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**Education and Training:**

<i>Year</i>	<i>Institution and Location</i>	<i>Degree</i>	<i>Area</i>
<b>UNDERGRADUATE:</b>			
1969-1973	West Virginia Institute of Technology Montgomery, WV	B.S., 1973	Biology
<b>GRADUATE:</b>			
1973-1980	West Virginia University Morgantown, WV	Ph.D., 1980	W. Kaczmarczk, Ph.D. Genetics
<b>POSTGRADUATE:</b>			
1980-1982	Mayo Foundation Rochester, MN	Post-Doc	Carlo Veneziale, M.D., Ph.D. Biochemistry
1982-1984	Mayo Clinic Rochester, MN	Post-Doc	Henry Homburger, M.D. Clinical Immunology

**Appointments and Positions:**

**ACADEMIC:**

1987-1989	University of Pittsburgh Pittsburgh, PA	Research Associate in Radiation Oncology
1989-1990	University of Pittsburgh Pittsburgh, PA	Research Instructor in Radiation Oncology
1990-2000	University of Pittsburgh Pittsburgh, PA	Research Assistant Professor Research Division Radiation Oncology
2000 - 2010	University of Pittsburgh Pittsburgh, PA	Research Associate Professor Research Division Radiation Oncology
2010 – Present	University of Pittsburgh Pittsburgh, PA	Research Professor Research Division Radiation Oncology

**NON-ACADEMIC:**

1980-1982	Mayo Foundation Rochester, MN	Postdoctoral Fellow in Cell Biology
1982-1984	Mayo Foundation	Special Projects Associate in Clinical
1984-1987	Allegheny-Singer Research Foundation Pittsburgh, PA	Immunochemist

**Memberships In Professional And Scientific Societies:**

American Association of Cancer Research	1989
American Society of Gene Therapy	1998
American Society of Hematology	1995
American Society for Therapeutic Radiology and Oncology	2003
International Society of Hematology	1995
Radiation Research Society	1989

**Honors:**

Alumnus of the year, West Virginia University Institute of Technology	1996
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**Publications:**

*Peer Reviewed Articles:*

1. **Epperly MW**, Donofrio J, Barham S, Venezia CM. Nuclear protein matrix of seminal vesicle epithelium. *J Steroid Biochem* 20:691-697, 1984.
2. Venezia C, **Epperly MW**, Barham S, Norvitch ME, Moore JT. Seminal vesicle epithelial individual cell growth and cell replenishment. In: *Control of Growth and Proliferation*. Carlo Venezia (ed), Van Nostrand Reinhold, New York, NY, pp. 1-10, 1984.
3. **Epperly MW**, Barham S, Norvitch M, Holicky E, Moore J, Venezia CM. The growth of individual seminal vesicle epithelial cells and their proliferation. *Proc Soc Exp Biol Med* 178:443-456, 1985.
4. **Epperly MW**, Bloomer WD. Systemic radiotherapy using auger and alpha emitting radionuclides. *Chemtech* 21:744-749, 1991.
5. **Epperly MW**, Damodaran KM, McLaughlin WH, Pillai KMR, Bloomer WD. Radiotoxicity of 17a[125]iodovinyl-11B-methoxyestradiol in MCF-7 human breast cancer cells. *J Steroid Biochem Molec Biol* 39:729-734, 1992.
6. Papadopoulou MV, **Epperly MW**, Shields DS, Bloomer WD. Radiosensitization and hypoxic cell toxicity of NLA-1 and NLA-2, two new bioreductive compounds. *Japanese J Cancer Res* 83:410-414, 1992.
7. Prezioso J, **Epperly MW**, Bloomer WD. Effects of tyrosine activity on the cytotoxicity of 4-S-cysteaminy phenol and N-acetyl-4-S-cysteaminy phenol in melanoma cells. *Cancer Letters* 63:73-79, 1992.
8. Ranadive GN, Rosenzweig HS, **Epperly MW**, S Bloomer WD. A technique to prepare boronated B72.3 monoclonal antibody for boron neutron capture therapy. *Nucl Med Biol* 20:1-6, 1993.
9. Ranadive GN, Rosenzweig HS, **Epperly MW**, Sesky T, Bloomer WD. A new method of technetium-99m labelling of monoclonal antibodies through sugar residues. A study with TAG-72 specific CC49 antibody. *Nucl Med Biol*, 20:719-726, 1993.
10. Koros AMC, Tobin MJ, **Epperly MW**, Levine G, McGinley JR. 186-Rhenium monoclonal antibody targets human small cell lung cancer cells in athymic nude mice: rapid screening model for therapy. *Anticancer Res* 13:1953-1956, 1993.
11. Damodaran KM, **Epperly MW**, Pillai KMR, Bloomer WD. A facile and improved synthesis of 17a-(2-[E]-{125-I}-iodovinyl)-19-nortestosterone, a no-carrier added ligand for progesterone receptor analyses. *J Labelled Compounds Radiopharm* 34:17-26, 1994.

12. **Epperly MW**, Deutsch M. 5-Iodo-2-deoxyuridine as cytotoxic chemotherapy and as a possible radiosensitizer in a mouse ovarian ascites tumor model. *Radiation Oncol Invest* 1:334-338, 1994.
13. Rosenzweig HS, Ranadive GN, Sesky T, **Epperly MW**, Bloomer WD. A novel method for the non-chromatographic purification of technetium-99m-labelled monoclonal antibodies: a study with B72.3 monoclonal antibody. *Nucl Med Biol* 21:171-178, 1994.
14. Jonnalagadda SS, Mokotoff M, Swanson DP, Brown ML, **Epperly MW**. 111-Indium-labelled laminin peptide fragments as potential diagnostic agents for metastatic cancers. *Proc 13th Am Peptide Symp, Peptides: Chemistry, Structure, and Biology*. RS Hodges and JA Smith (eds) ESCOM: Leiden, pp. 854-856, 1994.
15. Papadopoulou MV, Miller A, Sesky T, **Epperly MW**, Bloomer WD. Potentiation of antineoplastic drugs in vitro and in vivo by DNA intercalating bioreductive agents. *Radiat Oncol Invest* 1:206-217, 1994.
16. **Epperly MW**, Santucci MA, Reed J, Shields D, Halloran A, Greenberger JS. Expression of the human BCL-2 transgene increases the radiation resistance of a hematopoietic progenitor cell line. *Radiat Oncol Invest* 2:77-84, 1994.
17. Kalend AM, Bloomer WD, **Epperly MW**. Dosimetric consequences of 10-B(n,a)7-Li reaction occurring at the cellular membrane. *Int J Radiat Oncol Biol Phys* 31(1):171-178, 1995.
18. **Epperly MW**, Berry LM, Halloran A, Griffin J, Sherr J, Greenberger JS. Inhibition of G1 phase arrest induced by ionizing radiation in hematopoietic cells by overexpression in genes involved in the G1/S phase transition. *Radiat Res* 143:245-254, 1995.
19. Rosenstein M, **Epperly MW**, Hughey R, Prezioso J, Greenberger JS. Overexpression of the gamma glutamyltranspeptidase transgene does not alter the gamma-irradiation sensitivity of the IB3-1 normal bronchoepithelial or A549 human lung carcinoma cell line. *Radiat Oncol Invest* 3(1):9-16, 1995.
20. Znati C, Rosenstein M, Boucher Y, **Epperly MW**, Bloomer WD, Jain RK. Effect of radiation on interstitial fluid pressure and oxygenation in a human tumor xenograft. *Cancer Res* 56:964-968, 1996.
21. Greenberger JS, Anderson J, Berry LA, **Epperly MW**, Cronkite EP, Boggs SS. Effects of irradiation of CBA/Ca mice on hematopoietic stem cells and stromal cells in long term bone marrow cultures. *Leukemia* 10(3):514-527, 1996.
22. Greenberger JS, **Epperly MW**, Zeevi A, Brunson KW, Goltry KL, Pogue-Geile KL, Bray J, Berry LA. Stromal cell involvement in leukemogenesis and carcinogenesis. *In Vivo* 10:1-18, 1996.

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25. Feero WG, Rosenblatt JD, Huard J, Watkins SC, **Epperly MW**, Clemens PR, Kochanek S, Glorioso JC, Patridge TA, Hoffman EP. Viral gene delivery to skeletal muscle: insights on maturation-dependent loss of fiber infectivity for adenovirus and herpes simplex type I viral vectors. *Hum Gene Ther* 8:371, 1997.
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31. **Epperly MW**, Bray JA, Krager S, Berry LA, Gooding W, Engelhardt JF, Zwacka R, Travis EL, Greenberger JS. Intratracheal injection of adenovirus containing the human MnSOD transgene protects athymic nude mice from irradiation-induced organizing alveolitis. *Int J Radiat Oncol Phys* 43(1):169-181, 1999.
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44. **Epperly MW**, Gretton JA, DeFilippi SJ, Sikora CA, Liggitt D, Koe G, Greenberger JS. Modulation of radiation-induced cytokine elevation associated with esophagitis and esophageal stricture by manganese superoxide dismutase-plasmid/liposome (*SOD-PL*) gene therapy. *Radiat. Res.*, 155:2-14, 2001.
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57. **Epperly MW**, Guo HL, Gretton JE, and Greenberger JS. Bone marrow origin of myofibroblasts in irradiation pulmonary fibrosis. *Am J Respir Cell Mol Biol* 29:213-224, 2003.
58. Perry Y, **Epperly MW**, Finkelstein S, Klein ED, Greenberger JS, and James Leuketich. An Animal Model of Photodynamic Therapy Induced Proceedings of SPIE Vol 4949 Lasers in Surgery: Advanced Characterization, Therapeutics and Systems XIII, Edited by Lawrence S. Bass, Nikiforos Kollias, Reza S. Malek, Abraham Katzir, Udayan K. Shah, Brian J.F. Wong, Eugene A. Trowers, Timothy A. Woodward, Werner T. W. de Riese, David S. Robinson, Hans-Dieter Reidenbach, Keith D. Paulsen, and Kenton W. Gregory, (SPIE, Bellingham, WA, 2003, pages 395-404
59. **Epperly MW**, Bernarding M, Gretton J, Jefferson M, Nie S, Greenberger JS. Overexpression of the transgene for manganese superoxide dismutase (MnSOD) in 32D cl 3 cells prevents apoptosis induction by TNF- $\alpha$ , IL-3 withdrawal and ionizing irradiation. *Experimental Hematology* 31 (6):465-474, 2003.
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61. Cao B. Zheng B. Jankowski RJ. Kimura S. Ikezawa M. Deasy B. Cummins J. **Epperly M**. Qu-Petersen Z. Huard J. Muscle stem cells differentiate into haematopoietic lineages but retain myogenic potential. *Nature Cell Biology*. 5(7):640-6, 2003.
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72. **Michael W. Epperly**, Hongmei Shen, Mia Jefferson, and Joel S. Greenberger. In Vitro Differentiation capacity of esophageal progenitor cells with capacity for homing and repopulation of the ionizing irradiation-damaged esophagus. *In Vivo* 18:675-686, 2004.
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76. **Epperly Michael W**, Cao Shaonan, Goff Julie, Shields Donna, Zhou Shuanhu, Glowacki Julie, Greenberger Joel. Increased longevity of hematopoiesis in continuous bone marrow cultures and adipocytogenesis in marrow stromal cells derived from SMAD3<sup>-/-</sup> mice. *Experimental Hematology*, 33(3): 353-362, 2005.
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### **Publications in Non-Peer-Reviewed Journals:**

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355A. **Epperly Michael W**, Chaillet J Richard, Cao Shaonan, Zhang Xichen, and Greenberger Joel S. Use of MnSOD tet on transgenic mice as a model for evaluating irradiation protection and mitigation. AACR, May, 2012.

356A. Goff Julie P, Skoda Erin, Li Song, Gao Xiang, **Epperly Michael W**, Franicola Darcy, Houghton Frank, Wipf Peter, and Greenberger Joel S. Localization of mitochondrial targeted GS-nitroxide JP4-039 BODIPY FL conjugate during radioprotection and mitigation in vivo. AACR, May, 2012.

357A. Goff Julie, Shields Donna, Wang Hong, Skoda Erin, Sprachman Melissa, Wipf Peter, Atkinson Jeffrey, **Epperly Michael**, Kagan Valerian E, Lazo John S, and Greenberger Joel S. Identification of ionizing irradiation damage mitigators by evaluation of clonogenic survival of human umbilical cord blood progenitor cells. ASTRO, Boston, MA, September, 2012. P.S680, IJROBP, Vol. 84 (Suppl. 35), 2012, #2229.

358A. **Epperly Michael W**, Cao Shaonan, Dixon Tracy, Goff Julie P, Glowacki Julie, Wipf Peter, and Greenberger Joel S. Irradiation inhibition of bone repair in SAMP6 mice. ASTRO, Boston, MA, September, 2012. P. S674, IJROBP, Vol. 84 (Suppl. 35), 2012, #3214.

359A. Yang Yong, **Epperly Michael W**, Dixon Tracy M, Heron Dwight E, Greenberger Joel S, and Huq M Saiful. Total body irradiation at high dose rate using a True Beam accelerator results in increased survival in a mouse model. ASTRO, Boston, MA, September, 2012. P. S162, IJROBP, Vol. 84 (Suppl. 35), 2012, #3700.

360A. Kalash Ronny, Chaillet Richard, Houghton Frank, Zhang Xichen, **Epperly Michael W**, Cao Shaonan, and Greenberger Joel S. Irradiation induction of mRNA for redox-sensitive promoters and inflammatory cytokines in conditional Manganese Superoxide Dismutase (MnSOD) tet on-/- mouse bone marrow stromal cells. ASTRO, Boston, MA, September, 2012. P. S673, IJROBP, Vol. 84 (Suppl. 35), 2012, #5211.

361A. Kalash Ronny, Zhang Xichen, Houghton Frank, **Epperly Michael W**, Dixon Tracy M, and Greenberger Joel S. Elevated pulmonary MnSOD and endothelial gene expression heralds the onset of irradiation fibrosis. ASTRO, Boston, MA, September, 2012. P. S678, IJROBP, Vol. 84 (Suppl. 35), 2012, #3224.

362A. Sprachman Melissa M, **Epperly Michael W**, Wipf Peter, Shields Donna, Dixon Tracy M, Cao Shaonan, Goff Julie, and Greenberger Joel S. MMS350: a novel bifunctional sulfoxide with radiation protection and mitigation properties. ASTRO, Boston, MA, September, 2012. P. S680, IJROBP, Vol. 84 (Suppl. 35), 2012, #3228.

363A. **Epperly Michael W**, Chaillet J Richard, Goff Julie, Kalash Ronny, Shaffer Ben, Franicola Darcy, Houghton Frank, Cao Shaonan, Zhang Xichen, and Greenberger Joel S. Induction of MnSOD expression in MnSOD tet-on-/- murine bone marrow stromal cell lines correlates with temporal radiation resistance. ASTRO, Boston, MA, September, 2012. P. S677, IJROBP, Vol. 84 (Suppl. 35), 2012, #3223.

364A. Berhane Hebist, **Epperly Michael W**, Dixon Tracy M, Cao Shaonan, Shields Donna, Wipf Peter, Li Song, Gao Xiang, and Greenberger Joel S. Oral delivery of mitochondrial targeted GS-nitroxide JP4-039 protects Fanconi Anemia (FA) D2-/- mice from irradiation mucositis. ASTRO, Boston, MA, September, 2012. P. S677, IJROBP, Vol. 84 (Suppl. 35), 2012, #3222.

365A. Greenberger Joel S, Goff Julie P, Dixon Tracy M, Kim Hyun, Skoda Erin, Wipf Peter, Wang Hong, Li Song, Gao Xiang, and **Epperly Michael W**. Intraesophageal administration of radioprotector GS-Nitroxide (JP4-039) does not protect LSL-K-ras transgenic lung tumors. Radiation Research Society, October, 2012.

366A. **Epperly Michael W**, Cao Shaonan, Smith Tracy M, Friedlander Robert, and Greenberger Joel S. Lack of radioresistance of Caspase-1 homologous deletion recombinant negative mice. Radiation Research Society, October, 2012.

367A. Goff Julie, **Epperly Michael W**, Dixon Tracy M, Sprachman Melissa M, Wipf Peter, Zhang Xichen, and Greenberger Joel S. Live imaging of Luciferase positive bone marrow

stromal cell migration to form radiation pulmonary fibrosis. Radiation Research Society, October, 2012.

368A. Kanter David, O'Brien Matthew B, Shi Xiao-Hua, Beriwal Sushil, **Epperly Michael W**, Greenberger Joel S, and Sadovsky Yoel. The effect of ionizing radiation on murine fetal growth. S.G.I. Conference, 2012.

269A. Houghton Frank, **Epperly Michael W**, Chaillet J Richard, Cao Shaonan, Zhang Xichen, and Greenberger Joel S. Use of MnSOD tet on transgenic mice as a model for evaluating irradiation protection. UPCI Retreat, 6/12.

370A. Kanter David, O'Brien Matthew B, Beriwal Sushil, **Epperly Michael W**, Greenberger Joel S, and Sadovsky Yoel. The effect of ionizing radiation on murine fetal growth. UPCI Retreat, 6/12.

371A. Kalash Ronny, Houghton Frank, Zhang Xichen, Wang Hong, **Epperly Michael W**, and Greenberger Joel S. Pulmonary endothelial cell irradiation damage signaling initiates late fibrosis. ASH, 12/12.

372A. Goff Julie, Dixon Tracy M, **Epperly Michael W**, Sprachman Melissa M, Wipf Peter, Zhang Xichen, and Greenberger Joel S. Serial imaging of luciferase positive bone marrow stromal cell migration to form radiation pulmonary fibrosis. ASH, 12/12.

373A. Berhane Hebist, **Epperly Michael W**, Cao Shaonan, Zhang Xichen, Shields Donna, Goff Julie, Sprachman Melissa, Wipf Peter, Li Song, Gao Xiang, and Greenberger Joel S. Diminished oxidative stress responses in bone marrow stromal cell lines derived from Fanconi Anemia (FancD2<sup>-/-</sup>) mice. ASH, 12/12.

374A. Lazo John S, **Epperly Michael W**, Sharlow Elizabeth R, Lira Ana, Skoda Erin, Wipf Peter, Kagan Valerian, and Greenberger Joel S. Disruption of the PI3K axis abrogates ionizing radiation-induced cell death. Exp. Biology Annual Meeting, 2013.

375A. Kalash Ronny, Houghton Frank, Berhane Hebist, Wipf Peter, Shields Donna, **Epperly Michael W**, Chaillet J Richard, Cao Shaonan, Zhang Xichen, and Greenberger Joel S. GS nitroxide (JP4-039) induces radiation resistance of conditional MnSOD tet/tet murine bone marrow stromal cells. AACR, 2013.

376A. Berhane Hebist, Goff Julie P, Kalash Ronny, **Epperly Michael W**, Dixon Tracy, Francicola Darcy, and Greenberger Joel S. In field head and neck irradiation radiosensitivity of FancD2<sup>-/-</sup> mice and bystander effect reduction of distant marrow hematopoietic progenitor cells. AACR, 2013.

377A. Berhane Hebist, **Epperly Michael W**, Francicola Darcy, Goff Julie, Zhang Xichen, Shields Donna, Cao Shaonan, and Greenberger Joel S. Diminished oxidative stress responses and DNA repair in irradiated FancD2<sup>-/-</sup> mouse bone marrow stromal cell lines. ACRO, 2013.

389A. Kalash Ronny, Houghton Frank, Berhane Hebist, Chaillet J Richard, Zhang Xichen, Cao Shaonan, **Epperly Michael W**, Sprachman Melissa, Wipf Peter, and Greenberger Joel S. Small molecule radioprotectors JP4-039 and MMS350 alter irradiation induction of mRNA for redox-sensitive promoters and inflammatory cytokines in conditional Manganese Superoxide Dismutase (MnSOD) tet/tet mouse bone marrow stromal cell lines. ACRO, 2013.

390A. Houghton Frank, **Epperly Michael W**, Zhang Xichen, Nimgaonkar Vishwajit, and Greenberger Joel S. Radiosensitivity of human induced pluripotent stem cells (hiPSC) detectable by cell cycle analysis. ACGCT, 2013.

### ***Presentations***

1. **Epperly MW**, Jahroudi N, Rosenstein M, Shields D, Engelhardt J, Huang L, Greenberger JS. Protection of the lung from ionizing irradiation damage by inhalation gene therapy. The 37<sup>TH</sup> Annual Scientific Meeting of the American Society for Therapeutic Radiology & Oncology, Miami Beach, FL (October 8-11, 1995).

2. **Epperly MW**, Shiffer C, Escobar P, Bray JA, Watkins SC, Bigbee WL, Greenberger JS. Overexpression of MnSOD *in vitro* increases the radioresistance of 32D cl 3 hematopoietic progenitor cells. The 89<sup>TH</sup> Annual Meeting of the AACR, New Orleans, LA (March 28 - April 1, 1998).

3. **Epperly MW**, Bray JA, Escobar P, Bigbee WL, Watkins SC, Greenberger JS. Overexpression of the human MnSOD transgene *in vitro* protects 32D cl 3 murine hematopoietic progenitor cells from irradiation-induced apoptosis. The 40<sup>TH</sup> Annual Scientific Meeting of ASTRO, Phoenix, AZ (October 25-29, 1998).

4. **Epperly MW**, Bray JA, Defilippi S, Greenberger JS. Overexpression of manganese superoxide dismutase in the 32D cl 3 murine hematopoietic progenitor cell line prevents apoptosis induced by ionizing irradiation, IL-3 withdrawal, or exposure to TNF- $\alpha$ . The 28<sup>TH</sup> Annual Meeting of the International Society of Experimental Hematology, Monte Carlo, Monaco (July 10-14, 1999).

5. **Epperly MW**, Defilippi S, Sikora C, Gretton J, Greenberger JS. Radioprotection of lung and esophagus by overexpression of the human MnSOD transgene. International Conference on Low-Level Radiation Injury and Medical Countermeasures. Sponsored by the Armed Forces Radiobiology Research Institute, Bethesda, MD, November 8-10, 1999. LLR-99 (Session 2. Prevention and Treatments; Session 2B. Protective Devices and Strategies, p. 33.

6. **Epperly MW**, Defilippi SJ, Sikora CA, Gretton JE, Pierce L, Peterson J, Kagan V, Greenberger JS. Overexpression of the human MnSOD transgene prevents irradiation apoptosis of 32D cl 3 hematopoietic progenitor cells by stabilization of the mitochondria. The 29<sup>th</sup> Annual Scientific Meeting of the International Society Of Experimental Hematology, Tampa, FL, July 8-11, 2000. *Exp. Hematol.*, 28(7):Suppl. #1:35 (Abstract #14), 2000.

7. **Epperly MW**, Sikora CA, Gretton JE, DeFilippi SJ, Greenberger JS. Late upregulation of VCAM-1 and ICAM-1 in irradiated murine pulmonary endothelial and lung parenchymal cells precedes recruitment of bone marrow-derived macrophages and fibrosis. The 43<sup>rd</sup> Annual Meeting of the American Society for the Therapeutic Radiology and Oncology (ASTRO), San Francisco, CA, November 4-8, 2001.
8. **Epperly MW**, Greenberger JS, Gretton JE, Jefferson M, Bernarding M. Title: The importance of mitochondrial localization for the prevention irradiation-induced apoptosis by manganese superoxide dismutase. 31<sup>st</sup>. Annual Meeting International Society for Experimental Hematology, Montreal, Canada, July 5 – 9, 2002.
9. **Epperly MW**, Jefferson M, Guo HL, Gretton JE, Bernarding M, Greenberger JS. Title: Pre-but not post irradiation intratracheal injection of manganese superoxide dismutase-plasmid/liposomes (MnSOD-PL) protects the lung from irradiation damage. The 44<sup>th</sup> Annual Meeting of the American Society for the Therapeutic Radiology and Oncology, New Orleans, La, October 6 – 10, 2002.

## **Professional Activities:**

### **TEACHING:**

Dr. Epperly is the Course Director for the Radiobiology Course taught to the Radiation Oncology residents. Dr. Epperly was involved with establishment of the Radiobiology Course since the inception of the Radiation Oncology Residency Program in 2000. Dr. Epperly has been involved in the laboratory training of three medical students who have taken a one-year leave of absence between their third and fourth year of medical school to work in his lab to gain research experience before completing medical school. Other medical students have spent one rotation of their medical school experience in his laboratory to determine whether they wanted to pursue further research opportunities. Dr. Epperly has been involved in the training of two Ph.D. students and two postdoctoral fellows. Dr. Epperly has also been responsible for the Radiation Oncology Research Seminars.

## **SUMMARY OF CURRENT RESEARCH FUNDING**

### **ACTIVE**

2U19AI068021-11(Greenberger) NIH/NIAID CMCR “ <b>Signature-Directed, Sequential Delivery of Radiation Mitigators</b> ”	09/01/15-08/31/20	3.6 calendar months
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Project I

The goal of Project 1 of the CMCR grant is to develop new drugs to mitigate irradiation damage by targeting antioxidant and other small molecules to the mitochondria.

2U19AI068021-11 (Greenberger) 09/01/15-08/31/20 3.0 calendar months  
NIH/NIAID

**CMCR “Signature-Directed, Sequential Delivery of Radiation Mitigators”**

Core C

The goal of Core C of the CMCR grant is to support the four projects in the CMCR grant by in vitro and in vivo analysis of the ability of the new compounds to mitigate against irradiation damage.

2RO1 DK071085 (Kanai) 04/01/13 – 03/31/18 0.86 calendar months  
NIH **“Roles of Nitric Oxide”** The goal of this grant is to investigate the role of nitric oxide in radiation damage to the urinary bladder.

RO1 GM102989-01 (Li) 07/01/13 – 04/30/17 0.96 calendar months  
NIH **“Rational Design of Lipidic Vectors for Mitochondria-Targeted Antioxidants”** The goal of this project is to design new liposomal vector for the delivery of antioxidants to the mitochondria.

**PRIOR**

1U19A168021-01 (PI: Joel S. Greenberger, M.D.) 09/01/10-08/31/15  
Co-Investigator Project 1 and Director of Core F: Michael W. Epperly, Ph.D. 20% Effort  
**“Mitochondrial Targets Against Radiation Damage”**

NIH/NIAID Center for Medical Countermeasures Against Radiation (CMCR)

The goal of this project is to develop radioprotector/mitigator drugs focused on neutralizing mitochondrial specific steps in early response to irradiation damage which will prevent irreversible cell death.

NIH-2R01CA119927-08A1 (PI: Joel S. Greenberger, M.D.) 02/01/06-01/31/11  
Co-Investigator: Michael W. Epperly, Ph.D. 15% Effort

**“Mechanism of Irradiation Pulmonary Fibrosis”**

The goal of this grant is define critical steps in irradiation pulmonary fibrosis and identify new targets for therapeutic intervention, thereby decreasing patient side effects and facilitating dose escalation in the initial treatment or retreatment of recurrent thoracic cancers.

BARDA/HHS HHS0100200800062C (PI: Joel S. Greenberger, M.D.) 09/16/08-09/15/09  
Co-Investigator: Michael W. Epperly, Ph.D. 20% effort

**“Novel Mitochondrial Targeted Drugs for Treatment of the Irradiation-Induced Hematopoietic Syndrome”**

This contract will develop the optimal GS-nitroxide drug (JP4-039) from a library of novel small molecules to be a new mitigator when delivered 24 hours after irradiation to enhance bone marrow stromal cell recovery and

improve engraftment of circulating marrow stromal and hematopoietic stem cell progenitors in the irradiation damaged hematopoietic microenvironment.

NIH-1-R01-DK071085-1-DRG/NIH (PI: Anthony Kanai, Ph.D.) 4/01/05-03/31/10  
Co-Investigator: Michael W. Epperly, Ph.D. 10% effort

**“Roles of Nitric Oxide and Superoxide in Cystitis”**

The goal of this project is to investigate the production of nitric oxide and superoxide in the bladder following irradiation and their involvement in irradiation-induced cystitis of the bladder.

NIH-RC1-A1081284 (PI: Louis D. Falo, M.D.) 09/10/08-09/10/10  
Co-Investigator: Michael W. Epperly, Ph.D. 10% effort

**“Novel Cutaneous Radiation Injury Countermeasures”**

The goal of this project is to develop new small molecule drugs and delivery systems to deliver the drugs to the skin to prevent irradiation induced damage to the skin.

NIH-R01-CA83876-06 (PI: Joel S. Greenberger, M.D.) 08/02/06-06/30/11  
Co-Investigator: Michael W. Epperly, Ph.D. 25% Effort

**“Gene Therapy Reduction of Radiotherapy Esophagitis”**

The goal of this grant is to expand the molecular mechanism of esophageal radiation protection by MnSOD-PL administration.

1-R01-HL60132 – Competitive Renewal – DRG/NIH 2/01/02 - 1/31/07  
PI: Joel S. Greenberger, M.D. \$39,056  
Co-Investigator: Michael W. Epperly, Ph.D. (15% effort)

**“Lung Radiation Protection by MnSOD-Transgene Therapy”**

The goal of this grant will be to use validated, genetically modified animal models along with quantitative molecular methods to elucidate the cellular mechanism of irradiation lung fibrosis and the level(s) at which epitope-hemagglutinin (HA)-tagged manganese superoxide dismutase (MnSOD) transgene therapy protects.

1-R01-CA92389-01A1 04/01/03 - 03/31/07  
PI: Andrew A. Amoscato, M.D. \$28,752  
Co-Investigator: Michael W. Epperly, Ph.D. (5% effort)

**“Radiation-Induced Ceramide Generation”**

The goal of this grant is to look at the effect of irradiation on mitochondrial ceramide and its role in irradiation-induced apoptosis.

1-R01-CA83876-02 07/01/02 - 06/30/06  
PI: Joel S. Greenberger, M.D. \$30,158  
Co-Investigator: Michael W. Epperly, Ph.D. (27.5% effort)

**“Gene Therapy Reduction of Radiotherapy Esophagitis”**

The goal of this grant is to expand the molecular mechanisms of esophageal radiation protection by MnSOD-PL and the involvement of esophageal stem cells in irradiation protection.

1-R01-CA-101837-01A2-DRG/NIH 1/01/05 - 12/31/08  
**“MnSOD-PL Irradiation Protection of the Oral Cavity”** \$9,847  
PI: Joel S. Greenberger, M.D. (10% effort)  
Co-Investigator: Michael W. Epperly, Ph.D.

The goal of this grant is to investigate the protection of the oral cavity from irradiation damage by administration of MnSOD-PL, and to determine the effects of increased expression of MnSOD in on the antioxidant levels in tumors of the head and neck and normal tissue of the oral cavity.

NIH 1R01-CA92389-01A1

Lung Cancer SPORE (PI: Jill Siegfried, Ph.D.)

04/01/01 – 01/01/05

(Project #4: PI: Joel S. Greenberger, M.D., Co-I: Michael Epperly, Ph.D.)

\$17,145 (20% effort)

**"Protection of esophagus and normal lung from chemoradiotherapy (CRT) damage with radiosensitization of tumor in non-small cell lung carcinoma (NSCLC) patients by manganese superoxide dismutase-plasmid/liposome (MnSOD-PL) gene therapy."**

The goal of this project is to demonstrate in clinical trials that overexpression of MnSOD in normal tissue protects against irradiation and chemotherapy (chemoradiotherapy - CRT)-induced damage; demonstrate in a clinical trial that MnSOD-PL administration to the esophagus will result in decreased esophagitis in lung cancer patients undergoing CRT; that the optimal biological effective dose, safety of MnSOD-PL, and prevention of esophagitis will be evaluated; and that the studies in this project should lead to an improved quality of life for lung cancer patients requiring CRT.

**LIST OF CURRENT RESEARCH INTERESTS**

1. Use of gene therapy for protection of normal tissue from irradiation damage.
2. Development of new small molecules to protect tissue from irradiation damage.
3. Effects of irradiation on bone healing.
4. Use of antioxidant diets to protect astronauts from irradiation exposure during space travel.
5. Use of stem cells in repair of irradiation damage.

**RESEARCH PLANS**

Irradiation exposure has a dramatic effect of tissues in the body. It can result in alteration of many cellular activities such as development of fibrosis or cancer, premature aging or death. Currently, there is little that can be done to protect people from irradiation. Development of new methods of treating people exposed to irradiation needs to be intensified. To effectively develop ways to prevent the effects of irradiation, we must understand the mechanism of irradiation induced damage. In the past we have demonstrated the importance of stabilizing the mitochondria in the protection of the cell from irradiation. Many of the methods for preventing tissue damage from irradiation will use modalities which will protect the mitochondria. This may involve gene therapy techniques using plasmids carrying transgenes for proteins such as manganese superoxide dismutase or catalase as well as development of new small molecules that will deliver antioxidants to the mitochondria. We will also be investigating new diets which contain high levels of antioxidants to see if these diets can lead to increased concentrations of antioxidants in cells accompanied by increased survival following irradiation. The use of stem cells may have a profound effect on the repair of irradiated tissues. We have already demonstrated that increased expression of MnSOD at the time of irradiation results in increased migration of bone marrow stem cells to the irradiated damage resulting in increased survival. We will continue to investigate how hematopoietic stem cells or tissue specific stem cells can aid in the repair of irradiation damage. The overall objective of the lab will be to better understand the effects of irradiation on tissues and the development of new modalities to prevent the irradiation damage.

**Patents:**

1. Inventors: Drs. G. Ranadive, H.S. Rosenzweig, **M. W. Epperly**, and W.D. Bloomer

Organization: University of Pittsburgh

Title: “Regioselective chemical modification of monoclonal antibodies”

Frederick H. Colen, Esquire  
Reed, Smith, Shaw & McClay  
435 Sixth Street  
Pittsburgh, PA 15219-1996  
US Patent Application Serial No. 07/613,127, Filed 11/14/90  
US Patent #5,208,008; Issued 5/4/93  
Ref#90-230

2. Inventors: Drs. M. Papadopoulou-Rosenzweig, W.D. Bloomer, **M.W. Epperly**

Organization: University of Pittsburgh

Title: “Acridine-intercalator based hypoxia selective cytotoxins”

Frederick H. Colen, Esquire  
Reed, Smith, Shaw & McClay  
435 Sixth Street  
Pittsburgh, PA 15219-1996  
US Patent Application Serial No. 07/649,703, Filed 02/01/91; Ref#91-012

3. Inventor: Joel S. Greenberger, **Michael W. Epperly**

Organization: University of Pittsburgh Cancer Institute

Title: “Isolation of a transplantable esophageal/intestinal stem cell and methods of use thereof” Leslie Serunian, Esquire, Morgan & Finnegan, L.L.P., 345 Park Avenue, New York, NY, 10154-0053

Client Reference File#540; Attorney Reference File #2710-4009

USA Serial Patent #

Filing Date:

4. Inventor: Mitchell Fink, M.D., Joel Greenberger, M.D., **Michael Epperly, Ph.D.**

Title: “**Provisional patent application entitled “Radioprotective Agents”**”

Patent Application for Novel Radioprotective Agents

Our Ref: 027704.00027, Serial # PCT/USOG/28530, JH ref. 002.00B1PCT, Pitt Ref. 01007

Filing Date: 7/27/2005

5. Inventor: Anthony Kanai, Ph.D., Mark Zeidel, Ph.D., **Michael Epperly, Ph.D.**, Joel S. Greenberger, M.D.  
Title: **“Inhibition of Mitochondrial Nitric Oxide Synthase protects the bladder urothelium against radiation damage”**  
Our Ref.:  
Filing Date: 9/30/05  
Date Occurred: 2/1/03
  
7. Inventor: **Michael W. Epperly, Ph.D.**, Joel S. Greenberger, M.D., Jianfei, Jiang, Ph.D., Valerian E. Kagan, Ph.D., John S. Lazo, Ph.D., and Peter R. McDonald, Ph.D.  
Title: **“Radioprotective Agents”**  
United States Patent Application No. 8,883,852  
Issued November 11, 2014  
Webb reference:6527-112733  
Pitt Reference: 01830 0002.0158PCTUS.
  
8. Inventor: Peter Wipf, Ph.D., Natalia A. Belikova, Ph.D., Jianfei Jiang, Ph.D., Joel S. Greenberger, M.D., Joshua G. Pierce, Ph.D., and **Michael W. Epperly, Ph.D.**  
Title: **“Use of Targeted Nitroxide Agents in Preventing, Mitigating and Treating Radiation Injury”**  
US Patent Number: 8,822,541  
Issued September 2, 2014  
Pitt Reference number: 01734  
Klarquist Reference number 8123-88710-03
  
9. Inventors: Michael W. Epperly, Abhay Sudhir Gokhale; Joel S. Greenberger, Peter Wipf; Julianne Glowacki.  
Title: **“Use of Targeted Nitroxide Agents in Bone Healing”**  
Pitt Ref. No 01966  
Application No. 13/320,999 filed April 30, 2012  
US Patent No. 8,748,369 issued Date June 10, 2014.
  
10. Inventors: Michael W. Epperly, Joel S. Greenberger, Xiang Gao, Song Li, and Peter Wipf  
Title: **“Intraesophageal Administration of Targeted Nitroxide Agents for Protection Against Ionizing Irradiation-Induced Esophagitis”**  
Pitt Ref.: 02294  
JH Ref.: 0002.0233P  
Current Status: Submitted  
Submitted: 11/12/10
  
11. Inventors: Michael W. Epperly and Joel S. Greenberger

Title: “**Carbamazepine is a Radiation Protector and Radiation Mitigator**”

Pitt Ref: 02293

Current Status: Submitted

Submitted: 11/12/10

12. Inventors: Valerian E Kagan, Jeffrey Atkinson, Detcho A. Stoyanovsky, Michael Epperly, and Joel Greenberger.  
Title: “**Mitochondria-Targeted Specific Inhibitors of Cytochrome C Peroxidase Activity and Cardiolipin Oxidation as Protectors and Mitigators of Irradiation Injury**”  
Pitt Ref No.: 02602  
KS Ref. No.:  
Application No.:  
Filed: 10/31/11
13. Inventors: Peter Wipf, Joel S. Greenberger, Michael W. Epperly, and Melissa M. Sprachman  
Title: “**Bifunctional Compounds**”  
Pitt Ref No.: 02601  
KS Ref. No.: 8123-90010-04  
Application No.: PCT/US2012/061109  
US Patent Number: 9,200,035.  
Date Issued 12/02/2015
14. Inventors: John S. Lazo, Joel S. Greenberger, Michael W. Epperly, Elizabeth R. Sharlow, Peter Wipf, and Erin M. Skoda  
Title: “**Identification of Phosphoinositide-3-Kinase Inhibitors as Mitigators of Ionizing Radiation**”  
Pitt Ref No.: 02624  
KS Ref No.:  
Application No.: 61/589.289  
U.S. Patent Application No. 14/352,891  
Issued December 1, 2015
15. Inventors: Xiang Gao, Peter Wipf, Song Li, Michael W. Epperly, and Joel S. Greenberger  
Title: “**Formulations and Carrier Systems Including Compound Interactive Domains**”  
Pitt Ref. No.: 02645  
Attorney Ref. No.: 12-041P (Bartony & Hare)  
Patent Number 14/651,840  
Awarded: 10./29/2015

**Service**

Institutional Animal Care and Use Committee, University of Pittsburgh, (7/2015 to present).

DLAR Operations Committee, University of Pittsburgh, (9/2015 to Present).

National Organizations:

American Society for Radiation Oncology—Cancer and Radiation Biology Subcommittee (2006 to 2009).

Community Organizations:

Boy Scouts of America—Committee Member for Troop 36 (2004 to 2009).