK FACTORS OF MYOCARDIAL INFARCTION

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The role of Factor V Leiden mutation and Thr312Ala polymorphism of fibrinogen alpha-chain in genetic predisposition to myocardial infarction has been investigated. The method of polymerase chain reaction (PCR) was performed. DNA extracted from dried bloodspots was used as a matrix for PCR. Blood samples of 105 patients with acute myocardial infarction were investigated for Factor V Leiden mutation and 82 such samples were examined for Thr312Ala polymorphism. The control group consisted of 105 healthy people of more than 50 years old without cardiovascular pathology in anamnesis. It was obtained that the rate of Thr312Ala heterozygotes among patients with infarction myocardial was 1,3 times as high as in the control group. The frequency of Factor V Leiden mutation in patients with myocardial infarction was 2,4 times as high as in the control group. The obtained data show that Thr312Ala polymorphism of alpha-chain of fibrinogen as well as Factor V Leiden mutation is the factor of increased risk of myocardial infarction.

Keywords: Myocardial Infarction, Genetic Predisposition, Thr312Ala Polymorphism, Factor V Leiden, Fibrinogen

Presentation number: IM 13 Abstract number: ABS-57-ISABS-2009

GENETIC ANALYSIS OF DISEASES HMSNL AND LGMD2C IN ROMANI POPULATIONS

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The Romanies harbour some of the rare autosomal recessive disorders caused by founder mutations. Distribution frequencies of the Hereditary motor and sensory neuropathy Lom (HMSNL) and Limb-girdle muscular dystrophy 2C (LGMD2C) were analyzed in the Slovakian Romani population (n = 154) and Hungarian Romani population (n = 286). PCR-based RFLP assays were used to detect the mutations. Prevalence of certain mutations in various Roma groups indicates similar origin. Frequent mutations observed in the Romani groups are sporadic in other Non-Romani populations worldwide as published by others in the past. Thus, founder mutation analysis is important for predicting incidence of certain rare diseases not readily thought about in Non-Romanies yet possibly present in the local Romani populations, especially when diagnostic conundrums appear. It could have a great impact for public health interventions as well as it would allow planning and facilitating targeted preventative projects.

Keywords: population genetic, Romani, founder mutation, HMSNL, LGMD2C

Presentation number: IM 14 Abstract number: ABS-35-ISABS-2009

DISTRIBUTION OF HEPATITIS C VIRUS GENOTYPES AMONG INTRAVENOUS DRUG USERS IN SPLIT-DALMATIA COUNTY

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The aim of this retrospective study was to analyze the distribution of hepatitis C virus genotypes in patients with chronic hepatitis C acquiring infection by intravenous drug use. Data for intravenous drug users were obtained from the Register of chronic hepatitis C virus carriers at the Institute of Public Health Split–Dalmatia County and genotypes were obtained from the Laboratory for Clinical Genetics in the University Hospital Split. The hepatitis C virus genotype was determined from serum using Cobas Amplicor Hepatitis C Virus test (version 2.0) and Linear Array Hepatitis C Virus Genotyping test in the Laboratory for Clinical Genetics, University Hospital Split. From a total of 274 patients with chronic hepatitis C for which we had complete data, 233 (85%) were male, and only 41 (15%) female. The most registered genotype of hepatitis C virus was genotype 3 found in 52.2% of patients (125 male and 18 female patients, a total of 143 out of 274). The second most common was genotype 1, found in 122 (44.5%) patients (101 men and 21 women). Genotype 4 was found in only 9 patients (3.3%), while other genotypes (2, 5 and 6) were not registered. It can be concluded that the distribution of hepatitis C virus genotypes among intravenous drug users in Split-Dalmatia County is similar to that recorded in other countries of Southern Europe with domination of genotypes 3 and 1.

Keywords: Hepatitis C virus, HCV genotypes, Intravenous drug users, Chronic hepatitis C, RNA virus

Presentation number: IM 15 Abstract number: ABS-11-ISABS-2009

DETECTION OF COMMON CFTR MUTATIONS USING ARMS REAL-TIME PCR

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Traditionally, detection of mutations has been performed by RFLP analysis, SSCP or DGGE, which are relatively slow and technically demanding. Therefore novel methods based on Real-Time PCR are more convenient because they essentially shorten the time of analysis and avoid contamination. The aim of our study was to develop Real-Time amplification refractory mutation system (ARMS) for detection of most common mutations within the CFTR gene: dF508, W1282X, R117H, 621, N1303K. Method implies two reactions: first reaction contains primers complementary to the normal DNA sequence and the second reaction contains mutant-specific primers. Therefore, normal sample and homozygous mutant sample give single products and heterozygous sample gives product in both reactions. We have designed specific primers such that their 3' base was homologous to the normal or mutant DNA and added intentional mismatches to improve discrimination of alleles. We have optimized PCR conditions for amplification with SYBR Green. Developed methods were validated by testing 100 samples which had been genotyped by RFLP analysis; no differences were observed in the genotypes analyzed. Thereby, developed assays can be used as test kits for the molecular genetic diagnostics of CF patients and in the genetic screening programmes.

Keywords: molecular genetic diagnostics, CFTR, mutation, ARMS, Real-Time PCR

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INDIVIDUAL GENETIC VARIABLES IN RECURRENT PREGNANCY LOSS

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Recurrent Pregnancy Loss (RPL) represents an intriguing problem in obstetric practice in which genetic factors play a role. Enzymes such as P4501A1 (CYP1A1) metabolize organic compounds to reactive compounds which damage cells and DNA. N-acetyltransferase 2 (NAT2) is involved in the biotransformation metabolism of aromatic amines. Glutathione S-transferase (GST) catalyze the binding of a large variety of electrophils to the sulphydryl group of glutathione. During pregnancy, changes in blood coagulation may play a role in the occurrence of abortion. Factor V Leiden (FVL) gene, is associated with a hypercoagulable state and increased susceptibility for venous thrombosis. Factor II (prothrombin) gene is associated with higher plasma protrombin concentrations. Aim of this study was to investigate the possible role of I and II stage detoxification and coagulation systems genes polymorphisms in the pathogenesis of RPL. The polymorphic variants of those genes were analyzed in 24 women (case group) with RPL and in 171 women (control group) with the uncomplicated obstetric history. The frequency (80%) of NAT2 gene SS genotype in case group was significantly ($p<0.05$) higher than in control group (57%). Frequencies of GSTM1, GSTT1, CYP1A1, FII and FVL polymorphic variants were practically similar in both analyzed groups. It had been shown that NAT2 S/S genotype really can be involved in the process of RPL, which may be associated with changes in steroid hormones level. From our data the identification of NAT2 S/S genotype can be used as a marker for high risk recurrent pregnancy loss prediction in genetic testing family programs.

Keywords: Recurrent Pregnancy Loss, Polymorphism, Gene, Detoxification, Thrombophilia

Presentation number: IM 17 Abstract number: ABS-52-ISABS-2009

ENVIRONMENTAL VERSUS HEREDITARY FACTORS IN ETIOLOGY OF MENTAL RETARDATION

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Mental retardation is a very severe and common disease. The etiology of it is diverse and includes genetic and environmental factors. In this study we show the importance of environmental factors and hereditary antecedents in appearance of mental retardation. We investigated 596 children interned in Neuropsychiatry Infantile Section of Neurology and Psychiatry Clinical Hospital of Oradea, during the 1999-2001 period. In 596 examined children, 393 had different levels of mental retardation. We realised family investigations and genealogical trees. More than 65% of children with mental retardation have one or more affected relation in the family. The relations may be affected by congenital abnormalities and/ or mental diseases. The incidences of affected relations are important in groups with mild and moderate mental retardation. In the group with severe mental retardation, the incidence of affected relation is lower. Among 393 children with mental retardation, 216 have mild mental retardation, 87 have moderate mental retardation and 90 have severe mental retardation. These results may be an argument for the hypothesis that genetic factors are very important in the inheritance of mental retardation. The increased incidence in groups with mild and moderate mental retardation may be explained by harmful factors, critical age of parents and the presence of X fragil syndrome. It seems that, elementary, severe mental retardation appears because of genes and chromosomes disorders, and secondary because of dominant or recesive inheritance. Many of children (in more than 27% of cases) borned from alcoholic mothers have fetal alcoholic syndrom.

Keywords: Mental retardation, Family hereditary antecedents, Genetic factors, Harmful factors, Etiology

Presentation number: IM 18 Abstract number: ABS-53-ISABS-2009

CONTRIBUTIONS AS CONCERNS TO THE INCIDENCE OF CRANIOFACIAL DYSMORPHISM AND BONY ABNORMALITIES IN A POPULATION WITH MENTAL RETARDATION

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The mental retardation is a very severe illness because it is associated in many cases with different other malformative diseases. Also, the etiology of mental retardation is diverse, and depending on etiological cause, the number and types of traits in mentally affected person varies in large limits. Our study is about the incidence of cranial and facial dysmorphism and bony abnormalities in a population with mental retardation. We decided to make this research because of different etiology of mental retardation. Also, we wanted to establish if the cranial and facial dysmorphism and bony abnormalities are a important elements in description of different levels of mental retardation. This research was realised on 393 children with diverse levels of mental retardation, interned in Neuropsychiatry Infantile Section of Neurology and Psychiatry Clinical Hospital of Oradea, during the 1999-2001 period. The children were clinical examinated. We used the methods for chromosomes analysis. We observed that the incidence of craniofacial dysmorphism increased in accordance with the level of mental retardation. In the group with severe mental retardation, we obtained an incidence over the 40% of this abnormality. The explanation for these results may be the presence of some genes and chromosomes syndromes which associate craniofacial dysmorphism, too. The craniofacial dysmorphism is a common feature in the description of mental retardation disease. The incidence of this abnormality increase in accordance with the worsening of the mental retardation. We observed most common bony disorders in this population are congenital hip sprain, vertebral column abnormalities and club foot.

Keywords: etiology, mental retardation, craniofacial dysmorphism, bony abnormalities, genetic syndromes

Presentation number: IM 19 Abstract number: ABS-61-ISABS-2009

PERIPHERAL CD4+CD25+FOXP3+ LYMPHOCYTES AND IFN-γ GENOTYPE IN KIDNEY GRAFT RECIPIENTS- RISK FOR REJECTION?

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Interferon-γ as Th1 cytokine has detrimental role in acute allograft rejection, while recent data suggest that CD4+CD25+ FOXP3+ lymphocytes might be responsible for allograft tolerance. Study attempted to explore if certain IFN-γ production level, as presumed by genotype, was associated with transplant rejection and with proportion of peripheral CD4+CD25+FOXP3+ lymphocytes. Fifty three patients (age 50±12 years, 23 men) with stable cadaveric kidney graft function (creatinine clearance 68±27 ml/min) for more than a year (median 4 years, min. 1, max. 22) were included. Interferon-γ genotype was determined using PCR-SSP method. Peripheral mononuclear leukocytes (PMNL) were fenotyped by flow cytometry. History of acute rejection episodes was evidenced based on the clinical and/or biopsy data. The table shows distribution of IFN-γ genotypes and proportion of CD4+CD25+FOXP3+ lymphocytes in the patients with or without history of rejection. Those with genotype associated with low IFN-γ production were free of rejection episodes. Proportion of CD4+CD25+FOXP3+ lymphocytes did not differ between the patients with different IFN-γ genotypes and was not associated with history of acute allograft rejection. Low producers IFN-γ genotype might be protective against kidney allograft rejection, but that relation was not followed by distinct proportion of CD4+CD25+FOXP3+ lymphocytes, which were presumed as possible tolerance effectors.

Keywords: IFN- γ, lymphocytes, kidney, cytokine, genotype

ABOUT INVITED SPEAKERS

Melissa Barker ● *Applied Biosystems, Foster City, CA, USA*
Melissa Barker currently works at Applied Biosystems, part of Life Technologies, where she manages the laboratory responsible for next generation sequencing collaborations using the SOLiD platform. Prior to joining Applied Biosystems in 2007, Melissa spent 12 years working as part of the NIH funded Collaborative Family Registry for colorectal cancer, holding several positions including manager of the molecular profiling laboratory and biorepository for the Australasian Colorectal Cancer Family Registry in Brisbane, Australia. She holds an MSc degree in DNA profiling of Aboriginal Australians from Newcastle University.

Frederick Bieber ● *Harvard Medical School and Birgham and Women's Hospital, Boston, MA, USA*

Dr. Frederick R. Bieber serves as Medical Geneticist at Brigham and Women's Hospital and as Associate Professor of Pathology at Harvard Medical School in Boston, USA. His work focuses on the forensic aspects of DNA-based human identification, leading to his involvement in hundreds of civil and criminal cases. He has participated in the publication of over 100 articles, chapters, and books in human genetics, pathology and forensic medicine. Dr. Bieber has testified in state, federal, and military courts in the U.S. and abroad and has served on advisory boards of the Federal Bureau of Investigation, the Royal Canadian Mounted Police, and the United States Department of Defense. Dr. Bieber has received Distinguished Service and Public Service Awards from the Massachusetts District Attorney\'s Association, Massachusetts House of Representatives, Massachusetts State Police, Louisiana State Police, Federal Bureau of Investigation, and the U.S. Department of Justice.

Zoran Budimlija ● *NYC Office of Chief Medical Examiner, New York, NY, USA*

Not provided.

Cassandra Calloway ● *Children’s Hospital & Research Center Oakland, Oakland, CA, USA*

Not provided.

Theresa Caragine ● *New York City Office of Chief Medical Examiner (NYC OCME) Department of Forensic Biology*

Theresa Caragine is a Special Deputy Director in the Department of Forensic Biology at the Office of the Chief Medical Examiner (OCME). During her tenure at the OCME, Theresa directed the development and validation of protocols which generate DNA profiles from samples with very small amounts of DNA. In addition to her duties as one of the casework managers of this testing unit, Theresa manages a team which continues to optimize and implement novel technologies

for forensic casework. Theresa received a Bachelor of Science degree in Biology from Georgetown University and a Ph.D. in Molecular Oncology and Immunology from the Sackler Institute of Graduate Biomedical Sciences at New York University School of Medicine. She has worked in both clinical and research laboratories for the past eighteen years.

Michael Coble ● *Armed Forces DNA Identification Laboratory, Rockville, Maryland, USA*

Dr. Michael Coble is the Chief of the Research Section of the Armed Forces DNA Identification Laboratory (AFDIL) in Rockville, MD. He received his Master's in Forensic Science and Ph.D. in Genetics from the George Washington University and conducted his thesis research at AFDIL under the direction of Dr. Thomas Parsons. After completing his Ph.D., Dr. Coble worked as a National Research Council Post-Doctoral Fellow with Dr. John Butler and the human identity project team at the National Institute of Standards and Technology where he worked on a set of novel miniSTR markers for analyzing degraded nuclear DNA. Three of the markers characterized by Dr. Coble will be incorporated in the next generation forensic STR kit to be used in Europe. In 2006, Dr. Coble returned to AFDIL to direct the Research Section where he supervises seven full-time research scientists.

Henry Erlich ● *Roche Molecular Systems, Alameda, CA, USA*

Dr. Erlich is a molecular biologist, geneticist, and immunologist, and has been in the development and application of PCR in basic research, medical diagnostic, evolution and anthropology, and forensics. One of his major interests has been the analysis of polymorphism in the HLA genes and the development of HLA typing tests for tissue typing, disease susceptibility, individual identification, and, more generally, the genetics of complex disease. He has authored over 280 articles and is the recipient of various scientific awards. He recieved his B.A. from Harvard University and his Ph.D. in Genetics from the University of Washington, Seattle and has been a post-doctoral fellow in the Department of Biology at Princeton and the Department of Medicine at Stanford. He is currently on the faculty at Children's Hospital Oakland Research Institute.

Michael F. Hammer ● *University of Arizona, Tucson, USA*

Michael Hammer is a Research Scientist in the Arizona Research Laboratories (ARL) Division of Biotechnology at the University of Arizona, with joint appointments in Ecology and Evolutionary Biology and Anthropology. He received his Ph.D. in Genetics at the University of California, Berkeley, and did postdoctoral work in molecular biology and evolution of mouse t haplotypes at Princeton University and human genetic variation at Harvard University. He moved to

Arizona in 1991 to establish a molecular biology core facility and to pursue studies of the Y chromosome as a genealogical tool to infer human evolutionary history. His laboratory currently works on problems in forensic DNA, individual ancestry, community-scale genetics, human origins, sexual selection, and natural selection.

Eithan Galun ● *Hebrew University, Jerusalem, Israel*

Not provided.

Mitchell Holland ● *Forensic Science, Pennsylvania State University, University Park, PA, USA*

Dr. Holland holds a Bachelor of Science degree in Chemistry from Hobart Collage in Geneva, New York (1984). He earned his Ph.D. in Biochemistry at the University of Maryland, College Park (1989) and was a Postdoctoral Fellow at the Johns Hopkins University School of Medicine in Baltimore, Maryland where he studied Human Genetics (1990). Dr. Holland is a Fellow in the American Academy of Forensic Sciences, is on the Editorial Board of the Journal of Forensic Sciences, and has been a member of the Advisory Board of the International Journal of Legal Medicine. He is currently an Associate Professor of Biochemistry & Molecular Biology, and the Associate Director of the Forensic Science Program at Penn State University (since 2005). Before that he was the Senior Vice President and Laboratory Director of the Bode Technology Group from 2000-2005, and the Scientific Laboratory Director of AFDIL from 1991-2000.

Edwin Huffine ● *Bode Technology Group, Lorton, VA, USA*

Ed Huffine has overall responsibility for providing identification assistance and mass disaster response for regions that have experienced conflicts or natural disasters as well as assisting nations develop or upgrade their forensic systems. Providing these types of services requires frequent interaction with political, scientific, and diplomatic representatives of nations and various non-governmental organizations and potential donors. Mr. Huffine has more than 18-years of experience in forensic science and human DNA identification. From 1994 - 1999, he worked for the Armed Forces DNA Identification Laboratory (AFDIL) where he became the Chief of the section responsible for the identification of missing American service members from past conflicts as well as the testing of cases of special interest such as the bullet that allegedly killed John F. Kennedy. Mr. Huffine served as the Director of the Forensic Sciences Program for the International Commission on Missing Persons (ICMP) from 1999 - 2004.

Francis Kalush ● *Rockville, MD,USA*

Dr Francis Kalush currently is the „Diagnostics (In vivo and In Vitro) & Personalized Medicine“ Network Leader, in the Office Center Director, CDRH,

FDA. Dr Kalush coordinated submission of new drugs and in vitro diagnostic devices that are intended to guide use of those drugs in the Office of In Vitro Diagnostics. Prior to joining the FDA, Dr Francis Kalush was the Director, Pharmacogenomics at Celera Genomics. She directed the development of all Celera SNP databases, and products development in the field of pharmacogenomics/toxicogenomics and genetics markets. Francis graduated from the Department of Chemical Immunology at the Weizmann Institute of Science, she directed the research of the profile and role of cytokines in the development of experimental Systemic Lupus Erythematosus in mice, and assessed the role of estrogens in the disease through long term treatment with Tamoxifen.

Sree Kanthaswamy ● *University of California, Davis, CA, USA*

Dr. Sree Kanthaswamy received his PhD in 2001 from the University of California, Davis. He is currently an Assistant Research Geneticist at the Department of Anthropology and the California National Primate Research Center, University of California, Davis. His casework has included approximately 200 investigations locally and internationally using animal DNA evidence associated with civil or criminal complaints including murder, animal abuse, cattle rustling and severe dog mauling.

Jean-Pierre Kocher ● *Mayo Clinic College of Medicine, Rochester, MN, USA*

Dr. Jean-Pierre Kocher joined Mayo Clinic in October 2005 to develop and direct the activities of the Bioinformatics Core (BIC). The BIC's mission is to develop and maintain state of the art Services to help researchers engaged in genomics research. Since August 2008, Dr. Kocher is the chair of the newly created Division of Biomedical Statistics and Informatics (BSI). This BSI includes more then 280 members with experts in Biostatistics, Bioinformatics and Clinical Informatics. The division works collaboratively with basic science and clinical researchers, providing analytical and interpretative expertise to enable and validate discoveries with high impact on patient care. BSI leads also the development of statistical and informatics methodologies to provide novel approaches to mine and analyze clinical and biological data. Dr. Kocher's research activities focus on the development and application of computational methods to advance the understanding of the molecular mechanisms that underlie clinical disorders.

Doron Lancet ● *The Weizmann Institute of Science, Rehovot, Israel*

Doron Lancet is Professor at the department of Molecular Genetics, and heads the Crown Genome Center at the Weizmann Institute of Science, Israel. He pioneered genome research and infrastructure development, and initiated bioinformatics Systems Biology efforts at Weizmann and in Israel. A pioneer of smell research,

he currently studies the genomics, evolution and population genetics of human olfactory receptor genes. He developed GeneCards, a widely used human gene web compendium. He did research on human monogenic and polygenic disease, and published in transcriptomics and pharmacogenetics. More recently, he developed a computational network model for life's origins. Lancet is member of EMBO and a HUGO council member. He wrote a science column in Israel's major daily Haaretz, and continuously delivers public lectures on the impact of genomics. He was awarded the Wright Prize in olfaction (USA, 1998) and the Landau prize in Human genetics (Israel, 2008).

Henry Lee ● *University of New Haven, West Haven and Connecticut Forensic Science Laboratory, Meriden, CT, USA*

Dr. Henry C. Lee is one of the world's foremost forensic scientists. Dr. Lee's work has made him a landmark in modern-day forensic sciences. He has been a prominent player in many of the most challenging cases of the last 40 years. Dr. Lee's testimony figured prominently in the O. J. Simpson trial, and in convictions of the „Woodchipper“ murderer. Dr. Lee has assisted in the investigations of other famous crimes, such as the murder of Jon Benet Ramsey in Boulder, Colorado, the 1993 suicide of White House Counsel Vincent Foster, and the reinvestigation of the Kennedy assassination. In 1975, Dr. Lee joined the University of New Haven, where he created the school's Forensic Sciences program. He has taught at more than a dozen universities, law schools, and medical schools. Dr. Lee has authored hundreds of articles in professional journals and has co-authored more than 25 textbooks, covering the areas of; DNA, Fingerprints, Trace Evidence, Crime Scene Investigation and Crime Scene Reconstruction. Dr. Lee has been the recipient of numerous medals and awards, including the 1996 Medal of Justice from the Justice Foundation, and the 1998 Lifetime Achievement Award from the Science and Engineer Association. He has also been the recipient of the Distinguished Criminalist Award from the American Academy of Forensic Sciences; the J. Donero Award from the International Association of Identification, and in 1992 was elected a distinguished Fellow of the AAFS.

José A. Lorente ● *Department of Legal Medicine, University of Granada, Granada, Spain*

JOSE LORENTE, M.D., Ph.D. is Associate Professor of Legal and Forensic Medicine at the University of Granada, Spain. He’s Director of the Laboratory of Genetic Identification in Granada and also Director of the Pfizer – University of Granada – Andalusian Government Center for Genomics and Oncology. Dr. Lorente got his Ph.D. in 1989 and he was working at the Universities of Heidelberg and Munster in Germany (from 1989-1991) doing research on genetic identification. In 1992 and 1993 he was working at the FBI Academy with Dr. Budowle. He‘s the Scientific Director “Phoenix Program of Spain” – Spanish

Missing Persons Genetic Identification Program, that started in 1997 as the first program of its kind. He's starting now the "MISSING KIDS IDENTIFICATION PROGRAM", aka PROKIDS. Dr. Lorente has published over 100 scientific papers and has been a speaker in more than 25 countries all over the world.

Damir Marjanović ● *Institute for Genetic Engineering and Biotechnology Sarajevo, Sarajevo, B&H and Ruđer Bošković Institute, Zagreb, Croatia*

Positions: a) Head of the Laboratory for forensic genetics, Institute for genetic engineering and biotechnology, University of Sarajevo and one of the directors in Genos Company, Zagreb, Croatia b) Assistant professor Forensic Genetics, Faculty of Science and Forensic bio-anthropology, Faculty of Criminal Sciences , University of Sarajevo, Bosnia and Herzegovina Research field: a) forensic genetics c) molecular anthropology Personal data: 35 years old Bibliography: More than 80 publications (scientific papers, reviews, proceedings, abstracts etc).

Adele Mitchell ● *Office of Chief Medical Examiner of New York City, New York, NY, USA*

Dr. Adele Mitchell is a Research Scientist at the Office of Chief Medical Examiner of New York City. Dr. Mitchell's expertise is in statistical and population genetics. Her special interests are modeling stochastic effects and developing analytical methods for application to low copy number DNA. Previous work includes population genetics of endangered species, mapping genetic deletions in families, and modeling the effects of undetected genotyping error on family and population based tests for association between genetic variants and disease susceptibility. Academic appointments: Assistant Professor, Mount Sinai School of Medicine; Clinical Assistant Professor, New York University School of Medicine, both in New York City.

Thomas Parsons ● *International Commission on Missing Persons, Sarajevo, B&H*

Thomas Parsons is the Director of Forensic Science of the International Commission on Missing Persons (ICMP). He directs some ~100 staff members in forensic archaeology, anthropology, pathology and DNA. The ICMP is headquartered in Sarajevo, Bosnia, and was founded to assist governments in addressing the issues of missing persons from the conflict in the former Yugoslavia. Since 2003, ICMP has been acting on a global scale, providing DNA identification assistance in mass disasters such as the 2004 SE Asian tsunami, Hurricane Katrina in the US, and Typhoon Frank in the Philippines. The ICMP provides forensic and other assistance to the governments of Chile, Colombia, and Iraq, among others, and has offices in Bogota and Baghdad. Dr. Parsons was previously the Chief Scientist of the Armed Forces DNA Identification Laboratory,

and has published extensively in the fields of forensic DNA, population genetics, and molecular evolution.

Richard J. Roberts ● *New England Biolabs, Ipswich, MA, USA*

I work on restriction enzymes and DNA methylases and use bioinformatics extensively.

Antti Sajantila ● *Department of Forensic Medicine, University of Helsinki, Helsinki, Finland*

Currently the head of the forensic pahtology unit and the laboratory of forensic pathology at the Department of Forensic Medicine, University of Helsinki, Finland. Research intersts include population genetics and molecular anthropology, particularly the population history of finno-ugric speaking populations. In addition, the reasearch is focused on making the bridge between forensic genetics, pathology and toxicology by projects in genetics of sudden, unexpected death and post-mortem pharmacogenetics.

Aleksandar Sekulic ● *Scottsdale, AZ, USA*

Dr Sekulic has received an MD degree from the University of Zagreb Medical School, followed by a PhD degree in Immunology from the Mayo Graduate School and residency training in Dermatology at the Mayo College of Medicine in Rochester, Minnesota. He is currently an Assistant Professor in Dermatology at the Mayo Clinic in Scottsdale, AZ as well as an adjunct faculty member at the Translational Genomics Institute in Phoenix, AZ. Dr Sekulic's clinical expertise is centered on cutaneous oncology with specific emphasis on malignant melanoma. His research interests focus on genomics of cutaneous malignancies and the approaches for identification of molecular markers with potential utility in diagnosis, prognosis and treatment of skin cancers.

David I. Smith ● *Mayo Clinic College of Medicine, Rochester, MN, USA*

My name is David I Smith and I am a professor in Laboratory Medicine and Pathology at the Mayo Clinic. My research focuses on the genetic alterations that occur during cancer development. I am particularly interested in the role that long non-coding transcripts play in cancer development. In addition, I am responsible for developing the necessary infrastructure for Next Generation DNA sequencing at the Mayo Clinic. This technology will revolutionize how we conduct research and translate that into clinical practice. In my presentation, I will summarize our work using this technology to characterize oral cancers.

Mark Spigelman ● *Tel Aviv, Israel*

A human remains specialist/anthropologist, researching the history and development of microbial diseases utilizing microbiological techniques on Ancient human remains. Previously a consulting surgeon for 25 years in Sydney Australia and still in practise in the UK. Since becoming an Archaeologist/Anthropologist I have concentrated on developing the study of Paleomicrobiology and developing relationship between microbial diseases of the past and the diseases of today. Currently looking into the evolution of host resistance/susceptability and the evolution of the microbial genome from the Neolithic till modern times. Whilst concentrating currently on tuberculosis and leprosy we have also had success in finding Leischmania, Malaria and Schistosoma in ancient tissues other bio-molecules such as proteins and lipids are also being investigated. I have developed extensive techniques for minimally destructive sampling of human remains particularly endoscopic sampling of mummies-which I have now done on over 500 occasions.

Kári Stefánsson ● *deCODE Genetics, Reykjavik, Iceland*

Not provided.

Andre Terzic ● *Mayo Clinic College of Medicine, Rochester, MN, USA*

Dr. Andre Terzic holds the Marriott Professorship of Cardiovascular Disease Research at Mayo Clinic, where he is Professor of Medicine and Pharmacology, Medical Genetics, Director of Marriott Heart Disease Research Program, Co-Director Center for Individualized Medicine, and Associate Director for Research. By integrating advanced technology with a focus on clinical problems addressed at a fundamental level, Dr. Terzic has pioneered pathogenomic research of maladaptation in heart disease, and the application of cardioprotective and cardioregenerative therapeutic modalities. He has authored over 220 scientific manuscripts. Dr. Terzic is the recipient of numerous national and international awards including the Medal of Merit from the International Society for Heart Research, the Leon Goldberg Award from the American Society for Clinical Pharmacology and Therapeutics, the Klaus Unna Award from the University of Illinois, the Established Investigatorship from the American Heart Association. He is the Past President of the American Society for Clinical Pharmacology and Therapeutics.

Daniel Vanek ● *Forensic DNA Service, Prague, Czech Republic*

Graduated in Molecular Biology at the Charles University in Prague, CZE, head of Central DNA laboratory of the Czech Police for 10 years, 30 months spent in

Bosnia-Herzegovina (ICMP), now director of Forensic DNA Service. Major scientific interests: forensic genetics, archaeogenetics and genetic genealogy.

George Vasmatzis ● *Mayo Clinic College of Medicine, Rochester, MN, USA*

Dr. George Vasmatzis is a faculty member in the Department of Molecular Medicine and serves as the director of the Biomarker Discovery & Translation Laboratory within the Center of Individualized Medicine at Mayo Clinic, Rochester Minnesota. He is also an Assistant Professor in the Mayo Medical School. He has a Ph.D. in biomedical engineering and has acquired experience in diverse disciplines, including bioinformatics, molecular biology, and computational biology. His research program consists of a team of bioinformatics specialists, molecular biologists, epidemiologists, clinicians and pathologists. They combine computational and experimental techniques to facilitate discovery of genes that can be used as diagnostic markers, prognostic markers, or targets for therapy for lung and prostate cancers.

Scott A. Waldman ● *Jefferson Medical College, Thomas Jefferson University, PA, USA*

Dr. Scott Waldman obtained his PhD degree in Anatomy from Thomas Jefferson University, and his MD degree from Stanford University. He was a postdoctoral fellow at the University of Virginia and Stanford University in the Division of Clinical Pharmacology. He is currently the Chairman of the Department of Pharmacology and Experimental Therapeutics and the Director of the Division of Clinical Pharmacology. He is a past member of the American Board of Clinical Pharmacology, a past Regent of the American College of Clinical Pharmacology, and a past-President of the American Society for Clinical Pharmacology and Therapeutics. He is the Editor-in-Chief for Clinical Pharmacology and Therapeutics, Biomarkers in Medicine, and the Deputy Editor-in-Chief for Clinical and Translational Science. Dr. Waldman's research interests focus on tissue-specific pathways underlying intestinal tumorigenesis and their utility as targets for managing patients with colorectal cancer.

Elisa Wurmbach ● *New York City Office of Chief Medical Examiner (NYC OCME) Department of Forensic Biology*

I am a molecular biologist and received my PhD 1998 in Drosophila genetics. During my post-doc at the EMBL in Heidelberg (1998-2000) I started to generate and utilize microarrays. From 2000 to 2007, I worked at the Mount Sinai School of Medicine in New York where I specialized in genomics. In 2007 I joined the Office of Chief Medical Examiner in New York City as Research Scientist, where I initiated a pigmentation project about which I will give a presentation at the ISABS-meeting. In addition, I am an Adjunct Assistant Professor at Yeshiva University.

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Phone:	8187164735
Fax:	8187169471
E-Mail:	CustomerSevice@abacusdiagnostics.com
URL:	www.abacusdiagnostics.com
Keywords:	Manufacturer of Forensic and Crime Scene Investigation Products. Serving the worldwide Forensic Community since 1996.
Product(s):	Manufacturers of ABAcard® p30 for the forensic identification of Semen, Hematrace® for the forensic identification of human blood, SALIgAE® for the forensic identification of saliva, Hemascein™ to reveal latent bloodstains, FAB - SWAB, Uritrace™ for the forensic identification of urine.

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Organization Information	
Organization:	**Applied Biosystems**
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State/Province:	
ZIP or Postal Code:	64293
Country:	Germany
Phone:	+49 6151 9670 0
Fax:	+49 6151 9670 5599
E-Mail:	abdirect@eur.appliedbiosystems.com
URL:	http://www.appliedbiosystems.com
Keywords:	Applied Biosystems Inc., part of Life Technologies, is a global leader in the development and marketing of instrument-based systems, consumables, software, and services for academic research, the life science industry and commercial markets. The company commercializes innovative technology solutions for DNA, RNA, protein and small molecule analysis.
Product(s):	We offer instruments, consumables, software solutions and all related services for the following application: DNA Sequencing, Gene Expression, Genotyping, DNA/RNA Sample Prep, PCR and Real-Time PCR, Human Identification, Food and Environmental Testing, Forensic and Toxicology, Clinical Research, Metabolism Studies, Biomarker Analysis, Pharmakokinetics, Drug Development and Discovery

Biosistemi d.o.o.

Organization Information	
Organization:	**Biosistemi d.o.o.**
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City:	Zagreb
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ZIP or Postal Code:	10090
Country:	Croatia
Phone:	0038513460838
Fax:	0038513460840
E-Mail:	zdravko.nemet@biosistemi.hr; ivan.lukic@biosistemi.hr
URL:	www.biosistemi.hr
Keywords:	Applied Biosystems business partner for the territory of south east Europe, with offices in Zagreb, Belgrade and Bucharest.
Product(s):	Human identifications and molecular biology kits, reagents, software and instruments.

Genos d.o.o.

Organization Information	
Organization:	**Genos d.o.o.**
Address:	Planinska 1
City:	Zagreb
State/Province:	
ZIP or Postal Code:	10000
Country:	Croatia
Phone:	0038512352661
Fax:	0038512352663
E-Mail:	info@genos.hr
URL:	www.genos.hr
Keywords:	First private forensic DNA laboratory in this part of Europe providing all types of forensic DNA testing (human DNA identification- paternity testing, including prenatal paternity testing from blood and amniotic fluid), animal DNA analysis (canine, bovine, porcine); soon planning to introduce testing for coagulation factors and HPV.
Product(s):	distributor of Bode Technology Group buccal swab collectors

INEL- medicinska tehnika d.o.o.

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ZIP or Postal Code:	10000
Country:	Croatia
Phone:	0038516175150
Fax:	0038516520966
E-Mail:	info@inel-mt.hr
URL:	www.inel-mt.hr
Keywords:	INEL- medicinska tehnika is business partner and exclusive distributor for territory of Croatia for following manufacturers: Eppendorf AG, Qiagen, Leica-microsystems, Sarstedt, Fermentas and Tecan.
Product(s):	Molecular biology / microbiology kits, kits for human identification laboratories and all kind of laboratory consumables. Instruments and software for manually process and for automation in molecular laboratories and forensic investigation laboratories.

Leica Microsystems

Organization Information	
Organization:	**Leica Microsystems**
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State/Province:	
ZIP or Postal Code:	35578
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Phone:	0049 6441 292365
Fax:	0049 6441 292824
E-Mail:	Harald.Desch@leica-microsystems.com
URL:	www:leica-microsystems.com
Keywords:	Leica Microsystems is a leading global designer and producer of innovative, high-tech, precision optical systems for the analysis of microstructures. It is one of the market leaders in each of its business areas: Microscopy, Confocal Laser Scanning Microscopy with corresponding Imaging Systems, Specimen Preparation, and Medical Equipment. The company manufactures a broad range of products for numerous applications requiring microscopic imaging, measurement, and analysis. It also offers system solutions for life science including biotechnology and medicine, research and development of raw materials, and industrial quality assurance. The company is represented in over 100 countries with 10 manufacturing facilities in 8 countries, sales and service organizations in 19 countries and an international network of dealers. The international management is headquartered in Wetzlar, Germany
Product(s):	Microscopes, Specimen Preparation Systems, Macroscopes, Imaging Systems, Medical Equipment

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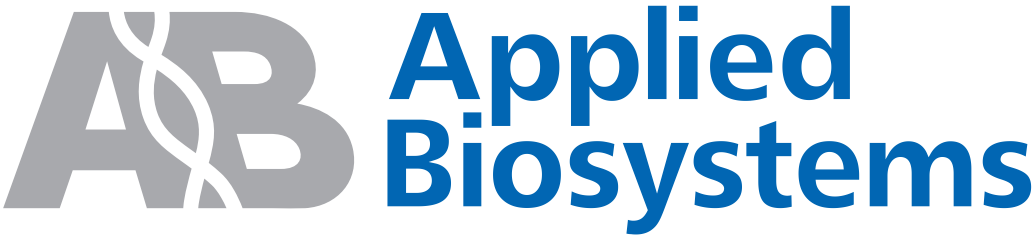


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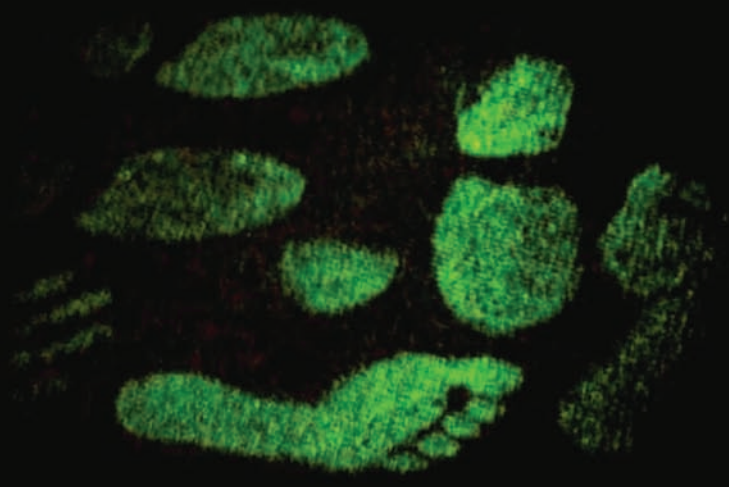

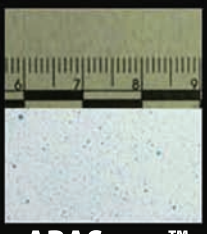

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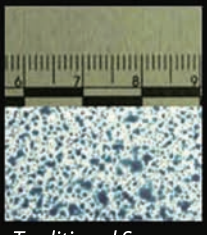

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