

## **Molecular and Clinical Mechanisms in Bloom's Syndrome and Related Disorders**

May 27-28, 2008

Location: University of Chicago Gleacher Center, downtown Chicago, Illinois

### DESCRIPTION

**Background:** Bloom's syndrome is a rare autosomal recessive disorder characterized by small size and sun sensitivity. Persons with Bloom's syndrome are also predisposed to the development of many different types of cancer. Bloom's syndrome is caused by mutations in the BLM helicase gene, which is a member of the RecQ family of DNA helicases. The RecQ gene WRN is mutated in Werner's syndrome and RECQL4 is mutated in Rothmund-Thomson syndrome. Both of these syndromes are characterized by premature aging. The RecQ family of helicases is implicated in the interplay between replication stress and repair of DNA damage by homologous recombination and these rare syndromes of the human present models for dissecting the role of these biological processes in the development of cancer and in the processes of aging.

**Scientific content:** This workshop will address key research topics surrounding the functions of the RecQ helicases and their influences on cancer and aging. We will discuss insights gathered from the study of model genetic organisms and human cells on the intersection between RecQ helicases and the responses to DNA-damage, examining (i) the biochemistry of RecQ helicases, (ii) RecQs' roles in DNA repair, (iii) RecQs' role in DNA replication, (iv) RecQ helicases and intra-S phase checkpoint signaling, (v) mouse models of RecQ helicase deficiency, (vi) the function of RecQ helicases at specialized DNA substrates such as telomeres, and (vii) RecQs' effects on cancer and aging. We will also discuss the advancement of potential therapies to prevent the genomic instability of Bloom's syndrome.

**Scientific goals:** To understand the role of BLM in DNA recombination and in maintenance of the genomic integrity. Understanding these functions will help define the mechanisms of genomic instability in Bloom's syndrome cells and elucidate the roles of mechanisms that maintain the integrity of the genome in the development of cancer and in the aging processes.

**Proposed format for scientific sessions:** Seven one and a half to two hour lecture sessions, a two-hour poster session, and poster presentations interleaved with sessions.

**Sponsored by the Office of Rare Diseases, NIH, The National Cancer Institute, the Ellison Medical Foundation and the Bloom syndrome Foundation.**

## Program Agenda

# Molecular and Clinical Mechanisms in Bloom's Syndrome and Related Disorders

Organizing Committee: Vilhelm A. Bohr, Nathan Ellis (Chair), Curtis C. Harris

## DAY 1

8:00            *Registration*

8:30            **Nathan Ellis** – Welcome

### **Session 1:** *Biochemistry of RecQ helicases*

Session chair: **Vilhelm Bohr**

8:35            **Patrick Sung** – *BLM/Topo III $\alpha$ /BLAP-dependent Holliday junction processing*

9:00            **Robert Bambara** – *Protection from illegitimate recombination: BLM helicase function on the lagging strand*

9:25            **James Keck** – *Structural and cellular mechanisms of bacterial RecQ DNA helicases*

9:50            **Poster Presentation Overview**

10:20-10:50   **Break**

### **Session 2:** *RecQ helicase functions in recombination*

Session chair: **Nancy Maizels**

10:50            **Douglas Bishop** – *The energetics of homologous recombination reactions*

11:15            **Alexander Mazin** – *Pro- and anti-recombination activities of the Bloom's syndrome helicase*

11:40            **Yilun Liu** – *RAD51 paralogs and the RecQ helicases - antagonistic roles in homologous recombination?*

## LUNCHEON I

12:05-1:00    **Lunch** (6<sup>th</sup> floor lunchroom)

## **POSTER SESSION I**

1:00-2:00    Posters (4<sup>th</sup> floor north lounge)

### **Session 3:** *Functions of the non-Bloom RecQ helicases*

Session chair: **Doug Bishop**

2:00            **Alessandro Vindigni** – *Structural and functional studies on the human RECQ1 helicase*

2:25            **Pavel Janscak** – *Biochemistry and function of RECQL5 protein*

2:50            **Igor Stagljar** – *Acetylation of RECQL4, the Rothmund-Thomson-, RAPADILINO- and Baller-Gerold-Syndrome gene product, by the histone acetyltransferase p300 regulates its subcellular localization*

3:15-3:45    **Break**

### **Session 4:** *ELLISON FOUNDATION SESSION: RecQ functions in cancer and aging*

Session chair: **Nathan Ellis**

3:45            **Vilhelm Bohr** – *Human RecQ helicase function in double- and single-strand DNA repair*

4:10            **Patricia Opresko** – *RecQ helicases' functions at telomeres*

4:35            **Ray Monnat** – *The Werner syndrome protein WRN as a fork 'spork'*

5:00-5:30    **Break**

## **EVENING RECEPTION** (with the Bloom's Connect group – 6<sup>th</sup> floor Board room)

5:30-7:00

Session chair: **Nathan Ellis and Vilhelm Bohr**

5:30            **James German** – *Clinical investigation and basic research: Bloom's syndrome and discovery*

5:45            **Maureen Sanz** – *Report from the Bloom's Syndrome Registry*

6:00 **Richard Gladstein** – *Mission of the Bloom's Syndrome Foundation*

6:15 Reception

## DAY 2

### Session 5: *RecQ* helicases and cellular physiology

Session chair: **Joanna Groden**

8:30 **Nancy Maizels** – *RecQ* helicases and the maintenance and expression of G-rich human genes

8:55 **Robert Brosh** – *Mechanisms of RecQ-like helicases in cellular DNA metabolism*

9:20 **Yves Pommier** – *BLM and replication stress responses: single-cell, single-DNA molecule and pharmacological analyses*

9:45-10:15 **Break**

### Session 6: *Models of RecQ* helicase deficiency

Session chair: **Curtis Harris**

10:15 **Joanna Groden** – *Tissue-specific effects of Blm haploinsufficiency on murine tumor initiation, progression and regression*

10:40 **Guangbin Luo** – *Interrogating the molecular mechanisms of RecQ helicase functions using knockout models*

11:05 **Shunichi Takeda** – *The reverse genetic study of the vertebrate Blm and Fbh1 DNA helicases using the chicken DT40 cell line and Medaka fish*

11:30 **Jeff Sekelsky** – *Analysis of synthetic lethality phenotypes provides insights into functions of Drosophila BLM in maintaining genome stability*

## LUNCHEON II

11:55-1:00 **Lunch** (6<sup>th</sup> floor lunchroom)

## POSTER SESSION II

1:00-2:00 Posters (4<sup>th</sup> floor north lounge)

### **Session 7: *RecQ* helicases in genome integrity**

Session chair: **Vilhelm Bohr**

2:00 **Steve Brill** – *Role of SUMO in the absence of the yeast Sgs1 DNA helicase*

2:25 **Qin Yang** – *RecQ helicases, telomere recombination and maintenance*

2:50 **Weidong Wang** – *A multiprotein complex that maintains genome stability and is involved in Bloom syndrome and Fanconi Anemia*

3:15-3:40 *Break*

### **Session 8: *Regulation of recombination by the BLM helicase***

Session chair: **Ray Monnat**

3:40 **Nathan Ellis** – *SUMO modification of BLM and the regulation of anti-recombination*

4:05 **Hocine Mankouri** – *S. cerevisiae sgs1 mutants as a model system to develop strategies to suppress Bloom's syndrome (BS) phenotypes*

4:30 **Ralph Scully** – *Control of sister-chromatid recombination in mammalian cells*

4:55 **Nathan Ellis and Vilhelm Bohr** – Final comments

5:00 Meeting ends

#### **Speakers**

Robert Bambara	University of Rochester
Douglas Bishop	University of Chicago
Vilhelm Bohr	National Institute of Aging
Steve Brill	Rutgers University
Robert Brosh	National Institute of Aging
Nathan Ellis	University of Chicago
James German	Weill Medical College of Cornell University
Richard Gladstein	Bloom's Syndrome Foundation
Joanna Groden	Ohio State University
Curtis Harris	National Cancer Institute
Pavel Janscak	Institute of Molecular Cancer Research
James Keck	University of Wisconsin
Yilun Liu	Yale University
Guangbin Luo	Case Western Reserve University

Nancy Maizels	University of Washington
Alexander Mazin	Drexel University College of Medicine
Ray Monnat	University of Washington
Patricia Opresko	University of Pittsburgh
Yves Pommier	National Cancer Institute
Maureen Sanz	Molloy College
Ralph Scully	Harvard Medical School
Jeff Sekelsky	University of North Carolina
Igor Stagljar	University of Toronto
Patrick Sung	Yale University
Shunichi Takeda	Kyoto University, Japan
Alessandro Vindigni	International Centre for Genetic Engineering and Biotechnology
Qin Yang	Washington University School of Medicine