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Cc: Pietkiewicz Joelle <jpietkiewicz@asmusa.org>,
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Subject: Important Invited Speaker Information - DNA Repair and
Mutagenesi
s Conference
Date: Fri, 20 Aug 1999 16:13:34 -0400
Importance: high
X-Priority: 1
MIME-Version: 1.0
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August 1999

Greetings from the American Society for Microbiology!

We're nearing the DNA Repair and Mutagenesis conference so we've favored speed over formality to send speaker/convener confirmation information to you. The conference program has been organized by Graham Walker, Errol Friedberg, and Susan Wallace. The conference will be held November 1-7, 1999, in Hilton Head, South Carolina.

ASM appreciates your willingness to participate in the upcoming conference as an invited speaker. Please consult the program attached below to view when your talk is scheduled and what we will print as your presentation title unless you let us know of corrections or a replacement title by Friday, October 8.

The conference will be held at the Westin Resort at Hilton Head Island, South Carolina. The hotel address is Two Grasslawn Avenue (Port Royal), Hilton Head Island, South Carolina, 29928. The hotel telephone number is 843-681-4000. The fax number is 843-681-1087.

Registration, poster sessions, meals, receptions, open mic nights, banquet/dance, and all general sessions will be held at the Westin Resort.
A guest registration fee will be offered on-site should you plan to bring a non-scientist guest to selected social functions during the conference.

The opening keynote lecture begins at 7:30 pm on Monday, November 1. ASM will be staffing a registration desk during the afternoon and evening of November 1, outside the Grand Ballroom, so please stop by when you get in to pick up your conference materials. The scientific portion of the conference will conclude by 5 pm on Sunday, November 7.

We ask that speakers make your own hotel reservations by calling the number above and mentioning that you are with the ASM DNA Repair and Mutagenesis conference in order to get our discounted rate. The hotel reservation deadline is October 1, but please call as soon as possible. Please note that a deposit is required at the time of reservation, and you will be asked to pay for the room charges when you check out and then apply to ASM for reimbursement, along with your travel and meal expenses as might be covered with the committed reimbursement.

ASM will commit to reimbursement of your travel, lodging, and food expenses related to participation in the conference up to $600 for each speaker. In addition, speakers receive complimentary registration, which includes most meals, several receptions, and the banquet/dance. If there are additional funds available (based on contributions we receive and registration revenue), we will be able to cover a portion of expenses above the committed amount. Please note that we are only able to reimburse for economy class airfare with tickets booked at least 14 days in advance of travel. We also are not able to reimburse for guest or entertainment expenses. Expense reimbursement request forms will be available to speakers on-site. Please contact me if you have questions about reimbursement.

Please make your own travel reservations immediately, if you haven't done so

already. Hilton Head does have a small airport with service from some major
east-coast cities. Savannah International airport is about 45 minutes away
from the resort and offers service to and from most areas. ASM has negotiated the following airline discount:

Delta Air Lines: 1-800-241-6760, Meeting ID code: DMN118962A
Delta Air Lines is offering a 5% discount off Delta's published round-trip fares from most locations, and 10% off unrestricted coach fares, or you may choose a zone fare, whichever works best from your
location. By purchasing your ticket 60 days or more in advance of your departure date, you can save an additional 5%. Whether booking your tickets
yourself, or through your favorite travel agent, using the meeting ID code
provided above will help you get the lowest fares possible.

Included with this e-mail is a form that is for you to print and fax back after filling in your current contact information, as you would like it included within the participant list. On the lower half of the form is a confirmation of the audiovisual equipment that we will provide and our request for you to list any additional equipment that you need for your presentation. ASM will make the necessary arrangements directly with the hotel audiovisual contractor.

Please fax back the speaker registration/audiovisual request form to me at
202-942-9340 by Friday, October 8. Your presentation title changes are due
by the same date, in order to have the information correct in the final program. If you have not yet submitted an abstract for your presentation,
please do so no later than October 8 via the ASM web site
http://www.asmusa.org/mtgsrc/dnarepg.htm. We have significantly upgraded our on-line abstract submission system and hope that it makes it easy for you to submit your abstract. One enhancement to the system is that you will
be able to view your abstract immediately upon submission, and will be able
to make corrections to it on-line. If you have any questions about submitting your invited presentation abstract, please contact me or my assistant Joelle, at 202-942-9261.

If others in your institution or company might be interested in participating in the conference, please let them know that the abstract deadline (for regular submissions) is August 25. And, please pass on the good news! The organizers have raised funds to provide postdoctoral fellow
travel grants to more experienced postdocs, and interested applicants should
check the appropriate box when submitting their abstract over the internet.
In addition, ASM is providing $400 travel grants to up to 50 graduate students and new postdocs (within one year of earning the doctoral degree).
Details are available on the conference web site.

Attachments that should appear at the bottom of this message are:

1) Program (revprog812.doc)
2) Speaker Registration and Audiovisual Equipment Request form (spkregav.doc)

I am available the remainder of this week and all next week (August 23-27)
should you have any questions or requests. My direct telephone number is included in my signature block.

If you would like a copy of this information on ASM letterhead, just let me
know and I will drop it in the mail. Thank you in advance for your participation at the ASM Conference on DNA Repair and Mutagenesis. I look
forward to welcoming you to Hilton Head.

Sincerely,

Lisa Nalker <<RevProg812.doc>> <<spkregav.doc>>

Lisa Nalker
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DNA Repair and Mutagenesis
November 1-7, 1999
Hilton Head, South Carolina

Contents of This Page:

Links to Other Pages:

General Information

IMPORTANT MESSAGE FOR ABSTRACT SUBMITTERS

Scientific Program Information

Scientific Program Organizers

Graham C. Walker, *Massachusetts Institute of Technology*
Errol Friedberg, *University of Texas*
Susan Wallace, *University of Vermont*

Final Program

Monday, November 1, 1999

2:00pm: Arrival and check-in

7:30pm: Welcome and Keynote Address

Mutability Doth Play Her Cruel Sports to Many Men's Decay: Variations on the Theme of Translesion Synthesis
Bryn Bridges, *MRC Cell Mutation Unit, University of Sussex*

Tuesday, November 2, 1999

9:00am-12:15pm: SESSION I. EXCISION REPAIR OF DNA DAMAGE I
Chair: Susan Wallace, *Department of Microbiology and Molecular Genetics, University of Vermont*

9:00am: Repair of Oxidative Base Damage
Susan Wallace, *Department of Microbiology and Molecular Genetics, University of Vermont*

9:25am: Human Uracil-DNA Glycosylase: Regulation and Structure-Function Relationships
Hans Krokan, *Institute of Cancer Research and Molecular Biology, Norwegian University of Science and Technology*

9:50am: Eukaryotic Alkylation DNA Repair
Leona Samson, *Cancer Cell Biology, Harvard School of Public Health*

10:15am: Crystal Structure of the E. coli AlkA Protein Complexed to DNA
Tom Ellenberger, *Harvard Medical School*

10:30am: Coffee Break

11:00am: Excision Repair of Oxidatively Damaged DNA Bases and Its Implication in Human Disease
Serge Boiteux, *Laboratoire de Radiobiologie du DNA, CEA/DSV/DRR*

11:25am: Structural and Mechanistic Studies of Base Excision DNA Repair
Greg Verdine, *Department of Chemistry and Chemical Biology, Harvard University*

11:50am: Base Excision Repair Initiation Revealed by Enzyme-DNA Co-Crystal Structures and DNA Binding Kinetics
John Tainer, *Department of Molecular Biology, The Scripps Research Institute*

12:15pm: Lunch and Afternoon Break

4:00pm-6:35pm: SESSION II: EXCISION REPAIR OF DNA DAMAGE II
Chair: Tomas Lindahl, *Imperial Cancer Research Fund, South Mimms*

4:00pm: Knock Out Mouse Models in the Study of Endogenous DNA Damage, Spontaneous Mutagenesis and Base Excision-Repair
Deborah Barnes, *Imperial Cancer Research Fund, South Mimms*

4:25pm: Base Excision Repair of Free Radical DNA Damage
Bruce Demple, *Department of Cancer Cell Biology, Harvard School of Public Health*

4:50pm: Completion of DNA Repair by Eukaryotic DNA Ligases
Alan Tomkinson, *Department of Molecular Medicine, University of Texas Science Center*

5:15pm: DNA Damage and Repair in Mitochondria
Ben van Houten, *National Institute of Environmental Health Sciences*

5:40pm: Nucleotide Excision Repair: Molecular Mechanisms and

Mouse Mutant /Human Disorders
Jan Hoeijmakers, *Eramus University, Rotterdam*

6:05pm: First Structural Insight into DNA Nucleotide Excision Repair: the Crystal Structure of the Ultimate DNA Damage Recognition Enzyme UvrB from Thermus thermophilus
Mischa Machius, *University of Texas Southwestern Medical Center at Dallas*

6:20pm: Structural Studies of Nucleotide Excision Repair
Caroline Kisker, *State University of New York at Stony Brook*

6:35pm: Dinner

8:00pm-10:00pm: Poster Session A

Wednesday, November 3, 1999

9:00am-12:30pm: SESSION III: TRANSCRIPTION AND DNA EXCISION REPAIR
Chair: Phil Hanawalt, *Department of Biological Sciences, Stanford University*

9:00am: What Happens Following Polymerase Arrest at a Lesion?
Phil Hanawalt, *Department of Biological Sciences, Stanford University*

9:25am: Transcription-Coupled Base Excision Repair of Oxidative Damage: Role of XPG
Priscilla Cooper, *Life Sciences Division, Lawrence Berkeley National Laboratory*

9:50am: A Role for BRCA1 and BRCA2 in Transcription-Coupled Repair
Stephen A. Leadon, *Department of Radiation Oncology, University of North Carolina*

10:15am: The NER Protein Machine in Mammalian Cells
Rick Wood, *Imperial Cancer Research Fund, Clare Hall Laboratories*

10:40am: Coffee Break

11:10: TFIIH: Its Function in Nucleotide Excision Repair and Transcription
Jean-Marc Egly, *Institut de Biologie Moleculaire et Cellulaire, University of Strasbourg*

11:35am: Interactions Between Chromatin Structure,

Transcription, Nucleotide Excision Repair, and Photolyase
Fritz Thoma, *Institute fuer Zellbiologie, ETH-Hoenggerberg*

12:00 noon: Absence of Spt4 Obviates the Need for Rad26 in Transcription Coupled Repair
Lars Jansen, *Leiden University*

12:15pm: Transcription-Coupled Nucleotide Excision Repair in Yeast Does Not Require Ubiquitylation of RNA Polymerase II or Proteasomal Function: Implications for Cockayne's Syndrome
Kevin Sweder, *Rutgers University College of Pharmacy*

12:30pm: Lunch and Afternoon Break

4:00pm-6:30pm: SESSION IV: UmuC/DinB/Rev1/Rad30 SUPERFAMILY OF DNA POLYMERASES
Chair: Errol Friedberg, *Department of Pathology, University of Texas Southwestern Medical Center at Dallas*

4:00pm: Translesion Replication: Proteins and Functions
Chris Lawrence, *Department of Biochemistry and Biophysics, University of Rochester Medical Center*

4:25pm: Replicative Bypass of DNA Damage by Yeast and Human Pol Eta
Satya Prakash, *Sealy Center for Molecular Science, University of Texas Medical Branch*

4:50pm: Molecular Steps in Translesion DNA Synthesis
Robert Fuchs, *Cancérogenèse et Mutagenèse Moléculaire et Structurale, ESBS, Strasbourg*

5:15pm: Biochemical Basis of SOS-induced "Error-prone" Repair: E. coli DNA Polymerase V, a Sloppier Copier
Myron Goodman, *Department of Biological Sciences, University of Southern California*

5:40pm: DNA Repair at a Price: Mutagenic Activity of the UmuC Protein
Zvi Livneh, *Department of Biological Chemistry, Weizmann Institute of Science*

6:05pm: Mammalian DinB Homologs
Valerie Gerlach, *Department of Pathology, University of Texas Southwestern Medical Center at Dallas*

6:30pm: Dinner

8:00pm-10:00pm: Poster Session B

Open Mike Night

Thursday, November 4, 1999

9:00am-12:10pm: SESSION V: CELLULAR RESPONSES TO DNA DAMAGE, CHECKPOINTS, AND DAMAGE TOLERANCE
Chair: Bryn Bridges, *MRC Cell Mutation Unit, University of Sussex*

9:00am: Inducible *E. coli* Proteins Involved in Mutagenesis and Control of Cell Cycle in Response to DNA Damage
Graham Walker, *Department of Biology, Massachusetts Institute of Technology*

9:25am: Recent Advances in Understanding Translesion DNA Synthesis: From *E. coli* to Humans
Roger Woodgate, *NICHD, NIH*

9:50am: Molecular Mechanism of Termination of the SOS Response by the DinI protein: Interaction with the RecA Protein
Oleg Voloshin, *Genetics and Biochemistry Branch, NIDDK, NIH*

10:05am: Cell Cycle and Transcriptional Responses to DNA Damage
Mingxia Huang, *Department of Biochemistry, Baylor College of Medicine*

10:30am: Coffee Break

11:00am: Arrest, Repair, Recovery and Adaptation to a Double-Strand Break
Jim Haber, *Rosensteil Center, Brandeis University*

11:25am: Essential Roles for S. cerevisiae Cyclin-Dependent Kinase in DNA Damage Checkpoint Arrest
Jonathan Fitzgerald, *University of Chicago*

11:40am: Identification of Two Damage-Responsive Repressors of a Eukaryotic DNA Repair Gene
Gwen Sancar, *University of North Carolina at Chapel Hill*

11:55am: Structure of DNA-dependent Protein Kinase and Requirements for its Activation by DNA
Gilbert Chu, *Stanford University Medical Center*

12:10pm: Lunch and Afternoon Break

4:00pm-6:30pm: SESSION VI: REPAIR OF MISMATCHED BASES
Chair: Paul Modrich, *Department of Biochemistry, Duke University Medical Center*

4:00pm: Functions of the MutS ATPase and the Role of the Human Mismatch Repair System in the Cellular Response to DNA Damage
Paul Modrich, *Department of Biochemistry, Duke University Medical Center*

4:25pm: Recognition of Heteroduplex DNA by the MutS Mismatch Repair Protein
Peggy Hsieh, *Genetics and Biochemistry Branch, NIDDK, NIH*

4:50pm: Initiation of DNA Mismatch Repair
Wei Yang, *Laboratory of Molecular Biology, NIDDK, NIH*

5:15pm: MutL Gene Functions in Yeast and Mice
Mike Liskay, *Department of Molecular and Medical Genetics, Oregon Health Sciences University*

5:40pm: Mismatch Repair and Cancer
Richard Kolodner, *Ludwig Institute for Cancer Research, UC San Diego School of Medicine*

6:05pm: Signal Transduction in Mismatch Repair
Rick Fishel, *Department of Microbiology and Immunology, Thomas Jefferson University*

6:30pm: Dinner

8:00pm-10:00pm: Poster Session C

Dance

Friday, November 5, 1999

9:00am-12:15pm: SESSION VII: MUTATION, GENOME-INSTABILITY, AND HYPERMUTATION
Chair: Miroslav Radman, *Laboratoire de Mutagenese, Institut J. Monod, Universite, Paris 7*

9:00am: Genetic Control of Mutation
Miroslav Radman, *Laboratoire de Mutagenese, Institut J. Monod, Universite, Paris*

9:25am: Genetic Regulation of Genome Stability in Yeast
Tom Petes, *Department of Biology, University of North Carolina*

9:50am: Mutagenesis and the Mismatch Repair System
Jeffrey H. Miller, *Department of Microbiology and Molecular Genetics, UCLA*

10:15am: Transcriptional Mutagenesis in Bacterial and Mammalian Cells
Paul Doetsch, *Department of Biochemistry, Emory University School of Medicine*

10:40am: Coffee Break

11:10am: Mechanism of Trinucleotide Repeat Expansion at FMR1
Steve Warren, *Howard Hughes Medical Institute, Emory University School of Medicine*

11:35am: Mutational Mechanisms for DNA Instability in Human Disease
Cynthia McMurray, *Mayo Clinic*

12:00 noon: Homologous Recombination as a Major Mechanism for the Maintanance of Genetic Integrity in Mammalian Cells
Maria Jasin, *Cell Biology Program, Sloan-Kettering Institute*

12:15pm: Lunch and Afternoon Break

4:00pm-6:30pm: SESSION VIII: REPAIR OF STRAND BREAKS
Chair: Martin Gellert, *Molecular Genetics Laboratory of Molecular Biology, NIDDK, NIH*

4:00pm: Actions of Rad 51 and Rad 52 in Double-Stranded Break Repair
Steve West, *Imperial Cancer Research Fund, Clare Hall Laboratories*

4:25pm: Recombination Proteins Underpin DNA Replication
Bob Lloyd, *Genetics Department, University of Nottingham*

4:50pm: Regulation of Yeast Recombination by Mismatch Repair Proteins
Sue Jinks-Robertson, *Department of Biology, Emory University*

5:15pm: Mechanism of DNA Strand Break Repair Mediated by the RAD52 Group Proteins

Patrick Sung, *Institute of Biotechnology and Department of Molecular Medicine University of Texas Health Science Center at San Antonio*

5:40pm: Double Strand Break Repair in Mammalian Cells
Penny Jeggo, *MRC Cell Mutation Unit, University of Sussex*

6:05pm: V(D)J Recombination: Links to Transposition and Double-Strand Break Repair
Martin Gellert, *Molecular Genetics Laboratory of Molecular Biology, NIDDK, NIH*

6:30pm: DNA Damage Sensing and Repair by DNA-PK
David Chen, *Lawrence Berkeley National Laboratory*

6:45pm: Dinner

8:00pm-10:00pm: Poster Session D

Open Mike Night

Saturday, November 6, 1999

9:00am-10:15am: SESSION IXa: REPLICATIONAL FIDELITY
Chair: Samuel Wilson, *Laboratory of Structural Biology, NIEHS, National Institutes of Health*

9:00am: Understanding Nucleotide Selection by DNA Polymerases Through Crystallography
Samuel Wilson, *Laboratory of Structural Biology, NIEHS, National Institutes of Health*

9:25am: Observing Mutagenesis in a Catalytically Active DNA Polymerase Crystal at 1.8 Å Resolution
Lorena Beese, *Department of Biochemistry, Duke University Medical Center*

9:50am: Structure-Function Studies of DNA Replication Fidelity
Tom Kunkel, *Laboratory of Molecular Genetics, National Institute of Environmental Health Sciences*

10:15am: Coffee Break

10:45am-12:30pm: SESSION IXb: LATE BREAKING DEVELOPMENTS
Chair: Samuel Wilson, *Laboratory of Structural Biology, NIEHS, National Institutes of Health*

10:45am: The Repair of OG:A Mismatches by MutY: The Importance of Being OG
Sheila David, *University of Utah*

11:00am: Structural Probes of DNA Lesion Bypass Mechanisms
John-Stephen Taylor, *Washington University*

11:15am: Repair of Ionizing Radiation Induced Damages
Yoke Wah Kow, *Emory University*

11:30am: So Many Nucleases, So Few Errors: The Interplay Between Replication and Repair Nucleases Genome Stability
Michael Resnick, *National Institute of Environmental Health Sciences, NIH*

11:45am: The Role of DNA Polymerase Delta/Epsilon in the Long-Patch Base Excision Repair
Eugenia Dogliotti, *Istituto Superiore di Sanita*

12:00 noon: The Fanconi Anemia Proteins FANCA, FANCC and FANCG/XRCC9 Interact in a Functional Nuclear Complex
Alan D'Andrea, *Dana-Farber Cancer Institute. Harvard Medical School*

12:15pm: The Novel DNA Repair Gene *MED1* is Mutated in Human Carcinomas Exhibiting Microsatellite Instability
Alfonso Bellacosa, *Fox Chase Cancer Center*

12:30pm: Lunch

2:00pm-4:45pm: SESSION X: REPAIR AND MUTATION IN CHALLENGING ENVIRONMENTS
Chair: Peter Setlow, *Department of Biochemistry, University of Connecticut Health Center*

2:00pm: How Does DNA in Spores of Bacillus Species Survive for Years and Years and Years?
Peter Setlow, *Department of Biochemistry, University of Connecticut Health Center*

2:25pm: The Complete Genome Sequence of the Extremely Radiation Resistant Bacterium *Deinococcus radiodurans*
Jonathan Eisen, *The Institute for Genomic Research*

2:50pm: DNA Repair and Adaptation to Life in Extremely Dry Environments

John Battista, *Department of Microbiology, Louisiana State University*

3:15pm: DNA Repair in UV and Oxidative Stress-Rich Environments
Akira Yasui, *Department of Molecular Genetics, Tohoku University*

3:40pm: DNA Replication in All Three Genomes of UV-Irradiated Plants
John Hays, *Oregon State University*

3:55pm: Spontaneous Mutagenesis in Nondividing Cells: Insights from the Study of Adaptive Mutation
Pat Foster, *Department of Biology, Indiana University*

4:20pm: Recombination-Dependent Hypermutation in Stationary Phase
Susan Rosenberg, *Department of Molecular and Human Genetics, Baylor College of Medicine*

BANQUET AND DANCE

Sunday, November 7, 1999

9:00am-12:15pm: SESSION XI: DEFECTS IN DNA REPAIR: CONSEQUENCES FOR HUMAN DISEASE AND AGING I
Chair: Priscilla Cooper, *Life Sciences Division, Lawrence Berkeley National Laboratory*

9:00am: Molecular Basis of Human Diseases with Nucleotide Excision Repair Deficiency
Kiyoji Tanaka, *Institute of Molecular and Cellular Biology, Osaka University*

9:25am: UV-induced Mutagenesis in Tumor Suppressor Genes of XP Skin Cancers
Alain Sarasin, *Laboratory of Molecular Genetics, Institut de Recherches sur le Cancer*

9:50am: The Involvement of DNA Helicase in Deficits in DNA Repair in Cancer and Aging
Larry Loeb, *Department of Pathology, University of Washington*

10:15am: Werner Syndrome
Junko Oshima, *Department of Pathology, University of Washington School of Medicine*

10:40am: Coffee Break

11:10am: Bloom's Syndrome Protein and Other RecQ Family Helicases
Ian Hickson, *Medical Oncology Unit, Imperial Cancer Research Fund, University of Oxford*

11:35am: The Bloom's Syndrome Mouse
Roger Schultz, *Department of Pathology, University of Texas Southwestern Medical Center*

12:00 noon: Werner Protein: Biochemical Properties and Interactions
Robert Brosh, *National Institute on Aging, National Institutes of Health*

12:15pm: Lunch

1:30pm-4:00pm: SESSION XII: DEFECTS IN DNA REPAIR: CONSEQUENCES FOR HUMAN DISEASE AND AGING II
Chair: Alan Lehmann, *MRC Cell Mutation Unit, Sussex University*

1:30pm: Diverse Clinical Outcomes of Mutations in the XPD Repair/Transcription Gene
Alan Lehmann, *MRC Cell Mutation Unit, Sussex University*

1:55pm: New Anti-Cancer Agents: Opportunities to Exploit Defects in DNA Repair
Stephen Friend, *Molecular Pharmacology, Fred Hutchinson Cancer Research Center*

2:20pm: Acute and Long Term Effects of DNA Damage in NER Deficient Transgenic Mice
Harry Vrieling, *MGC-Department of Radiation Genetics and Chemical Mutagenesis Leiden University Medical Centre*

2:45pm: ATM: At the Crossroads of Damage Repair and Signaling
Yossi Shiloh, *Department of Human Genetics, Tel Aviv University*

3:10pm: The hMre11/Rad50 Protein Complex: A Link Between Double Strand Break Repair and DNA Damage Dependent Cell Cycle Checkpoints
John Petrini, *Laboratory of Genetics, University of Wisconsin Medical School*

3:35pm: Closing

Errol Friedberg

Chris Lawrence
- translesion replication
- Rev7 - subunit of pol ζ
- Rev3 - subunit of pol ζ (catalytic)

Davies R
JBact 114:357
JBact 152:260

T7 + CT skew

- highly expressed genes have more skew
- what about wsy evolution

Graham Walker

SOS

- txn control
- post-txn (e.g. UmuD)

UmuD,D' manage events at replication fork

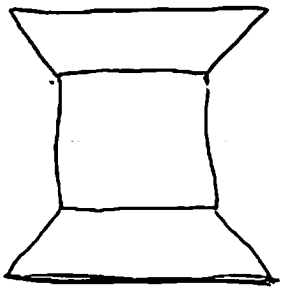
UmuD-UmuC = bact. Damage checkpoint

UmuD'-UmuC = translesion synthesis

related to signal peptidases

factory model of replication

- polymerase complex stays in one place even w/ UV in B subtilis



Roger Woodgate - new LexA regulated genes

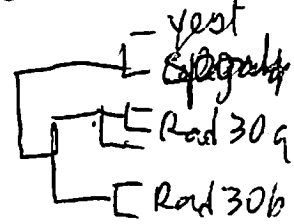
- see SOS ~~not~~ as a global response but as a DNA-damage response

- LexA regulation only a small component

- 21 genes shown experimentally to be LexA regulated
  ↓
  conserved SOS box
  ↓
  search
  ↓
  69 potential LexA genes including all 21 ~~30~~ previous LexA regulated
  ↓
  ~~northern~~ on remaining 49 +/- UV
  ↓
  9 new likely LexA regulated genes
  ↓
  some spatial clustering of all 30

- YSOA
- ndinR
- YDJQ - related to uvrA
- YDJM - two LexA boxes

hRad30B highly expressed in testes



Minxia Huang

J. Haber — DSBR

↙ Ku NHEJ

↘ RAD52-Rec. Repair

- Yeast + Human have similar NHEJ + RecR

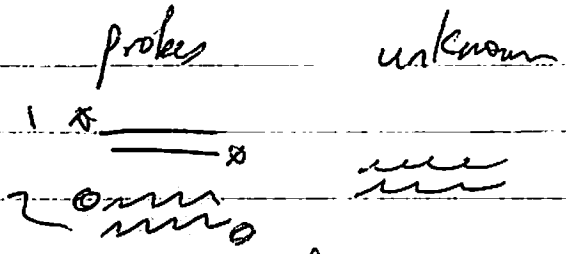
yeast

↓

persistent DNA damage

↓

eventually cells adapt



denature + mix

column w/ Mn+5

what % probe 1 vs probe 2

probe 1 >> probe 2 sample = 2/2
probe 1 = probe 2 sample = 1/2
probe 2 >> probe 1 sample 1/1

MutL structure

- Xtallized LN40 (40 kD aa of N term)

↓

not similar to PDB structures

↓

found that MutL + MutH = ATPase

↓

searched for ATPases

↓

similar structure w/ Gyrase + HSP90

w/ ATP non-hydrolyzable → MutL structure has major change and is a dimer

---

a MutS that cannot hydrolyze ATP can still stimulate MutH-endonuclease

MutL

- MutLα = MLH1, PMS1

MutLβ = MLH1, MLH3 (minor role in mismatch correction)
- only works w/ MutSβ

Miro Radman

- suggests that population level selection leads to selection for mutation rate increase

- stress induces mutagenesis

- multiple rounds of selection selects mutators

- CF patients - bacteria in lung
  1/3 of isolates are mutators vs. 1/10 in nature

- mutators will emerge whenever selective pressures are applied that require multiple changes

- if you take adapted mutator strain and restore Muts it still wins competition

- E. coli — Intact mut → 20% are mutators

- Mismatch —
  - ↑ mutation
  - ↑ recombination w/ heterologous

- incongruent muts phylogeny
  - all are neutral

Tom Petes

- rate of mutation for repetitive sequences

① mutations in msh5, msh6 homolog destabilize repeats

pol3 (pol δ) in yeast
- isolated mutants
- compared mutator rate w/ diff. expression of pol3 mutants
- low levels leads to mutator phenotype
- the mutators

~~wild type~~	sig
w/d type	} very few deletions between
mutant	direct repeats in mutants w/ low levels

② mito stability
- yeast mt has very poly AT
- expressed arg8 in mitochondria w/ poly AT out of frame

	mito	nucleus
poly AT +	3×10^{-10}	1×10^{-5}
poly AT −	1×10^{-7}	5×10^{-7}
poly GT +	3×10^{-7}	1×10^{-5}
poly GT −	4×10^{-6}	1×10^{-6}

don't have good means of rate per mito molecule

-mutants that destabilize mito.?

--MSH1 - 30-35x ↑ in mutation rate of poly GT but no effect on poly AT

∴ poly ATs prob. don't slip

Jeff Miller

-MRS pathway - mismatch repair saturation leads to cells becoming transiently MMR-

-exposure to mutagens leads to inc. in mutations not normally associated w/ those mutagens

-also occurs in pol mutants

cell
↓
tx w/ EMS
↓
wash out
↓
transfer in plasmid w/ poly G → high μ if tx. w/ EMS

Interspecies crosses may lead to saturation of MMR system - as well as ↑ in recombination

Fragile X

Sherman Paradox + anticipation

- expansion somehow not transmitted thru sperm
- old alleles appear to account for many cases
- repeat length + purity important
- two interruptions + few repeats = stable
- " " + many " = unstable
- one " + few repeats = unstable

XX → repeat not suppressed

XY → repeat suppressed

- All vertebrates have gene + even chicken has repeat (but CGT)

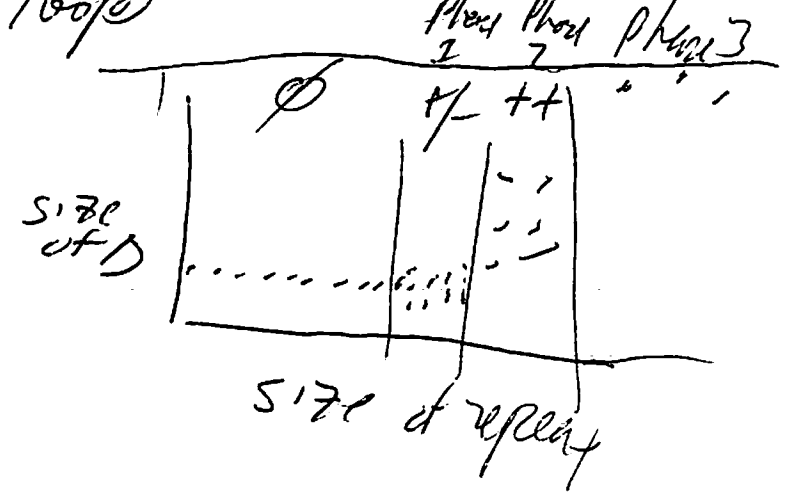
Hentzlin

suggests that DNA structure drives expansion

- best data comes from kinetics w/ different alleles

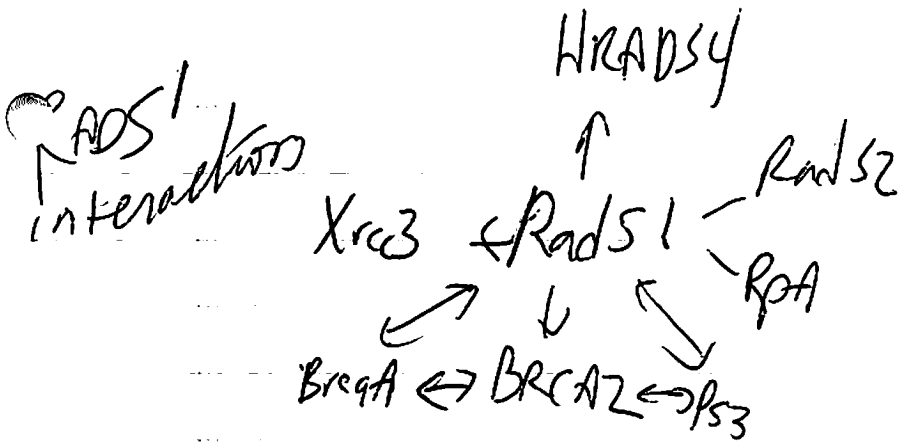
- proposes that 2ary structure inhibits repair ~~Arrest~~ by kinking loop

- what repair?



Homologous Recomb. in Mammals

- introduce DSB w/ SceI enzyme
- PCR test shows w = amts of NH + Homologous repair



Rad52

- involved in both SS annealing + recomb repair

Rad52 structure
ring
- 7 subunits

Replication + Recombination

RecBCD nuclease → RecA → D loop $\xrightarrow[\text{PriA}]{\text{RecG}}$ Holliday Junction

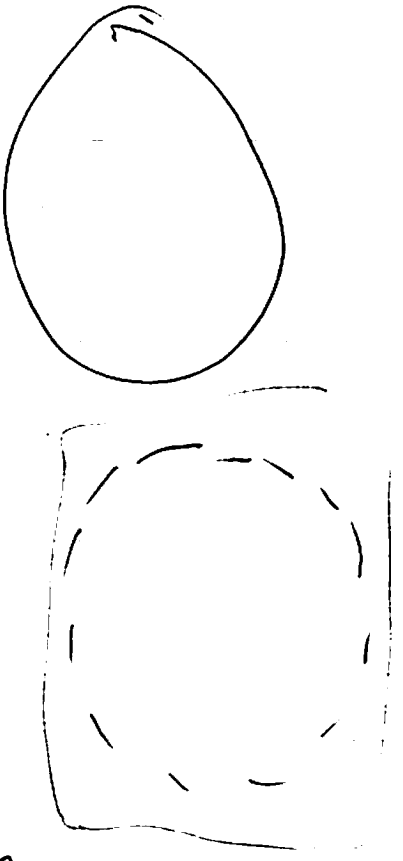
- KO of RecG or RuvABC does little

Stalled replication forks

PriA

RuvABC mutants can be affected by RNA polymerase ppGpp status

XRCC2 -



SMC

- SMC1 = HsSMC1, SMC1
- SMC2 = SMC2, XCAP-E, HCAP-E
- SMC3 =
- SMC4 = HCAP-C, CUT3
- RAD18 = Sp RAD18, ceRAD18
- PPR18 =

T4

uvsX, uvsY, gp32 = invasion
gp43, 45, 44/62 + DNF helicase = primy
gp41, 59, 61 = migration

rad A
rad C } involved in recomb,

R

Rad51+3 = ? Rad54
Rad6 x Rad9 =

3·3·3·3·2

Studio 51
Studio 54

54
27 x 2
18 x 3
9 x 6
2 x 3 x 3 x 3

Rad51 > Rad51
Rad54 > Rad52
Rad54 > Rad50
Rad54 > Rad24
Rad54 RULES

Rad54 probably
c-loop formation

ALL RADS1 AND NO RADS4 MAKES
JACK A DULL BOY

ALL RADS1 AND NO RADS4 MAKES
JACK A DULL BOY

ALL RADS1 AND NO RADS4 MAKES
JACK A DULL BOY

σ54 rules
σ51 does not exist

Damage by IR

ss breaks - BER
ds6 - Rec or NHEJ
abasic - BER
base damage - BER
protein-DNA x-link
DNA-DNA- x-links

Peter Setlow

R Cano - isolated bacteria from 30 mya bacteria

Bacilli - form spores + are resistant

Spore DNA protection

Spores
- no metabolism - no ATP (no repair)
- resistant to acute stress
- survive long periods w/ normal stress
- return to life via germination

Paradox
- at high T° expect lots of depurination
- but there isn't
- spores killed by heat don't have damage

SASP proteins - small acid soluble proteins
- multigene family (two in B. subtilis & make up 60% of types).
- no obvious motifs or homologs
- these are responsible for DNA protection
- protect from mutations
- recA mutations decr survival
- SOS regulation ... induced under conditions that cause DNA damage

Deinococcus

mesophiles (~30°C)
thermophiles (~55-60°C)

- no spores
- naturally transformable throughout growth
- 8-10 genome copies in log phase
- extreme resistance to UV, IR, dessication
- v. large shoulder for IR

6500
730

Why so resistant?

- there are no Earth environments w/ this level of IR

What are mechanisms?

Why?

- adaptation to dehydration

- dry environments
  - spores OR ionizing radiation resistant bacteria
    - multigenic = deinococcus, geodermatophilus, blastococcus, arthrobacter, chroococcidiopsis

- but Harasoyo did not see Δ in IR resistance w/ diff copy

grow in defined media + less chromosome
- only decr. survival at doses
higher than 5000 cGy

one = recA one = pol A

irrB = uvrD

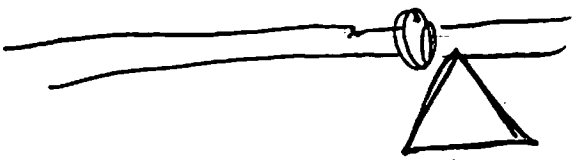
irrE = 01477 ~~01478~~
01476
irrF = 4057 ~~4056~~
4056 polA
irrI 4097 ~~4099~~
4099 = RAMP = Mn transport

John Hays -

Replication

nucl : mito : cpst
1 : 1 : 250

Arabidopsis chr II



- mito insertion

Quant. PCR

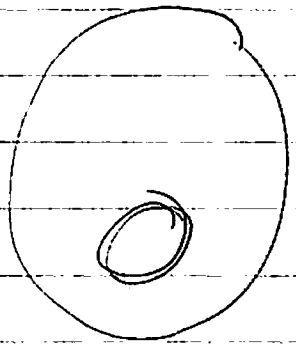
in vitro PTR

no in-vitro

Adaptive Mutation Mov

- when tet^S on ♯ episome you get high ♯ of mutations for

- two populations - low + high mutators



Genetics 148:1433
Canno model

Lunar dependent variation in mutation rates.