

AGENDA

Thursday – October 24, 2013

3:00 **Symposium check-in & registration opens**
Imperial Ballroom Foyer

4:00 - 6:00 ***FA 101: An Introduction to the Medicine & Biology of Fanconi Anemia***
Imperial Ballroom East

Note: This session is intended especially for those new to Fanconi anemia research and clinical care. However, all attendees interested in an overview of unanswered questions and new research and clinical directions in Fanconi anemia are encouraged to attend.

Introductions:

Grover C. Bagby Jr., MD

Chair, Scientific Advisory Board, Fanconi Anemia Research Fund
Oregon Health & Science University, Portland, Oregon

Faculty:

Alan D’Andrea, MD

Dana-Farber Cancer Institute, Boston, Massachusetts

Blanche Alter, MD, MPH

National Cancer Institute, Bethesda, Maryland

6:00 - 8:00 { **Welcome Reception**
 { **Poster Viewing**
 { *Imperial Ballroom West*
 { Presenters with an odd-numbered poster will be at their posters 6:00-7:00.
 { Presenters with an even-numbered poster will be at their posters 7:00-8:00.

Friday – October 25, 2013

7:00 - 8:00 { **Buffet Breakfast**
 { *Imperial Ballroom Center*
 { **Poster Viewing**
 { *Imperial Ballroom West*

{ **Plenary Session**
Imperial Ballroom East

8:00 - 8:25 **Welcome**
David Frohnmayer, JD
Co-founder and Advisor, Board of Directors
Fanconi Anemia Research Fund, Eugene, Oregon

Introduction
Grover C. Bagby Jr., MD
Chair, Scientific Advisory Board, Fanconi Anemia Research Fund
Oregon Health & Science University, Portland, Oregon

Special Session: Design and Conduct of Clinical Trials in Fanconi Anemia Patients

Chair: Jakub Tolar, MD, PhD
Scientific Advisory Board, Fanconi Anemia Research Fund
University of Minnesota, Minneapolis, Minnesota

8:25 - 8:30 **Session Overview: Jakub Tolar, MD, PhD**

8:30 - 8:40 **Jakub Tolar, MD, PhD**, University of Minnesota, Minneapolis, Minnesota

8:40 - 8:50 **Julian Sevilla, PhD**, Hospital Infantil Universitario Niño Jesús, Madrid, Spain

8:50 - 9:00 **Farid Boulad, MD**, Memorial Sloan-Kettering Cancer Center, New York, New York

9:00 - 9:10 **David Kutler, MD**, Weill Cornell Medical Center, New York, New York

9:10 - 9:20 **Rabin Tirouvanziam, PhD**, Emory University, Atlanta, Georgia

9:20 - 9:35 **Questions and Answers and Session Wrap-up: Jakub Tolar, MD, PhD**

Keynote Presentation: Genomics, Cancer and Personalized Medicine
(Please see page 12 for Keynote Presenter Statement.)

9:35 - 10:05 **Jeffrey Myers, MD, PhD**, University of Texas MD Anderson Cancer Center, Houston, Texas

10:05 - 10:15 Questions and Answers

10:15 - 10:35 **Break**

Session I: Head and Neck Squamous Cell Carcinoma

Chair: Ruud Brakenhoff, PhD

Vrije Universiteit Medical Center, Amsterdam, Netherlands

10:35 - 10:40 **Session Overview: Ruud Brakenhoff, PhD**

10:40 - 10:50 **Joel Greenberger, MD**, University of Pittsburgh Cancer Institute, Pittsburgh, Pennsylvania: *Head and Neck Irradiation Sensitivity and Distant Bone Marrow Suppression in FancD2-/- (FVB/N) Mice is Ameliorated by Intraoral Administration of GS-nitroxide (JP-4-039)*

10:50 - 10:55 Questions and Answers

10:55 - 11:05 **Sanne Martens-de Kemp, PhD**, Vrije Universiteit Medical Center, Amsterdam, Netherlands: *Identification of Drug Targets for the Treatment of Oral Cancer and Precancer in FA Patients*

11:05 - 11:10 Questions and Answers

11:10 - 11:20 **Stephanie Smetsers, MD, PhD Student**, Wilhemina Children's Hospital, Utrecht, Netherlands: *Prevalence of Oral Precursor Lesions in Fanconi Anemia Patients*

11:20 - 11:25 Questions and Answers

11:25 - 11:35 **Flavia Teles, DDS, DMSc**, The Forsyth Institute, Boston, Massachusetts: *Search for Microbial and Host-derived Determinants of Oral Carcinogenesis in Fanconi Anemia*

11:35 - 11:40 Questions and Answers

11:40 - 11:45 **Session Wrap-up: Ruud Brakenhoff, PhD**

11:45 - 12:55 { **Buffet Lunch**
Imperial Ballroom Center
Early Investigators Mentorship Lunch
Please pick up lunch in Imperial Ballroom Center and meet in Magnolia Room
Poster Viewing
Imperial Ballroom West

Session II: FA Pathway Regulation

Chair: Ray Monnat Jr., MD

**Scientific Advisory Board, Fanconi Anemia Research Fund
University of Washington, Seattle, Washington**

- 12:55 - 1:00 **Session Overview: Ray Monnat Jr., MD**
- 1:00 - 1:10 **Robert Brosh, PhD**, National Institute on Aging, Baltimore, Maryland: *Werner Syndrome Helicase has a Critical Role in DNA Damage Responses in the Absence of Fanconi Anemia Pathway*
- 1:10 - 1:15 Questions and Answers
- 1:15 - 1:25 **Wojciech Niedzwiedz, PhD**, University of Oxford, Oxford, United Kingdom: *Suppression of Global Reorganization of Chromatin Structure through Replication Requires Fanconi Anemia Related Helicase*
- 1:25 - 1:30 Questions and Answers
- 1:30 - 1:40 **Celine Jacquemont, PhD**, Fred Hutchinson Cancer Research Center, Seattle, Washington: *USP28 Inhibits the Fanconi Anemia Pathway and Homologous Recombination through Catalytic and Non-catalytic Activities*
- 1:40 - 1:45 Questions and Answers
- 1:45 - 1:55 **Andrew Deans, PhD**, St. Vincent's Institute, Fitzroy, Australia: *Cyclin-dependent Kinases Regulate FANCM to Restrict the Fanconi Anemia DNA Repair Pathway*
- 1:55 - 2:00 Questions and Answers
- 2:00 - 2:10 **Jenny Xie, PhD**, Dana-Farber Cancer Institute, Boston, Massachusetts: *RNF4 Degrades Sumoylated FANCA and Regulates the FA Pathway*
- 2:10 - 2:15 Questions and Answers
- 2:15 - 2:25 **Ronald Cheung, MD, PhD**, Fred Hutchinson Cancer Research Center, Seattle, Washington: *Identification of Wip1 as a Phosphatase that Regulates FANCD2 Phosphorylation*
- 2:25 - 2:30 Questions and Answers
- 2:30 - 2:40 **Maya Raghunandan, Graduate Student**, University of Minnesota, Minneapolis, Minnesota: *FANCD2 Controls the Replication Fork Restart Machinery Independently of the FA Core Complex*
- 2:40 - 2:45 Questions and Answers
- 2:45 - 2:50 **Session Wrap-up: Ray Monnat Jr., MD**
- 2:50 - 3:10 **Break**

Session III: Novel Analytical Models

Chair: Richard Gelinas, PhD
Scientific Advisory Board, Fanconi Anemia Research Fund
Board of Directors, Fanconi Anemia Research Fund
Institute for Systems Biology, Seattle, Washington

- 3:10 - 3:15 **Session Overview: Richard Gelinas, PhD**
- 3:15 - 3:25 **Alfredo Rodríguez Gómez, MSc**, Instituto Nacional de Pediatría, Mexico City, Mexico: *Network Modeling Identifies the Checkpoint Recovery as a Process that Enables Escape of Unrepaired Double Strand Breaks*
- 3:25 - 3:30 Questions and Answers
- 3:30 - 3:40 **Nidhi Sahni, PhD**, Dana-Farber Cancer Institute, Boston, Massachusetts: *Interpreting Fanconi Anemia Disease Variants through Systematic Edgotyping*
- 3:40 - 3:45 Questions and Answers
- 3:45 - 3:50 **Session Wrap-up: Richard Gelinas, PhD**

Session IV: Aldehydes and Enzymology

Chair: Markus Grompe, MD
Oregon Health & Science University, Portland, Oregon

- 3:50 - 3:55 **Session Overview: Markus Grompe, MD**
- 3:55 - 4:05 **Lucas Pontel, PhD**, MRC Laboratory of Molecular Biology, Cambridge, United Kingdom: *Ablation of Aldh5 with Fancd2 Leads to Rapid Onset of Bone Marrow Failure and Leukemia in Mice*
- 4:05 - 4:10 Questions and Answers
- 4:10 - 4:20 **Gerry Crossan, PhD**, MRC Laboratory of Molecular Biology, Cambridge, United Kingdom: *Aldh2 is Critical for the Maintenance of Fanconi Deficient Hematopoietic Stem Cells but not for their Generation*
- 4:20 - 4:25 Questions and Answers
- 4:25 - 4:35 **Markus Grompe, MD**, Oregon Health & Science University, Portland, Oregon: *Effects of the Aldehyde Scavenger Cysteamine in Fanconi Anemia Mice*
- 4:35 - 4:40 Questions and Answers
- 4:40 - 4:50 **Nigel Jones, PhD**, University of Liverpool, Liverpool, United Kingdom: *Investigating the Role of the Phospho-Ser7-FANCG Complex in Cellular Responses to Endogenous Aldehydes*
- 4:50 - 4:55 Questions and Answers
- 4:55 - 5:00 **Session Wrap-up: Markus Grompe, MD**

Saturday – October 26, 2013

7:00 - 8:00 { **Buffet Breakfast**
Imperial Ballroom Center
Poster Viewing
Imperial Ballroom West

Session V: Experimental Hematology

Chair: Helmut Hanenberg, MD

Indiana University School of Medicine, Indianapolis, Indiana

8:00 - 8:05 **Session Overview: Helmut Hanenberg, MD**

8:05 - 8:15 **Elizabeth Eklund, MD**, Northwestern University, Chicago, Illinois: *Activity of the Fanconi DNA Repair Pathway Prevents Bone Marrow Failure During Emergency Granulopoiesis*

8:15 - 8:20 Questions and Answers

8:20 - 8:30 **Amelie Lier, PhD Student**, Heidelberg Institute for Stem Cell Technology and Experimental Medicine, Heidelberg, Germany: *Stress-induced Exit from Dormancy Promotes HSC Depletion and Eventual Bone Marrow Failure in Fanca^{-/-} Mice*

8:30 - 8:35 Questions and Answers

8:35 - 8:45 **Michael Garbati, PhD**, Oregon Health & Science University, Portland, Oregon: *FANCA and FANCC Modulate TLR- and p38-dependent Expression of IL-1beta in Macrophages*

8:45 - 8:50 Questions and Answers

8:50 - 9:00 **Qingshuo Zhang, PhD**, Oregon Health & Science University, Portland, Oregon: *Oral Administration of a Direct SIRT1 Activating Compound Enhances Hematopoiesis in Fancd2^{-/-} Mice*

9:00 - 9:05 Questions and Answers

9:05 - 9:15 **Jordi Surrallés, PhD**, Universitat Autònoma de Barcelona, Barcelona, Spain: *Long-term Hematological Follow-up of Reverse Mosaicism in Fanconi Anemia Patients*

9:15 - 9:20 Questions and Answers

9:20 - 9:25 **Session Wrap-up: Helmut Hanenberg, MD**

Special Session: To Transplant or Not to Transplant: Point/Counterpoint

Chair: Eva Guinan, MD
Scientific Advisory Board, Fanconi Anemia Research Fund
Dana-Farber Cancer Institute, Boston, Massachusetts

- 9:25 - 9:30 **Session Overview: Eva Guinan, MD**
- 9:30 - 9:40 **Stella Davies, MBBS, PhD, MRCP**, Cincinnati Children's Hospital
Medical Center, Cincinnati, Ohio
- 9:40 - 9:50 **Blanche Alter, MD, MPH**, National Cancer Institute, Bethesda, Maryland
- 9:50 - 10:00 **Questions and Answers and Session Wrap-up: Eva Guinan, MD**
- 10:00 - 10:20 **Break**

Session VI: DNA Crosslink Incision and Repair

Chair: Agata Smogorzewska, MD, PhD
The Rockefeller University, New York, New York

- 10:20 - 10:25 **Session Overview: Agata Smogorzewska, MD, PhD**
- 10:25 - 10:35 **Jean Gautier, PhD**, Columbia University Medical Center, New York, New York:
Replication-independent Repair of DNA Interstrand Crosslinks
- 10:35 - 10:40 Questions and Answers
- 10:40 - 10:50 **Anaid Benitez, Graduate Student**, University of Miami, Miami, Florida:
Damage-dependent Regulation of MUS81-EME1 by Fanconi Anemia Complementation Group A Protein
- 10:50 - 10:55 Questions and Answers
- 10:55 - 11:05 **Daisy Klein Douwel, Graduate Student**, Hubrecht Institute, Utrecht, Netherlands:
XPF:ERCC1 is Responsible for the Unhooking Step in DNA Interstrand Crosslink Repair Coordinated by both FANCD2 and FANCP
- 11:05 - 11:10 Questions and Answers
- 11:10 - 11:20 **Jing Huang, PhD**, National Institute on Aging, Baltimore, Maryland:
Fanconi Anemia Protein FANCM Promotes Replication Traverse of DNA Interstrand Crosslinks
- 11:20 - 11:25 Questions and Answers
- 11:25 - 11:35 **Minoru Takata, MD, PhD**, Kyoto University, Kyoto, Japan: *FANCD2 in Chromatin Anchors CtIP and Regulates DNA End Resection During Crosslink Repair*
- 11:35 - 11:40 Questions and Answers

11:40 - 11:50 **Ravindra Amunugama, PhD**, Harvard Medical School, Boston, Massachusetts: *Molecular Mechanism of FANCM in DNA Interstrand Crosslink Repair*

11:50 - 11:55 Questions and Answers

11:55 - 1:55 { **Buffet Lunch**
Imperial Ballroom Center
Joint Board of Directors and Scientific Advisory Board Meeting
Cottonwood Room
Poster Viewing
Imperial Ballroom West

Session VI: DNA Crosslink Incision and Repair (continued)

1:55 - 2:05 **Elizabeth Garner, PhD**, The Rockefeller University, New York, New York: *Function of FANCP/SLX4-associated Nucleases MUS81 and SLX1 in the Resolution of Replication-induced Holliday Junctions*

2:05 - 2:10 Questions and Answers

2:10 - 2:20 **Michael Hodskinson, PhD**, MRC Laboratory of Molecular Biology, Cambridge, United Kingdom: *The Mechanism of Slx4-mediated Incision of a DNA Crosslink*

2:20 - 2:25 Questions and Answers

2:25 - 2:35 **Martin Cohn, PhD**, University of Oxford, Oxford, United Kingdom: *UHRF1/RNF106 Serves as a Sensor for DNA Interstrand Crosslinks in the Fanconi Anemia Pathway*

2:35 - 2:40 Questions and Answers

2:40 - 2:45 **Session Wrap-up: Agata Smogorzewska, MD, PhD**

Session VII: Centrosome and Spindle Assembly

Chair: Nigel Jones, PhD

University of Liverpool, Liverpool, United Kingdom

2:45 - 2:50 **Session Overview: Nigel Jones, PhD**

2:50 - 3:00 **Grzegorz Nalepa, MD, PhD**, Indiana University School of Medicine, Indianapolis, Indiana: *Fanconi Anemia Signaling Network Regulates the Spindle Assembly Checkpoint and Centrosome Maintenance*

3:00 - 3:05 Questions and Answers

- 3:05 - 3:15 **Jianqiu Zou, Graduate Student**, University of South Dakota, Vermillion, South Dakota: *FANCF and BRCA1 Cooperatively Promote Interstrand Crosslinker-induced Centrosome Amplification*
- 3:15 - 3:20 Questions and Answers
- 3:20 - 3:30 **Audrey Magron, PhD**, Laval University, Québec, Canada: *Stathmin, a New FANCC Interacting Protein Involved in the Regulation of Cellular Division*
- 3:30 - 3:35 Questions and Answers
- 3:35 - 3:40 **Session Wrap-up: Nigel Jones, PhD**
- 3:40 - 4:00 **Break**

Session VIII: Human Papillomavirus and Fanconi Anemia

Chair: Susanne Wells, PhD

Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

- 4:00 - 4:05 **Session Overview: Susanne Wells, PhD**
- 4:05 - 4:15 **Rachel Katzenellenbogen, MD**, Seattle Children's Research Institute, Seattle, Washington: *Detection of Human Papillomavirus (HPV) DNA in Fanconi Anemia Patient Oral Swabs*
- 4:15 - 4:20 Questions and Answers
- 4:20 - 4:30 **Parinda Mehta, MD**, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio: *Serology as a Biomarker for Immune Response to HPV Vaccination and Exposure in Patients with FA*
- 4:30 - 4:35 Questions and Answers
- 4:35 - 4:45 **Melinda Butsch Kovacic, MPH, PhD**, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio: *Individuals with Fanconi Anemia and their Susceptibility to Human Papillomavirus Infection*
- 4:45 - 4:50 Questions and Answers
- 4:50 - 4:55 **Session Wrap-up: Susanne Wells, PhD**

- 5:30 - 7:30 { **Poster Reception**
 Imperial Ballroom West
 Presenters with an odd-numbered poster will be at their posters 5:30-6:30.
 Presenters with an even-numbered poster will be at their posters 6:30-7:30.
- 7:30 - 9:30 { **Symposium Dinner**
 Imperial Ballroom Center

Sunday – October 27, 2013

7:00 - 8:00 { **Buffet Breakfast**
Imperial Ballroom Center
Poster Viewing
Imperial Ballroom West

Session IX: Endocrinology and Development

Chair: Susan Rose, MD

Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

8:00 - 8:05 **Session Overview: Susan Rose, MD**

8:05 - 8:15 **Neelam Giri, MD**, National Cancer Institute, Bethesda, Maryland: *Anti-Müllerian Hormone Deficiency Identifies Primary Ovarian Insufficiency in Females with Fanconi Anemia*

8:15 - 8:20 Questions and Answers

8:20 - 8:30 **Sule Unal, MD**, Hacettepe University, Ankara, Turkey: *The Earlier Diagnosis of Osteopenia/Osteoporosis in Fanconi Anemia Patients with Urinary Deoxypyridinoline Test*

8:30 - 8:35 Questions and Answers

8:35 - 8:45 **Stefan Meyer, MD, PhD**, University of Manchester, Manchester, United Kingdom: *Incidence and Patterns of Central Nervous System Abnormalities with Magnetic Resonance Imaging in Fanconi Anemia*

8:45 - 8:50 Questions and Answers

8:50 - 9:00 **Emilie Dubois, Graduate Student**, Laval University Cancer Research Center, Québec, Canada: *New In Vivo Models in Mouse and Drosophila Support a Role for the FANCI Protein at DNA Secondary Structures*

9:00 - 9:05 Questions and Answers

9:05 - 9:10 **Session Wrap-up: Susan Rose, MD**

Session X: FA Protein Interactions and Structure

Chair: Alexandra Sobeck, PhD

University of Minnesota, Minneapolis, Minnesota

- 9:10 - 9:15 **Session Overview: Alexandra Sobeck, PhD**
- 9:15 - 9:25 **Jung-Young Park, PhD**, Cincinnati Children's Research Foundation, Cincinnati, Ohio: *FANCO/RAD51C Binds to the FANCN/PALB2 WD40 Domain in the Fanconi Anemia-Breast Cancer Susceptibility Pathway*
- 9:25 - 9:30 Questions and Answers
- 9:30 - 9:40 **Chih-Chao Liang, Graduate Student**, University of Oxford, Oxford, United Kingdom: *Structural Insight into the Function of Full-length Human Fanconi Anemia FANCD2/FANCI Complex by Cryo-EM*
- 9:40 - 9:45 Questions and Answers
- 9:45 - 10:05 **Break**

Session X: FA Protein Interactions and Structure (continued)

- 10:05 - 10:15 **Gareth Williams, PhD**, Lawrence Berkeley National Laboratories, Berkeley, California: *High-resolution Crystal Structure of Rad51C (FANCO) Reveals Molecular Details of Disease-causing Mutations*
- 10:15 - 10:20 Questions and Answers
- 10:20 - 10:30 **Yie Liu, PhD**, National Institute on Aging, Baltimore, Maryland: *SLX4 and TRF2 Interaction is Required for Telomere Structure and Length Regulation*
- 10:30 - 10:35 Questions and Answers
- 10:35 - 10:40 **Session Wrap-up: Alexandra Sobeck, PhD**
- 10:40 - 12:00 **Symposium Town Hall: An Interactive Discussion about FA Research**
Chair: Grover C. Bagby Jr., MD
Chair, Scientific Advisory Board, Fanconi Anemia Research Fund
Oregon Health & Science University, Portland, Oregon

Keynote Presentation: Genomics, Cancer and Personalized Medicine

Jeffrey N. Myers, MD, PhD
University of Texas MD Anderson Cancer Center

Comprehensive Genomic Characterization of Head and Neck Squamous Cell Carcinoma

Oral cancer is the tenth most common form of cancer with 170,900 estimated new cases worldwide in 2011¹. Despite numerous improvements in the early detection and treatment of oral cancer, the mortality rate from this disease is high and has not improved significantly over the past several decades². With the goal of improving outcomes for patients suffering from this disease, our group and others, have begun to comprehensively identify and tabulate the genomic alterations that arise in oral and other head and neck squamous cell cancers in order to identify new targets for therapy as well as biomarkers for prognosis and treatment selection. This analysis has included 1) whole exome sequencing, 2) Single Nucleotide Polymorphism arrays to identify genome structural abnormalities such as copy number variations, 3) mRNA expression arrays, 4) microRNA expression arrays, and 5) DNA methylation arrays. Data from the first two platforms as well as a larger study by the The Cancer Genome Atlas (TCGA) has confirmed some previously identified gene alterations that have been known to occur in head and neck squamous cancer including a high rate of missense mutations in the TP53 tumor suppressor gene as well as frequent mutations and deletion of the p16 tumor suppressor gene^{3,4}. More novel findings include mutations in the Notch gene in 15-20% of cases, and somewhat less frequently seen mutations in the PI-3 Kinase, H-Ras, Caspase-8, and FBXW-7 genes. This presentation will summarize these events and their potential significance in head and neck squamous cancer development and progression as well as findings from the other platforms and will also provide some insights as to how some of these findings can be begin to be used to help patients with squamous cell carcinomas of the upper aerodigestive tract.

References:

- ¹Jemal, A., Bray, F., Center, M. M., Ferlay, J., Ward, E. and Forman, D. (2011), Global cancer statistics. *CA: A Cancer Journal for Clinicians*, 61: 69–90.
- ²Ow TJ, Myers JN. Current management of advanced resectable oral cavity squamous cell carcinoma. *Clin Exp Otorhinolaryngol* 4(1):1-10, 3/2011.
- ³Agrawal N et. Al. Exome sequencing of head and neck squamous cell carcinoma reveals inactivating mutations in NOTCH1. *Science*. 2011 Aug 26;333(6046):1154-7.
- ⁴Stransky N, et al. The mutational landscape of head and neck squamous cell carcinoma. *Science*. 2011 Aug 26;333(6046):1157-60
- ⁵Hayes DN, Grandis J, El-Naggar AK, et al: Comprehensive genomic characterization of squamous cell carcinoma of the head and neck in the Cancer Genome Atlas. AACR Annual Meeting. Abstract 1117. Presented April 7, 2013.