

Dutch Society of Human Genetics
(www.nvhg-nav.nl)

Two-Day Annual Symposium

21 & 22 September 2017



Wij zijn bijzonder erkentelijk voor de
financiële steun van
Stichting Simonsfonds



Logo: Tom de Vries Lentsch
Grafisch ontwerper / fotograaf

Dear colleagues,

Welcome to the annual symposium of the NVHG (Dutch Society for Human Genetics). This is a joint meeting organized together with the VKGL (Vereniging Klinisch Genetische Laboratoriumdiagnostiek), the VKGN (Vereniging Klinische Genetica Nederland) and the NACGG (Nederlandse Associatie voor Community Genetics en Public Health Genomics).



Almost every day, the newspapers report on exciting new developments in the field of human genetics, including exome/genome sequencing as well as non-invasive pre-natal testing which have been taken into the clinic. Thanks to these developments, the opportunities for accurate and rapid diagnostics and for personalized medicine are rapidly improving. In addition, the vast increase of genetics data is providing many new insights into mechanisms of disease and potential strategies for gene-based intervention strategies.

The program for this year's meeting is focused on the exciting progress that is being made in these areas and their clinical and societal impact. This symposium covers the entire width of pioneering Genetics research

conducted by national and international speakers, thereby providing a good overview of current genetics research in the Netherlands and beyond.

Next to the plenary sessions, the VKGN, VKGL and NACGG also organized interesting programs for the respective disciplines. For contrast and reflection, Thursday afternoon Dr. Thijs Porck will deliver a lecture on medieval medicine and curing of "old age".

This meeting would not have been possible without the generous support from our sponsors. We thank all of them and encourage all participants to see the representatives at the stands to take note of the products offered by them.

Finally, we thank all of you for your scientific support.

I wish you a great and inspiring meeting.

Hans van Bokhoven

General information

Venue

Hotel NH Eindhoven Conference Centre Koningshof
Locht 117
5504 RM Veldhoven
Eindhoven - Nederland
Tel.: +31 40 253 7475
www.nh-hotels.nl/hotel/nh-eindhoven-conference-centre-koningshof
nhkoningshof@nh-hotels.com

Registration

In the Lobby: open on Thursday September 21, 2017: 10.00 – 11.00 hrs

Reception and catering

Holland foyer

Dinner and party

Brabantzaal

Abstracts

- Abstracts guest speakers G 01 to G 09
- Abstracts talks: T 01 to T 16
- Abstracts posters : P 01 to P 31

Abstracts T 01 - T 16 and P 01 - P 31 are available as download through the NVHG website

For abstracts of the NACGG, VKGN and VKGL sessions we refer to these societies and the NVHG website

Posters

Poster boards have a size of 200 cm (height) and 100 cm (width)

Please put up your poster immediately after arrival. Do not forget to remove it at the end of the meeting

Language

The official language of the annual meeting will be English

Accreditation

Accreditation forms are available at the registration desk (GAIA ID number: 296910)

Badges

You are requested to hand in your badge at the end of the symposium

Presentations

You are requested to timely hand in an USB stick with your presentation to the chairperson of your symposium session

NVHG board and scientific organization

Prof. dr. Hans van Bokhoven (Board - Chairman)

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Prof. dr. Richard Sinke

Prof. dr. André Uitterlinden

Dr. Lisenka Vissers

Administrative organization

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September 21 & 22, 2017

The NVHG Two-Day Annual Symposium 2017 - Dutch Society of Human Genetics
Nederlandse Vereniging voor Humane Genetica (www.nvhg-nav.nl)

Program Thursday September 21, 2017

10:00-11:00 Registration

10.25-12.30 Opening & Plenary session

Room: Auditorium

Chair: Hans van Bokhoven

10.25 Opening

10.30-11.10 **Robert Green** (Boston, USA) (G 01)

Persistent Questions and Surprising Answers on the Path to Genomic Medicine

11.10-11.50 **Silvère van der Maarel** (Leiden, NL) (G 02)

Facioscapulohumeral muscular dystrophy

11.50-12.30 **Alexandre Reymond** (Lausanne, CH) (G 03)

Genome architecture and disease: the 16p11.2 paradigm

12.30-14.00 Lunch, room: Holland foyer

Business/private meetings: huishoudelijke vergadering VKGN en VKGL

13.15-14:00 Huishoudelijke vergadering VKGN

Room: room 82

13.15-14:00 Huishoudelijke vergadering VKGL

Room: room 83

14.00-16.00 **Parallel sessions**

14.00-16.00 Symposium 1A: VKGN

Making sense(s)

Room: Parkzaal

Chair: Mieke van Haelst



14.00-14.30 **Marleen Jansen** (Groningen, NL)
Individuals with combined visual and hearing loss

14.30-14.50 **Virginie Verhoeven** (Rotterdam, NL)
Polygenic visual disturbances

14.50-15.15 **Rob Collin** (Nijmegen, NL)
Gene therapies in retinopathies

15.15-15.35 **Marieke van Dooren** (Rotterdam, NL)
Clinical genetic approach of hearing loss

15.35-16.00 **Wilko Grolman** (Utrecht, NL)
Cochlear implantates: state of the art

14.00-16.00 Symposium 1B: VKGL

Room: Auditorium



14.00-14.40 **Ron van Schaik**, (Rotterdam, NL)
Pharmacogenetics in clinical care: a 15 year experience

14.40-15.20 **Lisenka Vissers** (Nijmegen, NL)
The concept of "one-genetic-test-fits-all-diseases": a genetic and cost-effectiveness perspective

15.20-16.00 **Ron Wanders** (Amsterdam, NL)
Translational metabolism: key to the future of inherited metabolic diseases



14.00-16.00 Symposium 1C: NACGG

Recontacting: (hoe) doe je dat?

Room: zaal 82

Chair: Lidewij Henneman (Amsterdam, NL)

14.00-14.30 **Helger Yntema** (Nijmegen, NL)

Heranalyse van exoom sequencing data: wanneer en waarom?

14.30-14.50 **Julia el Mecky** (Groningen, NL)

Ervaringen en perspectieven van patiënten en lab personeel met betrekking tot heranalyse en hercontact binnen de klinische genetica

14.50-15.10 **Gea Beunders** (Groningen, NL)

Heroproepen van kinderen met verstandelijke beperking door nieuwe genetische technieken: evaluatie van een Amsterdamse pilot op haalbaarheid en perspectief van ouders

15.10-15.40 **Gonneke Willemsen** (Amsterdam, NL)

Hercontact in onderzoek: een portal voor terugkoppeling van data aan deelnemers uit het Nederlands Tweelingregister

15.40-16.00 Slotdiscussie en afsluiting

16.00-17.30 Posters, coffee, tea
Presenters at posters

Room: room 65

17.30-18.30 Room: Auditorium
Chair: Raoul Hennekam

Thijs Porck, (Leiden, NL) (G 04)

Medieval medicine and the human life cycle: Curing old age in medieval England

Evening: (Brabantzaal)

18.30-19.00 Drinks

19.00-21.00 Dinner

21.00-00.30 Party

Program Friday September 22, 2017

9.00-10.10 **Plenary session**
Room: Auditorium



9.00-09.40 **Henk-Jan Guchelaar** (Leiden,NL) (G 05)
Implementation of pharmacogenomics into clinical practice

9.40-10.10 Winner Genetics Retreat: the annual Rolduc meeting 2017, **Heleen Masset** (Leuven, BE) (G 06)
Combining time-lapse imaging and genome-wide haplotyping reveals novel mechanisms underlying chimerism, mixoploidy and aneuploidy formation in human preimplantation embryos

10.10-11.10 **Parallel sessions**

10.10-11.10 **Symposium 2A**
Room: Auditorium
Chair: Richard Sinke

10.10-10.25 **Debby Hellebrekers** (Maastricht, NL) (T 01)
Next-generation sequencing of the mtDNA and exome is the preferred, first strategy to identify known and novel causes of mitochondrial disease

10.25-10.40 **Michal Mokry** (Utrecht, NL) (T 03)
Candidate gene identification based on 3D chromatin interactions: Genetics behind complex diseases just got even more complex

10.40-10.55 **Chantal Deden** (Nijmegen, NL) (T 05)
A retrospective analysis of genetic testing in pediatric patients while introducing rapid targeted whole genome sequencing for critically ill newborns

10.55-11.10 **Laura Vandervore** (Brussel/Rotterdam, NL/BE) (T 07)
RTTN is located at the centrosomes during mitosis and regulates centriole duplication

10.10-11.10 Symposium 2B

Room: Parkzaal

Chair: Lisenka Vissers

10.10-10.25 **Jakob Goldmann** (Nijmegen, NL) (T 02)

Germline de novo mutation clusters arise during oocyte aging in genomic regions with increased double-strand break incidence

10.25-10.40 **Edith Coonen** (Maastricht, NL) (T 04)

Refining embryo transfer strategies using embryonic ploidy status in PGD for translocations

10.40-10.55 **Matthew Hestand** (Amsterdam, NL) (T 06)

Fetal Fraction Evaluation in Non-Invasive Prenatal Testing (NIPT)

10.55-11.10 **Martin Elferink** (Utrecht, NL) (T 08)

Defining quality standards for clinical whole exome sequencing: a national collaborative study of the Dutch Society for Clinical Genetic Laboratory Diagnostics (VKGL)

11.15-11.45 Coffee-tea break

Room: Holland foyer

11.45-12.45 **Parallel sessions**

11.45-12.45 Symposium 3A

Room: Auditorium

Chair: André Uiterlinden

11.45-12.00 **Magdalena Harakalova** (Utrecht, NL) (T 09)

Transcriptional regulation in hypertrophic cardiomyopathy due to MYBPC3 founder mutations

12.00-12.15 **Jo Vanoevelen** (Maastricht, NL) (T 11)

Classification of Imna-variants by means of zebrafish phenotyping

12.15-12.30 **Machteld Oud** (Nijmegen, NL) (T 13)

Ciliary phenotyping in urine-derived patient cells to determine the pathogenicity of novel variants in ciliopathy genes

12.30-12.45 **Peter-Bram 't Hoen** (Leiden, NL) (T 15)

RNAseq in 296 phased trios provides a high resolution map of genomic imprinting

11.45-12.45 Symposium 3B
Room: Parkzaal
Chair: Roland Kuiper

11.45-12.00 **Bianca van den Bosch** (Maastricht, NL) (T 10)
Evolution of dihydropyrimidine dehydrogenase (DPD) diagnostics in a time-period of seven years

12.00-12.15 **Claudia Ruivenkamp** (Leiden, NL) (T 12)
Towards automated sharing of genetic variants between genome diagnostics laboratories and beyond: an initiative of the Dutch diagnostic data sharing consortium

12.15-12.30 **Stefan Lelieveld** (Nijmegen, NL) (T 14)
De novo missense mutation clustering identifies candidate neurodevelopmental disorder genes

12.30-12.45 **Rachel Schot** (Rotterdam, NL) (T 16)
SMPD4 mutations link primary microcephaly and severe encephalopathy to aberrant cytokinesis and membrane ceramide metabolism

12.45-14.00 Algemene ledenvergadering NVHG
Room: Parkzaal

13.00-14.00 Lunch (room: Holland foyer) and posterviewing (room: room 65)

14.00-16.00 Plenary session
Room: Auditorium
Chair: Hans van Bokhoven

14.00-14.40 **Joris Vermeesch** (Leuven, BE) (G 07)
The embryo is the cradle of chromosomal disorders

14.40-15.10 **Erik Sistermans** (Amsterdam, NL) (G 08)
NIPT in the Netherlands

15.10-15.50 **NVHG Lodewijk Sandkuijl lecture – Brenda Penninx** (Amsterdam, NL) (G 09)
Genetics & psychiatry: how 1+1 can be 3

15.50-16.00 **NVHG Awards**; Annual Award 2017, Poster Award 2017

16:00 Closure



Special Guest speaker

Thursday September 21, 2017 / 17.30 – 18.30 / Room: Auditorium

Medieval medicine and the human life cycle: Curing old age in medieval England

Thijs Porck, PhD, assistant professor of medieval English, Leiden University



Thijs Porck studied medieval history and English language and culture.

He wrote his Ph.D. thesis on old age in Anglo-Saxon England, entitled 'Growing Old among the Anglo-Saxons: The Cultural Conceptualisation of Old Age in Early Medieval England'.

Porck has published articles on Old English language and culture, *Beowulf* and J.R.R. Tolkien. He is also member of the editorial boards of various journals in the field of medieval studies and historical linguistics.

Porck has taught at university level since 2008, mostly at Leiden University, with a brief spell at Radboud University Nijmegen.

In 2014, he was awarded with the Humanities Faculty Teaching Prize for the most inspiring lecturer of the faculty

of Humanities at Leiden University. He writes about the early Middle Ages and his own research on his blog www.dutchanglosaxonist.com.

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Persistent Questions and Surprising Answers on the Path to Genomic Medicine

Prof. Robert C. Green

Brigham and Women's Hospital, Broad Institute and Harvard Medical School, Boston, USA

The use of genomics in the day-to-day practice of medicine has been slowed by persistent questions and beliefs around the return of genomic information. Is unanticipated genetic risk information distressing? Will consumers understand and act appropriately after receiving direct-to-consumer genetic testing? Can non-geneticist healthcare providers manage the results of genome sequencing in their patients? When healthy individuals are sequenced, do the results cause excessive and unnecessary healthcare spending or iatrogenic harm? How can genetic penetrance be estimated in the absence of family history? Should healthy infants be sequenced and should genetic risks for adult onset conditions be returned? In this presentation, experimental evidence from clinical research studies around these and other questions will be reviewed. Empirical studies in translational genomics are paving the way toward the integration of genetic technologies into the everyday practice of medicine.

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Facioscapulohumeral muscular dystrophy

Prof.dr.ir. Silvère M. van der Maarel

Leiden University Medical Center, Leiden, The Netherlands

Facioscapulohumeral dystrophy (FSHD) is an inherited myopathy characterized by progressive weakness and wasting of the facial and upper extremity muscles. FSHD is caused by partial chromatin relaxation of the D4Z4 repeat on chromosome 4q35. The polymorphic D4Z4 repeat normally varies between 8-100 units and adopts a repressive chromatin structure in somatic cells. Because of D4Z4 repeat contractions to a size of 1-10 units (FSHD1), or mutations in chromatin modifiers that are necessary to establish or maintain a repressive D4Z4 chromatin structure (FSHD2), in FSHD D4Z4 epigenetic silencing is incomplete causing ectopic *DUX4* expression in skeletal muscle. *DUX4* is transcription factor normally expressed in cleavage stage embryos and its ectopic expression in skeletal muscle activates a cascade of events leading to muscle degeneration.

Most FSHD2 patients have a mutation in *SMCHD1*. *SMCHD1* is a chromatin repressor that binds to D4Z4 and reduced *SMCHD1* repressor activity at D4Z4 leads to *DUX4* expression in skeletal muscle. *SMCHD1* is also a modifier for FSHD1 since mutations in *SMCHD1* increase *DUX4* expression and worsen disease presentation in some FSHD1 families. Rarely, mutations in the DNA methyltransferase 3B (*DNMT3B*) gene cause *DUX4* expression and disease presentation in FSHD1 and FSHD2. The modifying effects of these chromatin repressors may explain the marked inter- and intra-familial variability in disease onset and progression, and the frequent occurrence of borderline FSHD1 repeats in the population. Thus, FSHD1 and FSHD2 should be viewed as polar extremes of a disease continuum rather than separate disease entities.

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Genome architecture and disease: the 16p11.2 paradigm

Prof. Alexandre Remond

Center for Integrative Genomics, University of Lausanne, Genopode building, CH-1015 Lausanne, Switzerland

Copy number changes in 16p11.2 contribute significantly to neuropsychiatric traits. Besides the 600 kb BP4-BP5 (breakpoint) CNV found in 1% of individuals with autism spectrum disorders and schizophrenia and whose rearrangement causes reciprocal defects in head size and body weight, a second distal 220kb BP2-BP3 CNV is a likewise potent driver of neuropsychiatric, anatomical and metabolic pathologies. These two CNVs-prone regions at 16p11.2 are reciprocally engaged in complex chromatin looping and concomitant expression changes, as well as genetic interaction between genes mapping within both intervals, intimating a functional relationship between genes in these regions that might be relevant to pathomechanism.

These recurrent pathogenic deletions and duplications are mediated by a complex set of highly identical and directly oriented segmental duplications. This disease-predisposing architecture results from recent, Homo sapiens-specific duplications (i.e. absent in Neandertal and Denisova) of a segment including the BOLA2 gene, the latest among a series of genomic changes that dramatically restructured the region during hominid evolution.

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Medieval medicine and the human life cycle: Curing old age in medieval England

Dr. Thijs Porck

Leiden University, Leiden, The Netherlands

This lecture will provide an introduction to the theory and practice of medieval medicine, as well as a discussion of the role of the human life cycle in medical writings of the Middle Age. In particular, I will discuss the works of one thirteenth-century monk who claimed to have a cure for old age.

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Implementation of pharmacogenomics into clinical practice

Prof.dr. Henk-Jan Guchelaar

Dept of Clinical Pharmacy & Toxicology, Leiden Network of Personalised Therapeutics, Leiden University Medical Center, Leiden, The Netherlands

Pharmacogenomics is the study of genetic variability affecting an individual's response to a drug. Its use allows personalized medicine and reduction in 'trial and error' prescribing, leading to more efficacious, safer and cost effective drug therapy. Technical developments have moved the field from reactive genotyping to a pre-emptive panel approach: in this latter approach patients are tested for a panel of genetic variants even before drug prescribing has taken place. When these data are included in a patient's electronic medical record, this allows physicians and pharmacists to use this information at time of drug prescribing and medication surveillance.

Due to its highly developed infrastructure, The Netherlands healthcare system is at the forefront of implementing pharmacogenomics into routine clinical practice. Pre-emptive testing of f.e. *DPYD* before use of 5-fluorouracil or capecitabine and of *TPMT* before use of 6-mercaptopurine or azathioprine is standard in many centers in The Netherlands and patient's drug dosages are personalized based upon the pharmacogenomics test result.

Recently, an EU Horizon2020 project Ubiquitous Pharmacogenomics (U-PGx) was funded and investigates the approach of pre-emptive panel testing using a randomized clinical trial design in 7 EU countries and including a total of 8,100 patients. Feasibility, health outcome, especially the reduction of adverse drug events, and cost-effectiveness will be studied. The U-PGx consortium ultimately aims to formulate European strategies for further improving implementation of pharmacogenomics.

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Combining time-lapse imaging and genome-wide haplotyping reveals novel mechanisms underlying chimerism, mixoploidy and aneuploidy formation in human preimplantation embryos

Heleen Masset

Masset H. (1), Fernandez Gallardo E. (2), Peters M. (1,3), Rodriguez Iglesias B. (1), Dimitriadou E. (1), Destouni A. (1), Zamani Esteki M. (2), Debrock S. (4), Peeraer K. (4), Voet T. (2) & Vermeesch J.R. (1).

1 Laboratory for Cytogenetics and Genome Research, Center of Human Genetics, KU Leuven, Leuven, 3000, Belgium

2 Laboratory of Reproductive Genomics, Center of Human Genetics, KU Leuven, Leuven, 3000, Belgium

3 Competence Centre on Health Technologies, Tartu, Estonia

4 Leuven University Fertility Center, UZ Leuven, Leuven, 3000, Belgium

Introduction

Recently, we identified bovine cleavage stage embryos carrying distinct parental genomic blastomeres. We traced back the causal event to the first zygotic division and therefore coined the zygotic division leading to the segregation of parental genomes into distinct blastomere lineages with the term *heterogoneic*. These heterogoneic divisions resulted in biparental, androgenetic and/or gynogenetic blastomeres (i.e. paternal and maternal only, respectively) both in presence and absence of fertilization errors. Whether heterogoneic divisions exist in human remains unknown. In addition, most genome wide haplotyping studies have focused on understanding the causes for aneuploidy in normal fertilized embryos which are characterized by 2 pronuclei. In contrast, monopronuclear (1PN) and triprounuclear (3PN) embryos are discarded from being used in IVF cycles and little is known about the genomic constitution, developmental potential and the chromosomal stability of 1PN and 3PN derived human preimplantation embryos.

Used methods

Recently, we developed haplarithmis, enabling concurrent haplotyping and copy number profiling of single cells based on SNP arrays. By applying this novel methodology on human preimplantation embryos we are able to uncover the parental origin of the genomic content of single blastomeres. To identify heterogoneic cell divisions in human we performed single-cell analysis from blastocysts discarded from PGD cycles upon an aberrant biopsy result at day 3. In addition, we combine time-lapse imaging to monitor the cleavage divisions together with the genomic analysis of the cleavage cells of 1PN and 3PN human preimplantation embryos which are derived either through in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI).

Results

Here, we demonstrate the existence of heterogoneic cell divisions in human. Specifically, a single blastomere displayed paternal monosomy. Additionally, some chromosomes showed diploidy, maternal monosomy, nullisomy or uniparental disomy. Upon blastocyst dissociation nine biopsies, ranging from a single cell to clumps of 2 to 5 cells, were analyzed with haplarithmis. An identical profile to the aberrant biopsy was uncovered in a single cell and additionally, two single cells displayed a reciprocal maternal monosomic profile. Surprisingly, the remaining biopsies displayed diploid blastomeres except one blastomere carrying a paternal trisomy for a single chromosome. This is the first case of a heterogoneic division in a human cleavage preimplantation embryo. Moreover, we show the persistence of distinct blastomere lineages until blastocyst stage. A first 1 PN embryo containing only a maternal genome showed the cleavage to be activated. A second 1PN embryo turned out to be diploid, suggesting that pronuclear formation occurred asymmetrically. One of the triprounuclear embryos gave rise to three blastomeres following the first cleavage. Interestingly, two out of three blastomeres underwent fusion, which resulted in a diploid cell containing a different maternal genomic profile in comparison to the remaining blastomere. This suggests the persistence of a polar body with blastomere sized cells in the early-stage embryo.

Conclusions

These observations pinpoint novel mechanisms underlying chimerism/mixoploidy and aneuploidy, highlighting the genomic flexibility of human preimplantation embryos during early cleavages. In addition, we believe that paternal cell lines occasionally survive and can cause molar pregnancies.

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The embryo is the cradle of chromosomal disorders

Prof.dr. Joris R. Vermeesch

Centre for Human Genetics, UZLeuven, Leuven, Belgium

We developed a generic method that can be readily select for all transmitted genetic disorders in human and animal embryos. The method reconstructs genome-wide haplotype architectures as well as the copy-number and segregational origin of those haplotypes by employing phased parental genotypes and deciphering WGA-distorted SNP B-allele fractions using a process we coin haplarithmisis. We demonstrate the method can be applied as a generic method for preimplantation genetic diagnosis on single cells biopsied from human embryos enabling to diagnose both disease alleles genome wide, as well as numerical and structural chromosomal anomalies. Moreover, meiotic segregation errors can be distinguished from mitotic ones. During PGD, we discovered, unexpectedly, not only a high incidence of whole chromosomal aneuploidies but also of segmental chromosomal segmental deletions, duplications and amplifications that were reciprocal in sister blastomeres. We demonstrated since that chromosome breakages and fusions occur frequently in cleavage stage human embryos and instigate subsequent breakage-fusion-bridge cycles. We mapped the frequency and charting the landscape of segmental imbalances observed during PGT. When applied to human and bovine embryos, it was demonstrated that chromosome instability is comparable between bovine and human cleavage embryos. Interestingly, when applied to IVF embryos a novel form of genomic instability was uncovered whereby zygotes spontaneously segregate entire parental genomes into different cell lineages during the first post-zygotic cleavage division. We coin this "Heterogoneic" cell division. This mechanism is likely the main cause for chimaerism and mixoploidy in mammals and is the likely cause of ovarian teratomas and molar pregnancies.

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NIPT in the Netherlands

Dr. Erik A. Sistersmans

Clinical Genetics, VU University Medical Center Amsterdam, Amsterdam, The Netherlands

In the Netherlands, Non-Invasive Prenatal Testing (NIPT) has been available to women with high-risk pregnancies based on first trimester combined test (FCT) results or medical history since 2014 (TRIDENT-1 study). TRIDENT-2 started April 1st 2017, and aims at implementing NIPT for all pregnant women within the framework of the national prenatal screening program. This means that NIPT is now available for all pregnant women in the Netherlands (on average 180,000 women/year). To ensure that NIPT analysis is affordable to all women, the Minister of health invested €26 million/year in this screening. For TRIDENT-2, the entire chain from counselor to laboratory and back needed to be revised. The set-up of the project was closely supervised by the Ministry of Health and RIVM/CvB (Center for population studies) during monthly meetings. During the six months between approval of the project in September 2016 and the start in April 2017, ~3000 counselors were trained, informational booklets and websites for pregnant women and professionals were written and published; the laboratory capacity was increased 20-fold, the national prenatal screening database for ordering the NIPT test and reporting results was adapted and logistics for blood withdrawal and transportation were set up. Finally, a grant for questionnaire and interview studies to study the women's perspective was written and awarded. This was only possible because of the enthusiast and very active participation of many people from different groups, including midwives, laboratory personnel, doctors, lawyers, ICT-specialists and many others.

Already since the start of TRIDENT-1 a whole genome sequencing (WGS) approach is used, but in TRIDENT-2 women have the choice between receiving results for chromosomes 21, 13 and 18 only, or for all autosomes. Depending of the individual's choice, the laboratory will use a different set of bio-informatical filters to analyze the WGS data. Sex chromosomal abnormalities will not be analyzed and reported. All analysis are performed by the three clinical genetic laboratories in Maastricht, Rotterdam and Amsterdam using the same analysis software.

During the first 5 months approximately 30,000 NIPT analyses were requested. No major problems were encountered. Detailed information on the results will be presented at the meeting. We expect that this 3-year study will provide us with all the results needed for the final decision on the responsible introduction of NIPT in the Dutch National prenatal screening program.

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Genetics & psychiatry: how 1+1 can be 3

Prof.dr. Brenda Penninx

Department of Psychiatry, VU university Medical Center / GGZ inGeest, Amsterdam, The Netherlands

The last decade can be described as one of a 'genome wide analysis' breakthrough in human genetics. Due to technological and statistical developments, a huge upscaling of human genetic studies has emerged. This has revealed new leads in the pathophysiology of complex disorders, including psychiatric conditions. In my talk I will provide recent examples from large-scale collaborative genetic studies that illustrate how human genetics can inform pathophysiology, nosology, personalized medicine and treatment development in psychiatry.

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Abstracts Talks (T)

NVHG – Two Day Annual Meeting 2017

Nr	Name		Title	E-mail
T 01	Hellebrekers	Debby	Next-generation sequencing of the mtDNA and exome is the preferred, first strategy to identify known and novel causes of mitochondrial disease	debby.hellebrekers@mumc.nl
T 02	Goldmann	Jakob	Germline de novo mutation clusters arise during oocyte aging in genomic regions with increased double-strand break incidence	jakob.goldmann@radboudumc.nl
T 03	Mokry	Michal	Candidate gene identification based on 3D chromatin interactions: Genetics behind complex diseases just got even more complex	m.mokry@umcutrecht.nl
T 04	Coonen	Edith	Refining embryo transfer strategies using embryonic ploidy status in PGD for translocations	edith.coonen@mumc.nl
T 05	Deden	Chantal	A retrospective analysis of genetic testing in pediatric patients while introducing rapid targeted whole genome sequencing for critically ill newborns	chantal.deden@radboudumc.nl
T 06	Hestand	Matthew	Fetal Fraction Evaluation in Non-Invasive Prenatal Testing (NIPT)	m.hestand@vumc.nl
T 07	Vandervore	Laura	RTTN is located at the centrosomes during mitosis and regulates centriole duplication	lauravandervore@hotmail.com
T 08	Elferink	Martin	Defining quality standards for clinical whole exome sequencing: a national collaborative study of the Dutch Society for Clinical Genetic Laboratory Diagnostics (VKGL)	m.elferink@umcutrecht.nl
T 09	Harakalova	Magdalena	Transcriptional regulation in hypertrophic cardiomyopathy due to MYBPC3 founder mutations	m.harakalova@umcutrecht.nl
T 10	van den Bosch	Bianca	Evolution of dihydropyrimidine dehydrogenase (DPD) diagnostics in a time-period of seven years	bianca.vanden.bosch@mumc.nl
T 11	Vanoevelen	Jo	Classification of Imna-variants by means of zebrafish phenotyping	j.vanoevelen@maastrichtuniversity.nl
T 12	Ruivenkamp	Claudia	Towards automated sharing of genetic variants between genome diagnostics laboratories and beyond: an initiative of the Dutch diagnostic data sharing consortium	c.ruivenkamp@lumc.nl
T 13	Oud	Machteld	Ciliary phenotyping in urine-derived patient cells to determine the pathogenicity of novel variants in ciliopathy genes	machteld.oud@radboudumc.nl
T 14	Lelieveld	Stefan	De novo missense mutation clustering identifies candidate neurodevelopmental disorder genes	stefan.lelieveld@radboudumc.nl
T 15	't Hoen	Peter A.C.	RNAseq in 296 phased trios provides a high resolution map of genomic imprinting	p.a.c.hoen@lumc.nl
T 16	Schot	Rachel	SMPD4 mutations link primary microcephaly and severe encephalopathy to aberrant cytokinesis and membrane ceramide metabolism	r.schot@erasmusmc.nl

Abstracts Posters (P)

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Nr	Name		Title	E-mail
P01	't Hoen	Peter A.C.	Skewed X-inactivation is common in the general female population	p.a.c.hoen@lumc.nl
P02	Anvar	Yahya	Full-length mRNA sequencing uncovers a widespread coupling between transcription and mRNA processing	s.y.anvar@lumc.nl
P03	Appelhof	Bart	A Zebrafish Model for Pontocerebellar Hypoplasia.	b.appelhof@amc.nl
P04	Arshad	Maria	Association of rs182429 variant of the t-cell activation rho-gtpase activating protein (tagap) in pakistani rheumatoid arthritis patients	maria.arshad14@gmail.com
P05	Baas	Frank	Direct visualization of repetitive genome structures for the genetic diagnosis of FSHD	f.baas@lumc.nl
P06	Bouman	Katelijne	Multidisciplinary Dutch Guideline for Genotyping in Case of Fetal Ultrasound Anomalies	katelijnebouman@hotmail.com
P07	Demirdas	Serwet	Diagnosing Danon disease: a case-report of a young boy and his deceased mother	s.demirdas@erasmusmc.nl
P08	Diets	Illja	A specific de novo missense mutation in SMARCB1 causes severe intellectual disability and hydrocephalus	illja.diets@radboudumc.nl
P09	Eijkenboom	Ivo	A zebrafish model for small-fiber neuropathy	ivo.eijkenboom@maastrichtuniversity.nl
P10	Geuer	Sinje	Whole Exome Sequencing as first line diagnostic test for all genetic disorders	sinje.geuer@radboudumc.nl
P11	Grolleman	Judith	Multi-cancer phenotype including colorectal and breast cancer of patients with biallelic NTHL1 mutations	judith.grolleman@radboudumc.nl
P12	Harteveld	Cornelis L.	Breakpoint characterization of a rare alpha-thalassemia deletion using Next Generation Sequencing	c.l.harteveld@lumc.nl
P13	Hoffer	Mariëtte	ATAD3A deletions: a challenge in prenatal diagnosis	m.j.v.hoffer@lumc.nl
P14	Hoogeveen-Westerveld	Marianne	Functional analysis of variants of uncertain clinical significance in the RAS and mTOR signaling pathways.	m.hoogeveen-westerveld@erasmusmc.nl
P15	Koole	Wouter	Diagnostic clinical resequencing of polyposis-predisposition genes using single molecule Molecular Inversion Probes	wouter.koole@radboudumc.nl
P16	Lakeman	Phillis	Evaluation of an expanded carrier screening offer in a non-commercial setting	p.lakeman@amc.uva.nl
P17	Losekoot	Monique	The Leiden experience in diagnostics for short stature: gene panel based mutation analysis by next generation sequencing on the Ion Torrent PGM	m.losekoot@lumc.nl
P18	Medendorp	Niki	Counselors' experiences with uncertainties concerning Next Generation Sequencing. A focus group study.	n.m.medendorp@amc.uva.nl
P19	Nagyova	Ema	Targeted resequencing of coding and cardiac non-coding regulatory regions related to genes implicated in dilated cardiomyopathy	e.nagyova@umcutrecht.nl
P20	Pei	Jiayi	Genome-wide H3K27ac chromatin profiling in healthy and remodeled human myocardium	j.pei@umcutrecht.nl
P21	Ruivenkamp	Claudia	Enabling exome sequencing in non-genetic clinical practice: fast-WES as a routine diagnostic test	c.ruivenkamp@lumc.nl
P22	Schoot, van der	Vyne	Towards molecular understanding of ZBTB18 mutations: pointing the finger?	vyne.vander.schoot@mumc.nl
P23	Schuurmans	Juliette	Praktische Haalbaarheid van een Populatie-Brede Dragerschapstest voor Paren met Kinderwens Aangeboden door de Huisarts in Noord-Nederland	j.schuurmans@umcg.nl
P24	Sengul	Hatice Kubra	Identification of recurrently mutated genes in ADHD by targeted sequencing	hatice.sengul@radboudumc.nl

Abstracts Posters (P)

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Nr	Name		Title	E-mail
P25	Snoek	Rozemarijn	NPHP1 gene deletions cause ESRD in 0.9% of adult-onset cases	r.snoek-2@umcutrecht.nl
P26	WITHDRAWN			
P27	van Dijk	T.	Pontocerebellar hypoplasia with spinal muscular atrophy (PCH1): identification of SLC25A46 mutations in the original Dutch PCH1 family	t.vandijk@amc.nl
P28	van Duyvenvoorde	Hermine	Novel ACAN mutations in four children with short stature from two families without consistently advanced bone age	h.a.van_duyvenvoorde@lumc.nl
P29	van Slegtenhorst	Marjon	Major contributors identified for increase in diagnostic yield in our 10 years of experience in genetic testing for cardiomyopathies; data sharing, titin (TTN) mutations and stricter clinical inclusion criteria	m.vanslegtenhorst@erasmusmc.nl
P30	van Zutven	Laura	MAMLD1 deletions in three patients with proximal hypospadias	l.vanzutven@erasmusmc.nl
P31	Vanoevelen	Jo	A zebrafish model of classic galactosemia: paving the way for new insights on this metabolic disorder	j.vanoevelen@maastrichtuniversity.nl









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