BRCA 2021

A Vision of the Future | Une vision pour l'avenir

May 4 - 7, 2021 • Du 4 au 7 mai 2021 • Virtual Edition / Édition virtuelle

Eighth International Symposium on Hereditary Breast and Ovarian Cancer
8e Symposium international sur le cancer héréditaire du sein et de l'ovaire

AGENDA

(Revised March 1, 2021)
All times are in Eastern Daylight Time (UTC -4)

Tuesday, May 4, 2021

8:30 – 9:45 PARTICIPANTS LOG IN / NETWORKING ACTIVITIES

9:45 – 10:15 **Welcome and Introduction to the Programme**

Harley Eisman, MD, Co-Founder, Hereditary Breast and Ovarian Cancer Foundation, Montréal, QC, Canada

William Foulkes, MBBS, PhD, Director, Program in Cancer Genetics, McGill University, Montréal, QC, Canada

Session 1: Mutations, variants, databases 10:15 - 11:45

CHAIR: Lawrence Brody, PhD, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, USA

10:15 - 10:35 **LECTURE**
Variant interpretation in the genomic era
Jonathan Berg, MD, UNC School of Medicine, Chapel Hill, NC, USA

10:35 - 10:55 **LECTURE**
Functional classification of HRD gene variant using CRISPR screens
Lea Starita, PhD, University of Washington, Seattle, WA, USA

10:55 - 11:05 **PROFFERED PAPER 1 (S1-PP1)**
A VarCall Model for Classification of BRCA2 Variants Using Mouse Embryonic Stem Cells-based Functional Assays
Shyam Sharan, Ph.D, National Cancer Institute, NIH, Frederick, MD, USA

11:05 - 11:15 **PROFFERED PAPER 2 (S1-PP2)**
Germline Variants of 219 Genes in 1333 Ovarian Cancer Patients
Dr. Jana Soukupova, PhD, Charles University, Prague, Czech Republic

11:15 - 11:25 **PROFFERED PAPER 3 (S1-PP3)**
Variants of Low Allele Frequency in Panel Testing, Where Are They Coming From?
Raymond Kim, MD, PhD, FRCPC, FACMG, Princess Margaret Cancer Centre, Toronto, ON, Canada

11:25 - 11:45 **Question and discussion period (all speakers)**

11:45 - 12:45 MID-DAY BREAK

Tuesday, May 4, 2021 *(cont'd)*

Session 2: Pathology – Clinical Relevance 12:45 - 14:15

CHAIR: Blaise Clarke, MD, University Health Network, Toronto, ON, Canada

12:45 - 13:05 **LECTURE**
Breast cancer susceptibility genes, pathology and outcome
Marjanka Schmidt, PhD**,** Netherlands Cancer Institute, Amsterdam, and Leiden University Medical Center, Leiden, The Netherlands

13:05 - 13:25 **LECTURE**
Where do ovarian cancers originate and why does it matter?
Christopher Crum, MD, Brigham and Women's Hospital, Boston, MA, USA

13:25 - 13:35 **PROFFERED PAPER 1 (S2-PP1)**
Mechanisms That Impact the Cell Division Axis and Phenotype for BRCA1-mutant Mammary Epithelial Cells
Zhengcheng He, BSc., University of British Columbia, Vancouver, BC, Canada

13:35 - 13:45 **PROFFERED PAPER 2 (S2-PP2)**
Transcriptome-Based Profiles of Immune Cell Infiltration in BRCA1/2-Positive and BRCA1/2-Negative Male Breast Cancers
Valentina Silvestri, MSc., PhD, Sapienza University of Rome, Rome, Italy

13:45 - 13:55 **PROFFERED PAPER 3 (S2-PP3)**
Molecular and Genetic Characterisation of Contralateral Breast Cancer (CBC): The Importance of CBC Risk Stratification and Management
Colin McIlmunn, MB BCh, Queen's University Belfast, Belfast, Northern Ireland

13:55 - 14:15 **Question and discussion period (all speakers)**

14:15 - 14:45 BREAK

Session 3: Applied functional and computational genetics 14:45 - 16:15

CHAIR: Britta Weigelt, PhD, Memorial Sloan Kettering Cancer Center, New York, NY, USA

14:45 - 15:05 **LECTURE**
Mutational profiles - New approaches to genetic diagnosis and treatment
Serena Nik-Zainal, MD, PhD, University of Cambridge, Cambridge, UK

15:05 - 15:25 **LECTURE**
DNA Repair – Clinical relevance for breast cancer/ovarian cancer
Ralph Scully, MBBS, PhD, Beth Israel Deaconess Medical Center, Boston, MA, USA

15:25 - 15:35 **PROFFERED PAPER 1 (S3-PP1)**
Variation in the Functional Effects of Different Protein Truncating Mutations in BRCA1 and BRCA2 in Breast and Fallopian Tube Epithelial Cells
Simon Gayther, Cedars Sinai Medical Center, Los Angeles, CA, USA

15:35 - 15:45 **PROFFERED PAPER 2 (S3-PP2)**
Germline Genetic Testing Combined with Tumor Sequencing Has Significant Utility for Breast and Ovarian Cancer Patients
Sarah Nielsen, Invitae, San Francisco, CA, USA

Tuesday, May 4, 2021 *(cont'd)*

15:45 - 15:55 **PROFFERED PAPER 3 (S3-PP3)**
Etiologic Index: A Case-only Measure of BRCA1/2-associated Cancer Risk
Paz Polak, Mount Sinai Hospital, New York, NY, USA,

15:55 - 16:15 **Question and discussion period (all speakers)**

16:15 - 16:30 BREAK

Rapid-Fire Poster Session — 16:30 - 17:00

CHAIR: Patricia Tonin, PhD, McGill University, Montréal, QC, Canada

NEW this year: The Rapid-Fire Poster Session is an exciting, fast-paced session where five poster presenters will present key results of their research in 3-minute oral presentations.

POSTER SESSION 1 — 17:00 - 18:00

Wednesday, May 5, 2021

8:30 – 9:45 PARTICIPANTS LOG IN / NETWORKING ACTIVITIES

9:45 – 10:15 **Welcome and Introduction to the Programme**

Harley Eisman, MD, Co-Founder, Hereditary Breast and Ovarian Cancer Foundation, Montréal, QC, Canada

William Foulkes, MBBS, PhD, Director, Program in Cancer Genetics, McGill University, Montréal, QC, Canada

Remembering Henry Lynch

Lisa Madlensky, PhD, CGC, Moores UCSD Cancer Center, University of California San Diego, La Jolla, CA, USA

Steven Narod, MD, FRCPC, FRSC, Canada Research Chair in Breast Cancer, Women's College Research Institute, Toronto, ON, Canada

Session 4: Special Round Table: Population-based approaches to genetic testing and risk assessment – Beyond the current models — 10:15 - 11:45

MODERATORS:
Lawrence Brody, PhD, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, USA; **Clare Turnbull,** MD, PhD, MFPH, Institute of Cancer Research, London, UK

INTRO, OVERVIEW, CONSIDERATIONS
Paul Pharoah, BM, BCh, PhD, University of Cambridge, Cambridge, UK

Wednesday, May 5, 2021 *(cont'd)*

POPULATION TESTING

Integrated service provider program: the Geisinger experience
Adam Buchanan, MS, MPH, LGC, Genomic Medicine Institute, Geisinger Health System, Danville, PA, USA

National approaches: USA and beyond
Stephen Chanock, MD, National Cancer Institute, Rockville, MD, USA

Founder testing – the Israel approach: Is it generalizable?
Ephrat Levy-Lahad, MD, Shaare Zedek Medical Center, Jerusalem, Israel

11:45 - 13:30 MID-DAY BREAK

Session 5: Early diagnosis of breast and prostate Cancer in BRCA1 or BRCA2 heterozygotes — 13:30 - 14:30

CHAIR: Jeffrey Weitzel, MD, Duarte, CA, USA

13:30 - 13:50 **LECTURE**
MRI and the early diagnosis of breast cancer in BRCA1 and BRCA2 heterozygotes
Steven Narod, MD, FRCPC, FRSC, Canada Research Chair in Breast Cancer, Women's College Research Institute, Toronto, ON, Canada

13:50 - 14:00 **Question period**

14:00 - 14:20 **LECTURE**
Prostate cancer in men with BRCA1 or BRCA2 pathogenic variants - the IMPACT STUDY
Elena Castro, MD, PhD, CNIO-IBIMA Genitourinary Cancer Research Unit, Institute of Biomedical Research in Malaga (IBIMA), Málaga, Spain

14:20 - 14:30 **Question period**

14:30 - 14:45 BREAK

Session 6: Genetic counselling – New challenges — 14:45 - 16:15

CHAIR: Antonis Antoniou PhD, University of Cambridge, Cambridge, UK

14:45 - 15:05 **LECTURE**
Genetic Counseling for a general population: lessons learned
Kelly Tangney, MS, LCGC, Color Health, Inc., Burlingame, CA, USA

15:05 - 15:25 **LECTURE**
A practical approach to handling direct-to-consumer data
Lisa Madlensky, PhD, CGC, Moores UCSD Cancer Center, University of California San Diego, La Jolla, CA, USA

15:25 - 15:35 **PROFFERED PAPER 1 (S6-PP1)**
A Gynecologic Oncologist-led Mainstreaming Approach of Germline Genetic Testing for Patients with Ovarian Cancer; First Experiences of Healthcare Professionals and Patients
Kyra Bokkers, MD / PhD Student, University Medical Center Utrecht, Utrecht, The Netherlands

Wednesday, May 5, 2021 *(cont'd)*

15:35 - 15:45 **PROFFERED PAPER 2 (S6-PP2)**
Large Scale Group Genetic Counselling: A Novel Service Delivery Model in British Columbia
Zoe Lohn, MSc., BC Cancer, Vancouver, BC, Canada

15:45 - 15:55 **PROFFERED PAPER 3 (S6-PP3)**
Genetic Cancer Risk Assessment Outcomes for Latin American Participants in the GRACIAS (genetic risk assessment for cancer implementation and sustainment) study: Growing Reach, Cascade Testing, and Access to Risk Reduction Surgeries
Jeffrey Weitzel, MD, Duarte, CA, USA

15:55 - 16:15 **Question and discussion period (all speakers)**

16:15 - 16:45 BREAK

Wednesday Special Interest Groups (SIGs) 16:45 - 17:45

Moderated one-hour interactive discussions *with the aim of fostering bilateral knowledge transfer. Choice of the following 2 SIGs.*

SIG 1
Moderate risk genes – When and where are they useful?

In this session, the four experts will discuss the role of clinical testing for moderate risk breast and ovarian cancer susceptibility genes. They will review data on the cancer risks associated with pathogenic variants in each of the major moderate risk genes (e.g. ATM, BARD1, BRIP1, CHEK2, RAD51C, RAD51D) and will discuss emerging candidate genes. Models to assess risk will be discussed, as will counseling challenges. The pathology of tumors associated with pathogenic variants in these genes will be considered.

- **Paul James**, MD, PhD, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia *(session lead)*
- **Mark Robson**, MD, Memorial Sloan Kettering Cancer Center, New York, NY, USA
- **Lisa Madlensky,** PhD, CGC, Moores UCSD Cancer Center, University of California San Diego, La Jolla, CA, USA
- **Marjanka Schmidt,** PhD**,** Netherlands Cancer Institute, Amsterdam, and Leiden University Medical Center, Leiden, The Netherlands

SIG 2
Ethico-legal issues around usage of genomic data

Some of the issues that will be discussed in this interactive session include genetic counselling in the private direct to consumer testing era, patenting of genes and its influence on data sharing, secrecy *vs* open innovation, ethical aspects of large-scale genomic sequencing and genetic discrimination. Attendees will be encouraged to send in specific ethics questions in advance for discussion at the SIG.

- **Yann Joly,** PhD, AdE, McGill University, Montréal, QC, Canada *(session lead)*
- **Yvonne Bombard,** PhD, BSc, Li Ka Shing Knowledge Institute, St Michael's Hospital, Toronto, ON, Canada
- **Nathalie Bolduc,** MSc, Quebec Breast Cancer Foundation, Montréal, QC, Canada
- **Robert Cook-Deegan**, MD, Arizona State University, Washington, DC, USA

Thursday, May 6, 2021

8:30 – 9:45 PARTICIPANTS LOG IN / NETWORKING ACTIVITIES

9:45 – 10:00 **Introduction to the Programme**

Harley Eisman, MD, Co-Founder, Hereditary Breast and Ovarian Cancer Foundation, Montréal, QC, Canada

William Foulkes, MBBS, PhD, Director, Program in Cancer Genetics, McGill University, Montréal, QC, Canada

Session 7: New developments in HBOC management 10:00 - 11:30

CHAIR: Ephrat Levy-Lahad, MD, Shaare Zedek Medical Center, Jerusalem, Israel

10:00 - 10:20 **LECTURE**

Update on therapy for breast cancer for women with BRCA1/2 pathogenic variants

Mark Robson, MD**,** Memorial Sloan Kettering Cancer Center, New York, NY, USA

10:20 - 10:40 **LECTURE**

New treatments for BRCA-deficient ovarian cancer

Ursula Matulonis, MD, Dana-Farber Cancer Institute, Boston, MA, USA

10:40 - 10:50 **PROFFERED PAPER 1 (S7-PP1)**

The First Results of the Prospective Multicenter TUBA Study Investigating Salpingectomy with Delayed Oophorectomy in BRCA Mutation Carriers

Miranda Steenbeek, MD, PhD Student, Radboud University Medical Center, Nijmegen, The Netherlands

10:50 - 11:00 **PROFFERED PAPER 2 (S7-PP2)**

Oral Contraceptive Use and Cancer Incidence and Mortality for BRCA1 and BRCA2 Mutation Carriers: Absolute Risk-benefit Calculation Considering Breast, Ovarian and Endometrial Cancer

Matti Rookus, Netherlands Cancer Institute, Amsterdam, The Netherlands

11:00 - 11:10 **PROFFERED PAPER 3 (S7-PP3)**

A Positive Oestrogen Receptor Status and Breast Cancer Survival in Nordic BRCA2 Mutation Carriers

Laufey Tryggvadóttir, MSc., Professor, University of Iceland / Icelandic Cancer Registry

11:10 - 11:30 **Question and discussion period (all speakers)**

POSTER SESSION 2 11:30 - 13:00

13:00 - 14:30 MID-DAY BREAK

Thursday, May 6, 2021 *(cont'd)*

Thursday Special Interest Groups (SIGs) 14:30 - 15:30

Moderated one-hour interactive discussions *with the aim of fostering bilateral knowledge transfer. Choice of the following 2 SIGs..*

SIG 3
Rarer moderate to highly penetrant breast cancer syndromes – *CDH1, PTEN, TP53, NTHL1* and others

In this session, attendees will join the presenters in exploring clinico-pathological aspects of a set of well-known and less well-known breast and ovarian cancer susceptibility genes. Dr. Tischkowitz will focus on CDH1, Dr. Hoogerbrugge on PTEN and NTHL1 and Dr. Weitzel will discuss TP53. Attendees will be encouraged to send in specific cases in advance for discussion at the SIG.

- **Marc Tischkowitz,** MD, PhD, University of Cambridge, Cambridge, UK *(session lead)*
- **Nicoline Hoogerbrugge,** MD, PhD, Radboud University Medical Center, Nijmegen, The Netherlands
- **Jeffrey Weitzel**, MD, Duarte, CA, USA

SIG 4
Genetic counselling – How to expect the unexpected?

In this interactive case-based session, Dr. Hurley will explore advance concepts in genetic counselling and will show how counsellors can help clients cope with the challenges associated with discovering their genetic status.

- **Karen Hurley**, PhD, Cleveland Clinic, Cleveland, OH, USA

15:30 - 16:00 BREAK

Session 8: Polygenic risk scores in practice 16:00 - 17:30

CHAIR: Mark Robson, MD, Memorial Sloan Kettering Cancer Center, New York, NY, USA

16:00 - 16:20 **LECTURE**
Polygenic risk scores and the CanRisk breast and ovarian cancer risk prediction tool
Antonis Antoniou, PhD, University of Cambridge, Cambridge, UK

16:20 - 16:40 **LECTURE**
Multifactorial breast cancer risk assessment
Paul James, MD, PhD, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia

16:40 - 16:50 **PROFFERED PAPER 1** (S8-PP1)
Determining Women Preferences for Population Genetic Testing to Inform Implementation of Risk-Stratified Breast Screening
Alison Trainer, FRACP, PhD, Parkville Familial Cancer Center, Melbourne, Australia

16:50 - 17:00 **PROFFERED PAPER 2** (S8-PP2)
Personalized Risk Assessment for Prevention and Early Detection of Breast Cancer: Integration and Implementation (PERSPECTIVE I&I)
Jacques Simard, PhD, Centre de recherche CHU de Québec - Université Laval, Québec, QC, Canada

17:00 - 17:30 **Question and discussion period (all speakers)**

Friday, May 7, 2021

8:30 – 9:45 PARTICIPANTS LOG IN / NETWORKING ACTIVITIES

9:45 – 10:00 **Introduction to the Programme**

Harley Eisman, MD, Co-Founder, Hereditary Breast and Ovarian Cancer Foundation, Montréal, QC, Canada

William Foulkes, MBBS, PhD, Director, Program in Cancer Genetics, McGill University, Montréal, QC, Canada

Session 9: Insight from large datasets of women with breast cancer 10:00 - 11:45

CHAIR: Stephen Chanock, MD, National Cancer Institute, Rockville, MD, USA

10:00 - 10:20 **LECTURE**

Population-based studies of breast cancer risk in association with established and candidate breast cancer susceptibility genes

Fergus Couch, PhD, Mayo Clinic, Rochester, MN, USA

10:20 – 10:40 **LECTURE**

Generation and analysis of genomic data at population level: the UK experience

Clare Turnbull, MD, PhD, MFPH, Institute of Cancer Research, London, UK

10:40 - 10:50 **PROFFERED PAPER 1** (S9-PP1)

Breast Cancer Risk Genes: Association Analysis of Rare Coding Variants in 34 Genes in 60,466 Cases and 53,461 Controls from the BRIDGES Project

Douglas Easton, PhD, University of Cambridge, Cambridge, UK

10:50 - 11:00 **PROFFERED PAPER 2** (S9-PP2)

Are Germline Heterozygous Variants in NTHL1 Associated with Breast Cancer Predisposition? An International Multi-center Study of 46,000 Subjects

Ian Campbell, PhD, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia

11:00 - 11:10 **PROFFERED PAPER 3** (S9-PP3)

A Moderately Rare Unstable FANCI c.1813C>T; p.L605F Is Associated with Familial Ovarian Cancer

Caitlin Fierheller, BSc, PhD Candidate, McGill University, Montréal, QC, Canada

11:10 - 11:20 **PROFFERED PAPER 4** (S9-PP4)

The Contribution of Germline Pathogenic Variants Beyond BRCA1/2/PALB2 to Contralateral Breast Cancer in Women With a Younger Onset First Breast Cancer – a WECARE Study

Marc Tischkowitz, MD, PhD, University of Cambridge, Cambridge, UK

11:20 - 11:45 **Question and discussion period (all speakers)**

11:45 - 13:00 MID-DAY BREAK

Friday, May 7, 2021 ***(cont'd)***

Friday Special Interest Groups (SIGs) 13:00 - 14:00

Moderated one-hour interactive discussions *with the aim of fostering bilateral knowledge transfer. Choice of the following 2 SIGs..*

SIG 5
Hereditary prostate, pancreas and male breast cancer: Research updates and surveillance recommendations

In this session, the three presenters will discuss the latest research on prevention, early diagnosis and treatment of three cancers that are associated with germline mutations in HRD genes. Attendees will be encouraged to send in questions relating to these topics in advance for discussion at the SIG.

- **Elena Castro**, MD, PhD, CNIO-IBIMA Genitourinary Cancer Research Unit, Institute of Biomedical Research in Malaga (IBIMA), Málaga, Spain
- **George Zogopoulos**, MD, PhD, McGill University Health Centre, Montréal, QC, Canada
- **Justin Lorentz,** CGC, Sunnybrook Odette Cancer Centre, Toronto, ON, Canada

SIG 6
Ovarian cancer – a multi-faceted view

Ovarian cancer is one of the most preventable cancers. In this unique session, five leading experts will discuss the epidemiology of, and inherited contribution to, ovarian cancer, the role of risk assessment in management, the molecular genetics and pathology of the main subtypes of ovarian cancer, and where new treatments are taking the field.

- **Paul Pharoah,** BM, BCh, PhD, University of Cambridge, Cambridge, UK *(session lead)*
- **Antonis Antoniou** PhD, University of Cambridge, Cambridge, UK
- **Blaise Clarke**, MD, University Health Network, Toronto, ON, Canada
- **Ursula Matulonis,** MD, Dana-Farber Cancer Institute, Boston, MA, USA
- **Britta Weigelt**, PhD, Memorial Sloan Kettering Cancer Center, New York, NY, USA

14:00 - 14:30 BREAK

Closing Session: The Marla Miller Memorial Lecture 14:30 - 15:45

14:30 - 15:45

Introductory Remarks

William Foulkes, MBBS, PhD,
Director, McGill University Program in Cancer Genetics, Montréal, QC, Canada

LECTURE

The Icelandic approach to population-based testing for high risk alleles for breast and ovarian cancer

Kári Stefánsson, MD, PhD,
deCODE Genetics, Reykjavík, Iceland

Presentation by the Miller Family

Closing Remarks

Harley Eisman, MD,
Co-Founder, Hereditary Breast and Ovarian Cancer Foundation,
Montréal, Québec, Canada