

Timothy J. Jorgensen

Address: Department of Radiation Medicine
Lombardi Comprehensive Cancer Center
Georgetown University Medical Center
The Research Building/ Room E212A
3970 Reservoir Road, N.W.
Washington, D.C. 20057

Telephone: 202-687-1810
email: tjorge01@georgetown.edu

EDUCATION:

Fordham University

Fordham College
New York, New York

Bachelor of Science, 1977
Department of Biology

Fairleigh Dickinson University

Maxwell Becton Graduate College of Arts and Sciences
Rutherford, New Jersey

Master of Science, 1979
Department of Biological Sciences

Johns Hopkins University

Bloomberg School of Public Health
Baltimore, Maryland

Doctor of Philosophy, 1984
Department of Environmental Health Sciences
Division of Radiation Health

Graduate Certificate in Risk Science and Public Policy, 2002
Johns Hopkins Risk Science and Public Policy Institute

Master of Public Health, 2005
Department of Epidemiology
Cancer Epidemiology Program

POSTDOCTORAL:

Harvard Medical School

Dana-Farber Cancer Institute
Boston, Massachusetts

Research Fellow in Pathology, 1984-87

Department of Pathology
Division of Cancer Pharmacology

FELLOWSHIP:

Johns Hopkins University

Bloomberg School of Public Health
Baltimore, Maryland

Ruth L. Kirschstein Senior Fellow, 2003-2004

Department of Epidemiology
Cancer Epidemiology Program (Sponsor: Dr. Kathy J. Helzlsouer)

PROFESSIONAL EXPERIENCE:

1985 - 1986	Instructor (Part-time) Biology Department Harvard University Cambridge, Massachusetts
1987 - 1995	Assistant Professor Department of Radiation Medicine (1987-95), and Department of Biochemistry & Molecular Biology (1993-1995) Georgetown University School of Medicine
1988 - present	Member , Lombardi Comprehensive Cancer Center
1995 - present	Associate Professor (tenured 1996) Departments of Radiation Medicine, and Biochem. & Molecular Biology Georgetown University School of Medicine
2001 – present	Member , Cancer Genetics and Epi. Program, Lombardi Cancer Center
2003 – 2004	Visiting Scholar
2005 – present	Adjunct Associate Professor Department of Epidemiology Cancer Epidemiology Program Johns Hopkins Bloomberg School of Public Health

HONORS AND AWARDS:

Certificate of Merit for Outstanding Student Research, 1984
Delta Omega Society -- The Honorary Public Health Society

Cornelius Kruse Award for the Outstanding Thesis in Environmental Health Sciences, 1984

"DNA Damage to Mammalian Cells Caused by Low Doses of Ionizing Radiation"
Johns Hopkins University

Student Travel Award, 1984
Radiation Research Society

Individual National Research Service Award (F32), 1985-87
"Role of Gamma Endonuclease in DNA Repair"
National Cancer Institute
National Institutes of Health

Life Member, Alpha Chapter (Johns Hopkins) of Delta Omega -- The Honorary Public Health Society, 1986 - present

Faculty Travel Award, 1995
10th International Congress of Radiation Research (Wurzburg, Germany)
Radiation Research Society

Ruth L. Kirschstein Senior Fellow Award (F33), 2003-2004
"DNA Repair Gene Polymorphisms and Breast Cancer Risk"
National Cancer Institute
National Institutes of Health

PROFESSIONAL SERVICE:

Associate Editor, *Radiation Research* -- The International Journal of the Radiation Research Society
1994-98

Chairman, District of Columbia Legislative Committee of the American Association for Cancer Research
1992-94

Member, NIH Special Review Committee of RFA CA-91-07,
"Molecular Analysis of Radiation-Induced Genetic Damage"
November 24-26, 1991

Invited Participant, National Academy of Sciences Workshop
"New Approaches to a Biologically-Based Risk Model for Low Dose, Low Dose-Rate High LET Radiations"
January 20-21, 1996

Presenter, Junior Science and Humanities Symposia at GU (1995-present)

Member, NIH Special Review Committee for Program Project P01 CA25842-16,
"Modulation of Apoptosis to Improve Cancer Therapy"
April 14-16, 1996

Invited Participant, NIH/NCI "Molecular Radiation Biology and Oncology Workshop"
March 8-9, 1999

Member, NIH Study Section for Radiotherapy/Radiation Biology SBIR grants
1999-present

Member, NIH Special Review Committee for Program Project P01 CA97012-01,
"Molecular Gene and Radiation Therapies for Cancer"
February 6-8, 2002

Member, NIH Special Review Committee for Program Project P01 CA101869-01,
"DNA Repair Therapeutic Targets for Ovarian Cancer" March 1-3, 2003

Member, NIH Special Review Committee for Program Project P01 CA034936-19A1,
"A Mutational Model for Childhood Cancer" October 6-7, 2004

Member, NIH Center for Scientific Review Special Emphasis Panel on Oxidative
Damage Repair, November 10, 2004

Reviewer, Intel Science Talent Search, 2005

Ad Hoc Member (for radiation-related proposals), NIH/CSR Cancer Immunopathology
and Immunotherapy Study Section, 2005-present

Reviewer, DOD Prostate Cancer Research Program – Radiation Oncology, 2006

UNIVERSITY SERVICE:

Member, Board of Directors of GU Employees' Federal Credit Union (1992-2001)
[Board **Vice-President** (1992-93) and Board **President** (1993-97)]

Member, (1989-90 and 1993-present), GU Radiation Safety Committee

Chairman, GU Medical Center Cesium Irradiator Advisory Committee (1994-present)

Member, GU Medical School Research Committee (1993-96)

Interviewer, GU Medical School Office of Admissions (1988-96)

Member, Lombardi Center Flow Cytometry Core Advisory Committee (1991-present)

Member, Lombardi Center Library Committee (1991-96)

Member, Committee on Resources for the Educational Program/General Facilities
Georgetown School of Medicine, LCME Accreditation (2001-02)

PROFESSIONAL SOCIETIES:

Member, Radiation Research Society (1983 – present)

Member, American Association for Cancer Research (1988 – present)

Member, American Public Health Association (2000 – present)

Member, Society for Risk Analysis (2000 – present)

TEACHING ACTIVITIES:

LECTURING:

Course Director, of undergraduate "Radiation Biology" seminar course at Harvard University, 1985-86

Lecturer, in "Molecular Basis of Carcinogenesis" course at GU Graduate School, 1989-present

Course Director, of graduate "Radiation Biology" course at GU Graduate School, 1990-present

Lecturer, in "Introductory Tumor Biology" course at GU School of Medicine, 1993-present

Facilitator, in Problem Based Learning (PBL) "Biochemistry" course at GU School of Medicine, 1993-2003

Instructor, Biochemistry Graduate Student Tutorial at GU (1995-present)

Guest Lecturer, in "Topics in Cancer Causes and Cancer Prevention" course at the University of the District of Columbia (2002-2004)

Lecturer, in "Tumor Biology 520 – Cancer Prevention and Control, Part 1 Molecular Epidemiology" at GU (2004-present)

Lecturer, in "Tumor Biology 521 -- Topics in Molecular Epidemiology" at GU (2004-present)

Lecturer, in "Cancer Genetics" at GU (2005-present)

Guest Lecturer, Summer Institute, Health Policy and Management, at the Johns Hopkins Bloomberg School of Public Health (2003-present)

Guest Lecturer, "Etiology, Prevention, and Control of Cancer" course, at the Johns Hopkins Bloomberg School of Public Health (2005-present)

MENTORING:

Staff Radiation Biologist, GU Radiation Oncology Residency Training Program (1990-present)

Mentor, to Luis Rivero , Wanda Noguera, and Alexander Faje for their undergraduate Senior Theses in Georgetown College (LR graduated 5/90; WN graduated 5/92; AF graduated 5/01)

Mentor, to medical student Maurice FitzPatrick in molecular biology research techniques during his research elective clerkship (MF graduated 5/91)

Mentor, to Medical Oncology resident John Buatti M.D. during his Medical Oncology research elective (1989)

Mentor, to post-doctoral fellows Thomas Winters (1990-96), Isaf Al-Nabulsi (1992-94), Mubasher Dar (1993-96), Hui Tian (1998-2005)

Mentor, to doctoral student Manu Kohli in the GU Tumor Biology Training Program (1995-2000)

Mentor, to Sanford Katz M.D. during his one-year research rotation in the Radiation Oncology Residency Training Program (1999-2000)

Thesis Committee Member, for Luis Benevides (1994-95), Gabrielle Ortero (1994-1995), Jessica Jones (1996-99), Basel Eldadah (1996-98), Lorena dela Pena (1998-present), Aleeta Powe (1998-2000), Robert Newman (1999-2004), Stella Kim (2001-present), Meredith Tennis (2002-present), Luisel Sant-Ruiz (2003-present), Kimberly M. Batty (2002-present)

PUBLICATIONS:

CHAPTERS IN REFEREED BOOKS:

Jorgensen TJ: Photoreactivating enzyme. *In*: Parker S, (ed.), 1984 McGraw Hill Yearbook of Science and Technology pp. 342-344, 1984.

Jorgensen TJ: Biology of radiosensitive tissues and organs. *In* Mossman, KL and Mills, WA (eds.), The Biological Basis of Radiation Protection Practice. Williams and Wilkens, Baltimore, pp. 169-183, 1992.

JOURNAL ARTICLES:

Jorgensen TJ: Photoreactivating enzyme: A light-activated repair enzyme of microbes and man. *Bioscience* 31:671-674, 1981.

- Jorgensen TJ**, Munno F, Mitchell TG, and Hungerford D: Comparison of urinary cobalt concentrations in patients with porous Austin-Moore prostheses. *Clin. Orthopaed. Rel. Res.* 176:124-126, 1983.
- Furlong EA, **Jorgensen TJ**, and Henner WD: Production of dihydrothymidine stereoisomers in DNA by gamma irradiation. *Biochemistry* 25:4344-4349, 1986.
- Jorgensen TJ**, Olive PL, and Durand RE: DNA strand breakage in Chinese hamster V79 cells caused by low levels of incorporated ³H- and ¹⁴C-thymidine. *Int. J. Radiat. Biol.* 51:673-680, 1987.
- Henner WD, Kiker N, **Jorgensen TJ**, and Munck JN: Purification and aminoterminal aminoacid sequence of an apurinic/apyrimidinic endonuclease from calf thymus. *Nucleic Acids Res.* 15:5529-5544, 1987.
- Jorgensen TJ**, Kow YW, Wallace SS, and Henner WD: Mechanism of action of *Micrococcus luteus* gamma endonuclease. *Biochemistry* 26:6436-6443, 1987.
- Jorgensen TJ**, Furlong EA, and Henner WD: Gamma endonuclease of *Micrococcus luteus*: Action on irradiated DNA. *Radiat. Res.* 114:556-566, 1988.
- Thierry AR, **Jorgensen TJ**, Forst D, Belli JA, Dritschilo A, and Rahman A: Modulation of multidrug resistance in Chinese hamster cells by liposome-encapsulated doxorubicin. *Cancer Commun.* 1:311-316, 1989.
- Jorgensen TJ**, Prasad SC, Brennan TP, and Dritschilo A: Constraints to DNA unwinding near radiation-induced strand breaks in Ewing's sarcoma cells. *Radiat. Res.* 123:320-324, 1990.
- Briscoe PR and **Jorgensen TJ**: Improved RNA isolation from cells in tissue culture using the a commercial nucleic acid extractor. *Biotechniques* 10:594-596, 1991.
- Jorgensen TJ**, Leonard JC, Thraves PJ, and Dritschilo A: Baseline sister chromatid exchange in human cell lines with different levels of poly(ADP-ribose) polymerase. *Radiat. Res.* 127:107-110, 1991.
- Oudard S, Thierry A, **Jorgensen TJ**, and Rahman A: Sensitization of multidrug resistant colon cancer cells to doxorubicin by encapsulation in liposomes. *Cancer Chemother. Pharmacol.* 28:259-265, 1991.
- Winters TA, Weinfeld M, and **Jorgensen TJ**: Human HeLa cell enzymes that remove phosphoglycolate 3'-end-groups from DNA. *Nucleic Acids Res.* 20:2573-2580, 1992.
- Buatti JM, Rivero LR, and **Jorgensen TJ**: Radiation-induced DNA single-strand breaks in freshly isolated human leukocytes. *Radiat. Res.* 132:200-206, 1992.
- Kamesaki S, Kamesaki H, **Jorgensen TJ**, Tanizawa A, Pommier Y, and Cossman J: *bcl-2* protein inhibits etoposide-induced apoptosis through its effects on events subsequent to

topoisomerase II-induced initial DNA strand breaks and their repair. *Cancer Res.* 53:4251-4256, 1993.

Jorgensen TJ, Notario V, Thraves PJ, and Dritschilo A: Radiation response of NIH/3T3 mouse fibroblasts overexpressing human poly(ADP-ribose) polymerase. *Radiat. Oncol. Investigations* 1:189-197, 1993.

Winters TA, Henner WD, Russell P, McCullough A, and **Jorgensen TJ**: Removal of 3'-phosphoglycolate from DNA strand-break damage in an oligonucleotide substrate by recombinant human apurinic/apyrimidinic endonuclease 1. *Nucleic Acids Res.* 22: 1866-1873, 1994.

Jung M, Kern FG, **Jorgensen TJ**, McLeskey SW, Blair OC, and Dritschilo A: FGF-4 enhances G2 arrest and cell survival following exposure to ionizing radiation. *Cancer Res.* 54: 5194-5197, 1994.

Al-Nabulsi I, Takamiya Y, Voloshin Y, Dritschilo A, Martuza RL, and **Jorgensen TJ**: Expression of thymidine kinase is essential to low dose radiation resistance of rat glioma cells. *Cancer Res.* 54: 5614-5617, 1994.

Ziv Y, Bar-Shira A, **Jorgensen TJ**, Russell PS, Sartiel A, Shows TB, Eddy RL, Buchwald M, Legerski R, Schimke RT, and Shiloh Y: Human cDNA clones that modify the radiomimetic sensitivity of ataxia-telangiectasia (group A) cells. *Somat. Cell Mol. Genet.* 21:99-111, 1995.

Jorgensen TJ, Russell PS, and McRae DA. Radioresistant DNA synthesis in SV40-immortalized ataxia telangiectasia fibroblasts. *Radiat. Res.* 143:219-223, 1995.

Dar ME, and **Jorgensen TJ**. Deletions at short direct repeats and base substitutions are characteristic mutations for bleomycin-induced DNA double- and single-strand breaks, respectively, in a human shuttle vector system. *Nucleic Acids Res.* 23:3224-3230, 1995.

Gilad S, Khosravi R, Shkedy D, Uziel, T, Ziv, Y, Savitsky K, Rotman G, Smith S, Chessa L, **Jorgensen TJ**, Harnik R, Frydman M, Sanal O, Portnoi S, Goldwicz Z, Jaspers NGJ, Gatti RA, Lenoir G, Lavin MF, Tatsumi K, Wegner RD, Shiloh Y, and Bar-Shira A: Predominance of null mutations in ataxia-telangiectasia. *Human Molecular Genetics* 5:433-440, 1996.

Jorgensen TJ, and Shiloh Y: The ATM gene and the radiobiology of ataxia telangiectasia. *Int. J. Radiat. Biol.* 69:527-537, 1996.

Ziv Y, Bar-Shira A, Pecker I, Russell P, **Jorgensen TJ**, Zarfati I, and Shiloh Y: Recombinant ATM complements the cellular A-T phenotype. *Oncogene* 15:159-167, 1997.

Dar ME, Winters TA, and **Jorgensen TJ**: Identification of defective illegitimate recombinational repair of oxidatively-induced DNA double-strand breaks in ataxia-telangiectasia cells. *Mutation Res. DNA Repair* 384:169-179, 1997.

Gilad S, Chessa L, Khosravi R, Russell P, Galanty Y, Piane M, Gatti RA, **Jorgensen TJ**, Shiloh Y, and Bar-Shira A: Genotype-phenotype relationships in ataxia-telangiectasia (A-T) and A-T variants. *American Journal of Human Genetics* 62:551-561, 1998.

Kohli M, and **Jorgensen TJ**: The influence of SV40 immortalization of human fibroblasts on p53-dependent radiation responses. *Biochem. Biophys. Res. Comm.* 257:168-176, 1999.

Winters AT, Russell PS, Kohli M, Dar ME, Neumann RD, and **Jorgensen TJ**: Determination of human DNA polymerase utilization for the repair of a model ionizing radiation-induced DNA strand break lesion in a defined vector substrate. *Nucleic Acids Res.* 27:2423-2433, 1999.

Walker JR, McGeagh K, Sundaresan P, **Jorgensen TJ**, Rabkin SD, and Martuza RL: Local systematic therapy of human prostate cancer with the conditionally replicating herpes simplex virus vector G207. *Human Gene Therapy* 10:2237-2243, 1999.

Kohli M, and **Jorgensen TJ**: Lack of dependence on p53 for DNA double strand break repair of episomal vectors in human lymphoblasts. *Biochem. Biophys. Res. Comm.* 264:702-708, 1999.

Tian H, Wittmack EK, and **Jorgensen TJ**: p21^{WAF1/CIP1} antisense therapy radiosensitizes human colon cancer by converting growth arrest to apoptosis. *Cancer Res.* 60: 679-684, 2000.

Jorgensen TJ, Katz S, Wittmack EK, Varghese S, Todo T, Rabkin SD, and Martuza RL: Ionizing radiation does not alter the antitumor activity of herpes simplex virus vector G207 in subcutaneous tumor models of human and murine prostate cancer. *Neoplasia* 3:451-456, 2001.

Tian H, Faje AT, Lee SL, and **Jorgensen TJ**: DNA damage-induced phosphorylation of Chk1 at S345 is associated with p53-dependent checkpoint pathways. *Neoplasia* 4:171-180, 2002.

Brewster AM, **Jorgensen TJ**, Ruczinski I, Yao H, Hoffman S, Thuita L, Newschaffer C, Lunn RM, Bell D, and Helzlsouer KJ: Polymorphisms of the DNA repair genes XPD (Lys751Gln) and XRCC1 (Arg399Gln and Arg194Trp): Relationship to breast cancer risk and familial predisposition to breast cancer. *Breast Cancer Research and Treatment* 95(1): 73-80, 2005.

Crowe SL, Movsesyan VA, **Jorgensen TJ**, Kondratyev A: Rapid phosphorylation of histone H2AX following ionotropic glutamate receptor activation. *Europ. J. Neuroscience* 23 (9): 2351-2361, 2006.

Jorgensen TJ, Visvanathan K, Ingo Ruczinski I, Lucy Thuita L, and Helzlsouer KJ: Breast cancer risk is not associated with polymorphic forms of xeroderma pigmentosum genes in a cohort of women from Washington County, Maryland. *Breast Cancer Research and Treatment* (in press), 2006.

Jorgensen TJ, Tian H, Ferguson D, Joseph IBJK, Menon K, and Frost D: Chemosensitization and radiosensitization of human lung and colon cancers by antimitotic agent, ABT-751, in athymic murine xenograft models of subcutaneous tumor growth. *Cancer Chemother Pharmacol* (submitted), 2006.

Chen J, Yenokyan G, **Jorgensen TJ**, Ruczinski I, Yao Y, Alani R, Lieigois N, Hoffman SC, Hoffman-Bolton J, Strickland PT, Hezlsouer KJ, Alberg AJ: Nonmelanoma skin cancer as a marker of risk for subsequent malignancy: A community-based prospective cohort study. JNCI (submitted), 2006.

RESEARCH SUPPORT:

Active:

NCI R01 CA097705 (Shields)

10/01/02 - 9/30/07

Molecular Epidemiology of Secondary Lung Cancer

The goals of this proposal are to determine risk factors for secondary lung cancer in women with breast cancer and treated with radiotherapy. Risk factor data for smoking and radiotherapy will be examined in the context of genetic traits that modify these risks and their impact on molecular markers in breast and lung tumors, such as mutations in the p53 gene.

NCI R01 CA64472 (Notario)

4/1/03 - 3/31/08

Function of the *PCPH* oncogene in mammalian carcinogenesis

The goals of this project are to identify and characterize: (1) mechanisms of transformation by mt-PCPH or the deregulated expression of PCPH; (2) involvement of PCPH in the regulation of cellular ATP protocols; (3) functional interactions between PCPH and mTOR in yeast cells; and (4) Participation of PCPH in human cancer.

NCI P01 CA74175-07 (Dritschilo)

4/1/03 - 3/31/07

Mechanisms of Cellular Responses to Ionizing Radiation

Core B: **Technology** (Jorgensen)

The technology core supports the common technical needs of all of the projects within the Program Project. Support includes readily available experimental instrumentation, technical advice and expertise in the use of instruments, technical assistance in conducting experiments, and assistance in experimental design and interpretation of data.

NCI R01 CA105069-01 (Alberg) (subcontract to Georgetown/Jorgensen) 6/1/05-5/31/10

DNA Repair, Skin Cancer and Overall Cancer Risk

A personal history of nonmelanoma skin cancer (NMSC) is associated with an increased risk of both on cutaneous malignancies and subsequent skin and lip cancers. The basis for this observation remains unclear, but the risk of subsequent non-skin cancers suggests a high cancer risk phenotype. A likely candidate underlying this susceptibility to both cutaneous and noncutaneous malignancies is inter-individual differences in DNA repair. Because of the strong link between Nucleotide Excision Repair (NER) and NMSC, and because of the importance of bulky DNA adducts to all cancers, the NER pathway is the most relevant DNA repair pathway. We hypothesize that polymorphisms in genes in the NER pathway may be the underlying susceptibility factor.

Recently Completed:

NCI F33 CA09817-01 (Jorgensen)

10/01/03 - 9/30/04

Ruth L. Kirschstein Senior Fellow Award

DNA Repair Gene Polymorphisms and Breast Cancer Risk

Investigations of potential gene-environment interactions may improve our understanding of the etiology of breast cancer. Dr. Jorgensen worked as a Visiting Scholar in the Department of Epidemiology at Johns Hopkins University, during a year-long sabbatical from Georgetown. The findings from this study will aid in understanding potential genetic susceptibility factors related to breast carcinogenesis, and will help in identifying women at increased breast cancer risk who may benefit from targeted interventions.

Abbott Pharmaceuticals (Jorgensen)

4/1/04 – 3/31/05

Radiosensitization of Human Colon Cancer by Antimitotic Agent, ABT-751, in a Mouse Xenograft Model

The specific aim of this study is to determine whether there are additive or synergistic interactions between ABT-751 and ionizing radiation for inhibition of tumor growth in a subcutaneous athymic xenograft mouse model of human colon cancer.