

BIOGRAPHICAL SKETCH plus recent bibliography

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

Philip C. Hanawalt	POSITION TITLE The Morris Herzstein Professor of Biology		
eRA COMMONS USER NAME Hanawalt, Philip			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date	FIELD OF STUDY
Deep Springs College, CA	---	06/1950	Liberal Arts
Oberlin College, OH	B.A.	06/1954	Physics
Yale University, CT	M.S., Ph.D.	09/1958	Physics, Biophysics
University of Copenhagen, Denmark	Postdoc	07/1960	Bacterial Physiology
California Institute of Technology, CA	Postdoc	09/1961	Molecular Biology

A. Personal Statement

My experience includes over 54 years of research and teaching; mentoring undergraduates, graduate students (29 Ph.D.'s) and postdocs at Stanford University. Having co-discovered the ubiquitous process of DNA excision repair in 1963-'64, my students and I discovered the sub-pathway of transcription-coupled repair (TCR) in mammalian cells, yeast and bacteria several decades later. My current interest focuses upon mechanisms and genetic control of TCR, and the search for gratuitous forms of TCR that may contribute to genomic instability. We study the behavior of RNA polymerases (T7 RNAP and mammalian RNAPII) encountering DNA lesions, guanine-rich DNA sequences and non-canonical DNA structures to learn the precise signals that initiate TCR to overcome transcription blockage. We also study the differences between the hereditary diseases, Cockayne syndrome (CS) and UV-sensitive syndrome; of which both are deficient in TCR and present no cancers, while CS patients, in particular, exhibit features of premature aging, and their cells may be defective in processing oxidative DNA damage. We have developed an ultrasensitive comet-FISH assay for quantifying 8-oxo-guanine and its repair in expressed genes. We are also developing an approach, utilizing peptide nucleic acid (PNA) targeted to unique expressed genes, to generate stable R-loops (RNA-DNA hybrids), in order to potentially render the very act of transcription "toxic" for selected tumor cells.

1. Hanawalt PC, Spivak G (2008) "Transcription-coupled DNA Repair: Two decades of progress and surprises" *Nature Reviews: Molecular Cell Biology* 9:958-970. PMID 19023283
2. Belotserkovskii BP, Mirkin SM and Hanawalt PC, (2013) "DNA sequences that interfere with transcription: Implications for genome function and stability" *Chemical Reviews*, thematic issue on "Gene Expression", 113:8620-8637.
3. Guo J, Hanawalt PC and Spivak G, (2013) "Comet-FISH with strand-specific probes reveals transcription-coupled repair of 8-oxoGuanine in human cells." *Nucleic Acids Res.* 41:7700-7712.
4. Belotserkovskii BP, Hanawalt PC (2015) "PNA binding to the non-template DNA strand interferes with transcription, suggesting a blockage mechanism mediated by R-loop formation". *Molec. Carcinogenesis* (Open Access on PubMed, Aug. 2014.) 54: 1508-1512.

B. Positions and Honors

Positions (at Stanford University, California)

1961-65 Research Biophysicist and Lecturer
1965-70 Associate Professor of Biology
1968-85 Director, Biophysics Graduate Program
1970- Professor of Biology
1979- Professor of Dermatology (Joint appointment in Stanford Medical School)
1982-89 Chair, Department of Biological Sciences
1988-90 Chair, Second Senate *ad hoc* Committee on the Professoriate
1997-02 The Howard H. and Jessie T. Watkins University Professor at Stanford
2006- Member, Stanford Comprehensive Cancer Center
2009-17 The Dr. Morris Herzstein Professorship in Biology

Other Experience and Professional Memberships

- 1966-70 Physiological Chemistry Study Section, NIH
1971 Program Chair, Biophysical Society Annual Mtg.; Executive Board Member (1969-71)
1974 Chair/Organizer, First Int. Conf. on "Molecular Mechanisms for Repair of DNA", Squaw Valley, CA
1975 Co-Chair, ICN-UCLA Conf. on "DNA Replication and its Regulation", Squaw Valley, CA
1976-83 Advisory Comm. to Bruce Ames, Environmental Health Science Ctr., Univ. California, Berkeley
1981-84 Chemical Pathology Study Section, NIH
1982-93 Co-Founding Editor, *DNA Repair (Mutation Research)*
1984-90 Scientific Advisory Bd., Univ. TX Cancer Ctr. Science Park, Smithville (Chair, 1988-90)
1985 Pre-doctoral Fellowship Review Panel, National Science Foundation (NSF)
1987-90 Board of Scientific Counselors, Division of Biometry and Risk Assessment, NIEHS, NIH
1987-92 Advisory Committee, Brookhaven National Laboratory, Biology Department (Chair, 1992)
1993-94 Program Chair and President, Environmental Mutagen Society (EMS)
1994-97 Board of Directors, American Association for Cancer Research (AACR)
1994 Chair, *Ad Hoc* Committee on Research Integrity and Ethics, AACR
1994-98 Scientific Advisory Board, Office of Environmental Health Hazard Assessment, California EPA
1995-01 Board of Reviewing Editors, *Science*
1995-01 Toxicology Advisory Committee, The Burroughs-Wellcome Fund (Chair, 1997-2000)
1995-99 Scientific Advisory Board, Fogarty International Center, NIH
1995-98 Board on Radiation Effects Research, NAS/NRC Commission on Life Sciences
1996 External Review Comm. for MRC Molecular/Cell Medicine, Cell Mutation Unit, Brighton, U.K.
1996-98 External Review Working Group, NIEHS, NIH
1996 Chair, Gordon Research Conference on "Mutagenesis"
1998-01 Council for Extramural Grants, American Cancer Society (ACS)
1998-07 Board of Trustees, Oberlin College (Chair, Committee on Academic Affairs)
1999 Chair, Gordon Research Conference on "Mammalian DNA Repair"
2001 Genetics Study Section Boundaries Team, CSR, NIH
2001-14 Ext. Advisory Bd. "Structural Biology of DNA Repair" Program, Lawrence Berkeley Lab, CA
2001 Intramural site visiting committee, NICHD, NIH
2003-10 Senior Editor, *Cancer Research*
2003- Editorial Board, *Proceedings of the National Academy of Sciences U.S.A.*
2005- Editorial Board, *Genes and Environment*, Journal of the Japanese EMS
2005-10 International Advisory Board, Princess Chulabhorn Research Inst., Bangkok, Thailand
2005-08 Special Conference Committee, AACR (also 1991-94)
2006 Working Group on Integrated Translational Research on DNA Repair, NIEHS, NIH
2007- Editorial Board, *Mechanisms of Ageing and Development*
2009 Intramural site visiting committee, NCI, NIH
2010-13 External Examiner, Biotechnology Program, Universiti Tunku Abdul Rahman, Kampar, Malaysia
2010 External Reviewer for Cancer Research UK (Quinquennial Review)
2013- Associate Editor, *DNA Repair*, to organize annual issues on "Cutting-Edge Perspectives"
2014 Chair, Gordon Research Conference on "DNA Damage, Mutation and Cancer"

Honors and Professional Recognition

- 1981 Elected Fellow, American Association for the Advancement of Science
1982 Inaugural Annual Lecture, Lord Dowding Fund for Humane Research, London
1987-01 Outstanding Investigator Research Grant, National Cancer Institute, NIH
1989 Elected Member, National Academy of Sciences, U.S.A.
1991 Annual Excellence-in-Teaching Award, Northern California Chapter, Phi Beta Kappa
1992 Annual Award for Excellence in Basic Science, Environmental Mutagen Society (EMS)
1992 Peter and Helen Bing Award for Distinguished Teaching, Stanford University
1993 Elected Fellow, American Academy of Microbiology
1996 Annual Research Award, American Society for Photobiology
1996 Second Severo Ochoa Memorial Honors Lecture, New York University
1997 International *Mutation Research* Award for Excellence in Scientific Achievement

1997 Honorary Doctor of Science, Oberlin College, Ohio
 1999 Princess Takamatsu Cancer Foundation Lectureship (Tokyo, Sendai, Kumamoto, Fukuoka), Japan
 2000 Inaugural John Abelson Family Lecture, Washington State University, Pullman
 2001 Annual Student Mentoring Award, EMS
 2001 Elected Foreign Associate, European Molecular Biology Organization (EMBO)
 2001-05 Senior Scholar Research Award, Ellison Medical Foundation
 2002 J.B. Little Award/Lecture in Radiation Sciences, Harvard School of Public Health, Boston
 2003 Rothschild-Yvette Mayent Curie Institute Award and Lectureship, Paris, France
 2004 Keynote Lecture, ASM International Conference on DNA Repair and Mutagenesis, Bermuda
 2005 President / Organizer, 9th Int. Conference on Environmental Mutagens, San Francisco
 2005 Special Issue, *Mut. Res.* v577, "Molecular Mechanisms of DNA Repair", dedicated to P. Hanawalt
 2006 *Doctor Honoris Causa*, University of Bio Bio, Concepcion, Chile
 2007 Centennial Lecture, "Sunrise Session", 99th AACR Annual Meeting, Los Angeles, CA
 2007 Visiting Scholar/Lectureship, Graduate School of Frontier BioSciences, Osaka University, Japan
 2008 Elected Fellow, American Academy of Arts and Sciences
 2008 *Doctor Honoris Causa*, University of Seville, Spain
 2009 Keynote Lecture, 11th Ann. Midwest DNA Repair Symposium, Ann Arbor, MI (Also, 1st Symp.1999)
 2009 Keynote Lecture, Symp. on DNA Repair and Human Health, Ctr. for Integrative Genetics, Lausanne
 2009 Keynote Lecture, 10th Int. Conference on Environmental Mutagens, Florence, Italy
 2010 Three publications selected for "Centennial Classics Series" in *J.Biological Chemistry*
 2011 AACR - Princess Takamatsu Lectureship Award, presented at AACR Annual Mtg., Orlando, FL
 2012 Keynote Lecture, 3rd Erling Seeberg Symposium on DNA Repair, Trondheim & Ørland, Norway
 2012 *Doctor Honoris Causa*, University of Buenos Aires, Argentina
 2013 Plenary Lecture, 11th Int. Conference on Environmental Mutagens, Foz do Iguassu, Brazil
 2014 Allan V. Cox Medal for Faculty Excellence Fostering Undergraduate Research at Stanford
 2014 Keynote lecture, 16th International Congress on Photobiology, Cordoba, Argentina
 2014 Appointed to Fulbright Specialist Roster, Council for International Exchange of Scholars (CIES)
 2014 *Doctor Honoris Causa*, National University of El Litoral, Santa Fe, Argentina
 2014 Fulbright Specialist Grant to teach course in "Genomic Maintenance", Santa Fe, Argentina
 2015 Fulbright Specialist Grant to teach in Hollaender Course, La Paz, Bolivia
 2015 Wilbur Lucius Cross Medal from the Yale University Graduate School Alumni Association
 2015 *Doctor Honoris Causa*, Universidad Mayor de San Andreas, La Paz, Bolivia

C. Contributions to Science

1. During my postdoctoral apprenticeship at the University of Copenhagen, I discovered that RNA and protein synthesis are required to initiate the bacterial DNA replication cycle, thereby establishing an approach for synchronizing DNA replication in *Escherichia coli*. My results were important to the formulation of the replicon model by Jacob, Brenner and Cuzin in 1963.
2. My Ph.D. thesis research at Yale University included studies on the recovery of DNA synthesis in UV irradiated bacteria and the photoreactivation of macromolecular syntheses. That work provided the underpinning for the subsequent discovery of pyrimidine dimer excision by my mentor, Richard Setlow, and for my discovery of repair replication in 1963-'64 in collaboration with my first graduate student, David Pettijohn. Those studies constituted the discovery of the ubiquitous pathway of nucleotide excision repair. Base excision repair and mismatch repair were reported by others a decade later.
3. My postdoctoral associate, Hiroaki Nakayama, and I discovered the recQ gene in E.coli, while searching for a mutant that was resistant to thymineless death. My graduate student, Justin Courcelle, and I characterized the role of the RecQ helicase in processing arrested replication forks. Five RecQ homologues have been reported in human cells, including WRN, for which mutants cause premature aging, BLM, for which mutants have high levels of sister chromatid exchanges, and RTS, for which mutants are also cancer prone. Lessons learned from studies of RecQ underscore the value of basic research in bacterial systems that can have profound implications for human health.

4. My students and I discovered transcription-coupled DNA repair (TCR) in mammalian cells, yeast and bacteria; for many years we have pioneered this important field. Interestingly, humans with deficiencies in TCR present no cancers of any type. Sequenced genomes from tumors often provide the “mutational signature” for the causal agent and they additionally indicate the extent to which TCR is operating for repair of the damage due to the particular agent. Some types of DNA damage are recognized by TCR but not by the global genomic pathway of nucleotide excision repair.
5. Most recently we have provided important insights toward an understanding of the behavior of RNA polymerases encountering non-canonical DNA structures and unusual sequences. These studies have culminated in our current focus on a unique approach to selectively inactivate tumor cells by forming stable R-loops in certain expressed genes that are not expressed in the population of normal cells. Potentially this may develop as a novel approach for cancer chemotherapy.

See Home Page for Complete CV and All Publications: <http://www.stanford.edu~hanawalt/>

D. Current Research Support

2R01-CA77712 Hanawalt (PI) 04/01/09 – 07/31/17

Role of Transcription in Genomic Stability

We are characterizing unique features of transcription complexes encountering different impediments; non-canonical DNA structures, guanine-rich sequences, strand breaks and other lesions, to reveal signals for initiating TCR and possible gratuitous repair. These studies will hopefully provide clues for innovative approaches in chemotherapy for cancer, including the generation of stable R-loops in unique active genes in tumor cells to render the very act of transcription selectively toxic for those cells.

E. Completed Research Support

1R01-ES018834 Hanawalt (PI) 04/01/10 – 09/30/15

Oxidative DNA damage processing; role in human pathology and aging

We developed novel approaches for elucidating effects of oxidative DNA lesions on transcription, and for repair analysis at physiologically relevant levels in transcriptionally active and silent genomic domains

R01 CA77712 Hanawalt (PI) 04/01/03-03/31/09.

Role of RNA Polymerase II in DNA Repair

We characterized translocating RNA polymerases at site-specific DNA lesions *in vitro*; Effects of transcription factors (eg. TFIIIS) were evaluated, and comparative analyses with carried out with TCR *in vivo*.

R01 CA90915 Hanawalt (PI) 01/28/02-12/31/08

Transcription-coupled DNA Repair and Human Disease

Comparative analyses of TCR in cells from Cockayne syndrome and UV-sensitive syndrome with respect to

5R 35 CA44349 Hanawalt (PI) 06/01/87-11/30/01

Outstanding Investigator Grant : Cellular Processing of Damaged DNA; Role in Oncogenesis different genotoxic exposures, including reactive oxygen species. Genetic analyses of these diseases.

RO1 CA91456 Hanawalt (PI) 01/28/02-12/31/08

Transcription-coupled DNA Repair in *E. coli*

Role of bacterial RNA polymerase and T7 RNA polymerase in TCR. Studies on thymineless death and roles of RecQ and other DNA repair enzymes in processing arrested replication forks.

AG-SS-0550-00 Hanawalt (PI) 01/01/01-12/31/04

Ellison Medical Foundation Sr. Scholar Award : DNA Repair in Human Neurons

F. Publications, from 2008:

Tornaletti S, Park-Snyder S, Hanawalt PC. G4-forming sequences in the non transcribed DNA strand pose blocks to T7 RNA polymerase and mammalian RNA polymerase II. *J Biol Chem.* 283: 12756- 12762 (2008).

Hanawalt PC. Emerging links between premature aging and defective DNA repair. *Mechanisms of Aging and Development* 129: 503–505 (2008).

Ditlevson J V, Tornaletti S, Belotserkovskii BP, Teijeiro V, Wang G, Vasquez KM, **Hanawalt PC.** Inhibitory Effect of a Short Z-DNA Forming Sequence on Transcription Elongation by T7 RNA Polymerase. *Nucleic Acids Research* 36: 3163–3170 (2008).

Hanawalt PC, Spivak G “Transcription-coupled DNA Repair: Two decades of progress and surprises” *Nature Reviews: Molecular Cell Biology* 9:958-970 (2008).

Spivak G, Cox RA, **Hanawalt PC.** New applications of the Comet assay: Comet-FISH and transcription coupled DNA repair. *Mutat.Res.* 681: 44 – 50 (2009)

Belotserkovskii BP, **Hanawalt PC.** Peptide nucleic acid (PNA) binding and its effect on *in vitro* transcription in Friedreich’s ataxia triplet repeats. *Molec. Carcinogenesis* 48:299-308 (2009)

Vasquez KM, **Hanawalt PC.** Intrinsic genomic instability from naturally occurring DNA structures: An introduction to a Special Issue *Molec. Carcinogenesis* 48:271-272 (2009)

Nardo T, Oneda R, Spivak G, Vaz B, Mortier L, Thomas P, Orioli D, Laugel V, Stary A, **Hanawalt PC,** Sarasin A, Stefanini M. A UV-sensitive syndrome patient with a specific CSA mutation (2009)

Hanawalt PC, Spivak G. Foreword, for Medical Intelligence Unit: *Molecular Mechanisms of Cockayne Syndrome* (SI Ahmad, editor), Landes Bioscience, Austin TX {ISBN: 978-1-58-706-321-3} (2009)

Sangurdekar DP, Hamann BL, Smirnov D, Srienc F, **Hanawalt PC,** Khodursky AB, "Thymineless death is associated with loss of essential genetic information from the replication origin." *Molecular Microbiology* 6:1455-1467 (2010)

Fonville N, Bates D, Hastings PJ, **Hanawalt PC,** Rosenberg SM, "Role of RecA and the SOS response in thymineless death in *Escherichia coli*." *PloS Genetics* 6:e1000865 (2010)

Belotserkovskii BP, Liu R, Tornaletti S, Krasilnikova MM, Mirkin SM, **Hanawalt PC,** "Mechanisms and implications of transcription blockage by guanine-rich DNA sequences" *Proc. Nat. Acad. Sci. USA*, 107: 12816 - 12821 (2010)

Hanawalt PC, “Growing up with DNA repair and joining the EMS.” *Environmental and Molecular Mutagenesis* 51:890-896 (2010)

Ganesan A and **Hanawalt PC,** “Transcription-coupled nucleotide excision repair of a gene transcribed by bacteriophage T7 RNA polymerase in *Escherichia coli*.” *DNA Repair* 9:958-963 (2010)

Kresge N, Simoni RD, Hill RL, “Discovery and characterization of DNA excision repair pathways: the work of Philip Courtland **Hanawalt**.” *J. Biol. Chem.* 285: e9-11 (2010)

Hanawalt PC, Belotserkovskii B, Spivak, G, “Role of transcription in genomic stability or instability.” *in DNA Repair and Human Cancers, Princess Takamatsu 40th International Symposium.* 40:123-126 (2010)

Belotserkovskii B, **Hanawalt PC,** “Anchoring Nascent RNA to the DNA Template Could Interfere with Transcription.” *Biophys. Journal* 100: 675-684 (2011)

Salinas-Rios V, Belotserkovskii BP, **Hanawalt PC** “DNA slip-outs cause RNA polymerase II arrest in vitro: potential implications for genetic instability”. *Nucl. Acids Res.* 39:7444-54 (2011).

Hanawalt PC and Ford JM, “DNA repair defects and human disease” for *Brenner’s Encyclopedia of Genetics*, 2nd Edition, Elsevier (2012)

Hanawalt PC, “Lesions sensing and decision points in the DNA damage response.” Chapter 3.4 *in The Cellular Response to the Genotoxic Insult: The Question of Threshold for Genotoxic Carcinogens.* (ed. by Helmut Greim and Richard J. Albertini. *The Royal Society of Chemistry* (2012)

Ganesan A, Spivak G and **Hanawalt PC,** “Transcription-coupled DNA repair in prokaryotes.” *Mol. Bio and Trans. Sci.* (CP. Doetsch, Ed.) Vol. 110: 25-40 (2012)

Hanawalt PC, “Repairing DNA for 80 years: The timeline of my life.” *DNA Repair* 5: 452, e1-11 (2012)

Falik-Zaccai TC, Erel-Segal R, Horev L, Bitterman-Deutsch O, Koka S, Chaim S, Keren Z, Kalfon L, Gross B, Segal Z, Orgal S, Shoval Y, Slor H, Spivak G and **Hanawalt PC,** “A novel XPD mutation in a compound heterozygote; the mutation in the second allele is present in three homozygous patients with mild sun sensitivity.” *Enviro. Molecular Mutagenesis* 53:505-514 (2012)

Neil AJ, Belotserkovskii BP and **Hanawalt PC,** “Transcription blockage by bulky end termini at single-strand breaks in the DNA template: Differential effects of 5’ and 3’ adducts.” *Biochemistry* 44: 8964-8970 (2012)

Belotserkovskii BP, Neil AJ, Saleh SS, Shin JH, Mirkin SM and **Hanawalt PC,** “Transcription blockage by homopurine DNA sequences: role of sequence composition and single-strand breaks.” *Nucleic Acids Res.* 3: 1817-1828 (2013)

Guo J, **Hanawalt PC** and Spivak G, "Comet-FISH with strand-specific probes reveals transcription- coupled repair of 8-oxoguanine in human cells." *Nucleic Acids Res.* 41:1-13 (2013)

Belotserkovskii BP, Mirkin SM and **Hanawalt PC**, "DNA sequences that interfere with transcription: Implications for genome function and stability" *Chemical Reviews*, thematic issue on "Gene Expression", 113:8620-8637 (2013)

Hanawalt PC, "The Awakening of DNA Repair at Yale." *Yale Journal of Biology and Medicine*, 86:517- 523 (2013)

Hanawalt PC, Wilson SH, Preface for special issue on "Cutting Edge Perspectives in Genomic Maintenance" edited by Hanawalt, *DNA Repair*, 19:1-2 (2014)

Hanawalt PC, "Role of transcription domain-associated DNA repair in mutational heterogeneity", Cell Press (News Blog), Posted 20 Nov. 2014. . <file://localhost/http://news.cell.com/cellreports/cell-reports/role-of-transcription-domain-associated-dna-repair-in-mutational-heterogeneity-commentary-by-philip-hanawalt>)

Belotserkovskii BP, **Hanawalt PC**, "PNA binding to the non-template DNA strand interferes with transcription, suggesting a blockage mechanism mediated by R-loop formation" *Molecular Carcinogenesis*, Epub ahead of print (Aug 2014), 54: 1508-1512 (2015)

Spivak G, **Hanawalt PC**, "Photosensitive Human Syndromes" *Mutation Research*, 776:24-30 (2015)

Hanawalt PC, "A balanced perspective on unbalanced growth and thymineless death" *Frontiers in Microbiology*, June 2015, V.6, Article 504; doi:10.3389/fmicb.2015.00504 (2015)

Khodursky A, Guzman EC, **Hanawalt PC**, "Thymineless death lives on: New insights into a classic phenomenon", *Annual Review of Microbiology*, 69:247-263 (2015)

Pandey S, Ogloblina AM, Belotserkovskii BP, Dolinnaya NG, Yakubovskaya MG, Mirkin SM, **Hanawalt PC**, "Transcription blockage by stable H-DNA analogs in vitro", *Nucleic Acids Res.* 43:6994-7004 (2015)

Tanasova M, Goeldi S, Meyer F, **Hanawalt PC**, Spivak G, Sturla SJ, "Altered minor-groove hydrogen bonds in DNA block transcription elongation by T7 RNA polymerase", *ChemBioChem*, (2015) doi:10.1002/cbic.201500077 Open Access (2015)

Hanawalt PC, Wilson SH, "Cutting-edge perspectives in genomic maintenance II. Preface", edited by Hanawalt , *DNA Repair*, 32: 1-2 (2015)

Hanawalt P, Grollman A, Mitra S, "A tribute in memory of Richard B. (Dick) Setlow (1921-2015)", *DNA Repair*, 33:111-114 (2015)

Hanawalt P, "Historical perspective on the DNA damage response" (Invited Review) *DNA Repair* 36:2-7 (2015)

Ganesan A, **Hanawalt P**, "Photobiological origins of the field of genomic maintenance" (Invited review), *Photochem.Photobiol.* On Line: October 2015; In Press for January (2016)