# Steven P. Zielske

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2010 – 2014	Assistant Professor Department of Radiation Oncology, Wayne State University, Detroit, Michigan
2011 – 2014	Member, Cancer Biology Training Program, Wayne State University
2011 – 2014	Associate Member, Department of Oncology, Karmanos Cancer Institute
2011 – 2014	Member, Molecular Therapeutics Program, Karmanos Cancer Institute
2010 – 2014	Associate Member, Center for Molecular Medicine and Genetics, Wayne State University

Education					
Jul. 2005 – Mar. 2010	Departr	<b>ch Fellowship</b> nent of Radiation O Theodore Lawren	Radiobiology; cancer stem cells chocology, <b>University of Michigan</b> , Ann Arbor, Michigan ce, M.D., Ph.D.		
Feb. 2003 – Jun. 2005	<b>Postdoctoral Fellowship</b> Human immunodeficiency virus molecular biology Program in Molecular Medicine, <b>University of Massachusetts Medical School</b> , Worcester, MA Mentor: Mario Stevenson, Ph.D.				
Jul. 1998 – May 2003	Ph.D. Molecular Virology Division of Hematology/Oncology, Case Western Reserve University, Cleveland, Ohio Mentor: Stanton L. Gerson, M.D. Dissertation title: Transduction of Hematopoietic Stem Cells Using Lentiviral Vectors in Models of Drug Resistance Gene Therapy: Determinants of Transduction and Selection.				
Sep. 1996 – Aug. 1998	M.A.	Biology	St. Cloud State University, St. Cloud, Minnesota		
Sep. 1991 – May 1991	B.A.	Chemistry	Gustavus Adolphus College, St. Peter, Minnesota		

Employment				
1995 - 1996	Research Assistant I: Supervisor: Raymond R. Crowe, M.D., Department of Psychiatry, University of Iowa			
1992 - 1995	Research Assistant I: Supervisor: Joe D. Coulter, Ph.D., Department of Anatomy, University of Iowa			
1987 - 1991	Microcomputer Lab Monitor: Academic Computing, Gustavus Adolphus College			
1987 - 1991	Biology Stockroom Assistant: Department of Biology, Gustavus Adolphus College			

## **Grant Support**

Completed

2/1/12 – 3/31/14. (Zielske and Huttemann) \$50,000

Karmanos Cancer Institute

Effect of optimized radiosensitizing therapy on mitochondrial respiration and apoptosis in breast cancer

1/1/11 – 12/31/11. (Zielske) \$30,000

Wendy Will Case Cancer Fund

The hedgehog pathway and the radiation and chemotherapy response of breast cancer

7/1/08 – 9/30/09. (Zielske) \$75,000

Lung Cancer Research Foundation

Investigation of Mesenchymal Stem Cells for Treatment of Radiation Therapy-induced Lung Injury.

10/1/07 - 6/30/09. (Zielske)

Elsa Pardee Foundation

Enzyme-Prodrug Gene Therapy of Cancer using Mesenchymal Stem Cells.

1/1/07 – 12/31/08. (Zielske) \$95,700.

American Cancer Society PF-07-229-01-MGO

#### LUNGevity Foundation - American Cancer Society Postdoctoral Fellowship in Lung Cancer

\$84.650.

Enzyme-Prodrug Gene Therapy of Cancer using Mesenchymal Stem Cells.

9/1/05 - 8/31/06.

NIH Kirschstein National Research Service Award T32CA09676

Targeting Brain Tumors with Mesenchymal Stem Cells and Enzyme/Prodrug Gene Therapy

7/2003 – 6/2005. NIH Kirschstein National Research Service Award (T32Al07349). 1/2001 – 1/2003. NIH Kirschstein National Research Service Award (T32AG00105).

Teaching Experience				
1999	Tutor: Cell and Molecular Biology. Case Western Reserve University.			
1996-1998	Teaching Assistant: <i>Principles of Biology, Human Biology,</i> and <i>Laboratory Methods in Immunology.</i> St. Cloud State University.			
2008 (fall)	Co-instructor: Radiation Biology (EHS 583 / RTT 423), University of Michigan.			
2010-2014	Co-instructor: Radiation Biology for Residents in Radiation Oncology, Wayne State University			
2011-2014	Co-instructor: Principles of Cancer Therapy, Wayne State University			

## Mentoring

Postdoctoral fellows	Undergraduate students
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Hosam Elbaz, Ph.D. (2012 – 2014) Elizabeth Norgard (2003-2004)

Amar Patel (2013) Fatima Eid (2013)

#### Ethan Brock (2013) Research Assistants

Sajah Ahmed (2007 – 2009) Deborah Antwih (2010 – 2013) Kristina Gabbara (2011 – 2013) Aisha Fasih (2011 – 2013) Morgan Laney (2013 – 2014)

## **Scholarly Activities**

### Ad hoc manuscript reviewer:

Stem Cells (18)

**Graduate Students**Brittany Haynes (2012)

**Medical students** 

Cole Kreofsky (2011)

Intl Journal of Radiation Oncology, Biology, Physics (10)

Translational Oncology (4)

Molecules (3) Cancer Research (2) Anti-Cancer Drugs (2) Mutagenesis (1) Clinical Medicine: Pathology (1)

Clinical Medicine Reviews in Oncology (1) International Journal of Molecular Sciences (1) Environmental and Molecular Mutagenesis (1) Breast Cancer Research and Treatment (1) Free Radical Biology and Medicine (1)

#### Professional memberships:

Radiation Research Society

American Association of Cancer Research

2013: Grant Review Committee, Henry Ford Health System

2000-2001: Organizing Committee, Case Annual Graduate Student Research Symposium

#### **Oral Abstract Presentations**

- 1. **Zielske, SP**, Reese, JS, Lingas, KT, and Gerson, SL **2002**. Human NOD/SCID Repopulating Cells Lentivirus-Transduced with P140K MGMT have a Selective Advantage and are Enriched in Vivo after BG/BCNU Treatment without Pre-transplant Irradiation Conditioning. 1st Annual Gene Therapy Symposium for Heart, Lung, and Blood Diseases: Davis, California.
- 2. **Zielske, SP**; Norgard, E.; Stevenson, MA **2004**. Evaluation of Karyopherin-Mediated Nuclear Import of the HIV Printegration Complex. Cold Spring Harbor Laboratory Retrovirus Meeting: Cold Spring Harbor, New York.
- 3. **Zielske, SP**; Stevenson, MA **2005**. The SUMO Pathway Inhibits HIV Infection of Macrophages. <u>Cold Spring Harbor Laboratory</u> Retrovirus Meeting: Cold Spring Harbor, New York.

## **Peer Reviewed Publications**

- 1. Patki, AH, **Zielske, SP**, Sieg, SF, and Lederman, MM **2000**. Preferential S Phase Entry and Apoptosis of CD4+ T Lymphocytes of HIV-1-Infected Patients after *in Vitro* Cultivation. *Clinical Immunology* 97:241-7.
- Davis, BM, Encell, LP, Zielske, SP, Christians, FC, Liu, L, Friebert, SE, Loeb, LA, and Gerson, SL 2001. Applied Molecular Evolution of O<sup>6</sup>-Benzylguanine-resistant DNA Alkyltransferases in Human Hematopoietic Cells. *Proceedings of the National Academy of Sciences USA* 98:4950-4.
- 3. **Zielske, SP** and Gerson, SL **2002**. Lentiviral Transduction of P140K MGMT into Human CD34<sup>+</sup> Hematopoietic Progenitors at Low Multiplicity of Infection Confers Significant Resistance to BG/BCNU and Allows Selection in Vitro. *Molecular Therapy* 5: 381-7.
- 4. Ballas, CB, **Zielske**, **SP**, and Gerson, SL **2002**. Adult Bone Marrow Stem Cells for Cell and Gene Therapies: Implications for Greater Use. *Journal of Cellular Biochemistry* S38:20-8.
- Wadhwa, PD, Zielske, SP, Roth, JC, Ballas, CB, Bowman, JE, and Gerson, SL 2002. Cancer Gene Therapy: Scientific Basis. Annual Review in Medicine 53:437-52.
- 6. **Zielske, SP** and Gerson, SL **2003.** Cytokines Including SCF Alone Enhance Lentiviral Transduction in Non-dividing LTCIC and NOD/SCID Repopulating Cells. *Molecular Therapy* 7: 325-33.
- 7. **Zielske**, **SP** and Gerson, SL **2003**. SarCNU Mediates Selection of P140K MGMT Transduced Human CD34+ Cells in Vitro. *Blood Cells*, *Molecules*, *and Diseases* 31:48-50.
- 8. Volweiller, J; **Zielske, SP**; Reese, JS; Gerson, SL **2003.** Hematopoietic Stem Cell Gene Therapy: Progress Towards Therapeutic Targets. *Bone Marrow Transplantation* 32:1-7.
- Zielske, SP, Reese, JS, Lingas, KT, Donze, J, and Gerson, SL 2003. In Vivo Selection of MGMT(P140K) Lentivirus-Transduced Human NOD/SCID Repopulating Cells Without Pre-Transplant Irradiation Conditioning. *Journal of Clinical Investigation* 112:1561-70. PMID: 14617757
- 10. **Zielske**, **SP**; Lingas, KT; Li, Y; Gerson, SL **2004**. Limited Lentiviral Transgene Expression with Increasing Copy Number: Lack of Copy Number Selection by Drug Treatment. *Molecular Therapy* 9:923-31.
- 11. **Zielske**, **SP**; Braun, SE **2004**. Cytokines: Value Added Products in Hematopoietic Stem Cell Gene Therapy. *Molecular Therapy* 10:211-9.
- 12. **Zielske, SP**; Stevenson, M. **2005**. Importin 7 May Be Dispensable for HIV-1 and SIV Infection of Primary Macrophages. *Journal of Virology* 79:11541-6.
- 13. **Zielske, SP**; Stevenson, M. **2006.** Modest but Reproducible Inhibition of HIV-1 Infection in Macrophages Following LEDGFp75 Silencing. *Journal of Virology* 80:7275-80.
- 14. Nyati, MK; Feng, FY; Maheshwari, D; Varambally, S; **Zielske, SP**; Ahsan, A; Chun, PY; Arora, VA; Davis, MA; Jung, M; Ljungman, M; Canan, CE; Chinnaiyan, AM; Lawrence, TS. **2006**. Ataxia telangiectasia mutated down-regulates phospho-extracellular signal-regulated kinase 1/2 via activation of MKP-1 in response to radiation. *Cancer Research* 66:11554-9.

- 15. **Zielske, SP**; Livant, DL; Lawrence, TS. **2009.** Radiation Therapy Increases Mesenchymal Stem Cell Localization to Tumors. *International Journal of Radiation Oncology, Biology, Physics.* **75**:843-53.
- 16. **Zielske, SP**; Spalding, AC; Lawrence, TS. **2010**. Loss of tumor-initiating cell activity in cyclophosphamide-treated breast xenografts. *Translational Oncology*. 3:149-52. PMID: 20563255
- 17. Watson, RL; Spalding, AC; **Zielske, SP**; Morgan, M; Kim, AC; Bommer, GT; Eldar-Finkelman, H; Giordano, T; Fearon, ER; Hammer, GD; Lawrence, TS; Ben-Josef, E. **2010**. GSK3β and β-catenin modulate radiation cytotoxicity in pancreatic cancer. *Neoplasia*. 12:357-65. PMID: 20454507
- 18. **Zielske, SP**; Spalding, AC; Wicha, M; Lawrence, TS. **2011**. Ablation of breast cancer stem cells with radiation. *Translational Oncology*. 4:217-23. PMID: 21804918
- 19. Antwih, DA; Gabbara, KM; Lancaster, WD; Ruden, DM; **Zielske, SP**. **2013.** Radiation-induced epigenetic DNA methylation modification of radiation-response pathways. *Epigenetics*. 8:839-48.
- 20. Elbaz, HA; Lee, I; Antwih, DA; Liu, J; Huttemann, M; **Zielske, SP**. **2014.** Epicatechin stimulates mitochondrial activity and selectively sensitizes cancer cells to radiation. *PLoS ONE*. 9(2): e88322. doi:10.1371/journal.pone.0088322
- 21. Fasih, A; Elbaz, HA; Huttemann, M; Konski, AA; **Zielske, SP**. **2014**. Radiosensitization of pancreatic cancer cells by metformin through the AMPK pathway. *Radiation Research*. 182:50-59.
- 22. **Zielske, S. 2015**. Epigenetic DNA methylation in radiation biology: On the field or on the sidelines? *Journal of Cellular Biochemistry*. 116:212-7.

## **Patent**

(-)Epicatechin as a cancer treatment enhancing drug. Huttemann, M; **Zielske, SP**; Malek, MH; Lee, I; Elbaz, HA. Provisional Patent #61/817,226

## **Book Chapters**

- 1. Roth, JC, **Zielske**, **SP**, Wadhwa, PD, Ballas, CB, Bowman, JE, Reese, JS, and Gerson, SL **2001**. *Gene Therapy Models*. In: **The Cancer Handbook**, MacMillan Publishers, England.
- 2. Koc, ON, **Zielske, SP**, Roth, JC, Reese, JS, and Gerson, SL **2002**. *Transfer of Drug Resistance Genes into Hematopoietic Progenitors*. In: **Gene Therapy of Cancer**, 2<sup>nd</sup> Ed. Academic Press. Latime and Gerson, Editors.
- 3. **Zielske, SP**; Davis, BM **2006**. *Hematopoietic Stem Cell Gene Therapy: Advances in Transduction Efficiency and in vivo Selection*. In: **Stem Cell Therapy**, Nova Science Publishers, New York. Grier, Editor.
- 4. **Zielske, SP**. **2013**. The Role of Epigenetics in Radiation Therapy and the DNA Damage Response. In: **Epigenetics and Cancer**, Springer Science+Business Media, Germany. F. Sarkar, Editor.
- Huttemann, M; Doan, JW; Goustin, AS; Sinkler, C; Mahapatra, G; Shay, J; Liu, J; Elbaz, H; Aras, S; Grossman, LI; Ding, Y; Zielske, SP; Malek, MH; Sanderson, TH; Lee, I. 2014. Regulation of cytochrome c in respiration, apoptosis, neurodegeneration and cancer the good, the bad and the ugly. In: Cytochromes b and c: Electrochemistry, Biological Functions and Pathophysiological Implications. Nova Science Publishers, New York. R. Thom, Editor.

## **Invited Lectures/Seminars**

- 1. Thoracic Oncology Group, University of Michigan. Radiation and mesenchymal stem cell homing to tumors. (7/12/07)
- 2. Division of Hematology/Oncology, Case Western Reserve University. Radiation Sensitivity of breast cancer stem cells. (6/1/09)
- 3. Department of Radiation Oncology, Ohio State University. Radiation sensitivity of breast cancer stem cells. (11/9/09)
- Department of Radiation Oncology, Wayne State University. Radiation sensitivity of breast cancer stem cells. (3/2/10)
- 5. Center for Molecular Medicine and Genetics, Wayne State University. *Normal and malignant stem cells in radiation oncology:* opportunities and challenges. (5/18/10)
- 6. Breast Cancer Biology Program, Karmanos Cancer Institute. Radiation resistance of breast cancer stem cells. (3/17/11)
- 7. Prostate Cancer Research Team, Karmanos Cancer Institute. Epigenetic DNA methylation of the radiation response. (7/20/12)
- 8. Division of Translational Radiation Sciences, University of Maryland Baltimore. *Epigenetics in the radiation response and the impact on resistance*. (6/25/14)
- 9. Division of Molecular Radiation Biology Research, University of Texas Southwestern Medical Branch at Dallas. *Epigenetics in the radiation response and the impact on resistance*. (9/9/14)

## **Meeting Abstracts**

- 1. Ritchie, TC, Kluge, D, **Zielske, SP**, and Coulter, JD **1996**. NT75, the S-7B8 Antigen, is a Complex Composed of SNAP-25 and Synaptobrevin/VAMP. 26th Annual Meeting of the Society for Neuroscience, Washington D.C.
- 2. **Zielske, SP 1997**. Construction of Eukaryotic Expression Vectors for Transfection of lck and HIV nef Genes. North Central Branch Meeting of the American Society for Microbiology, St. Cloud, Minnesota.
- 3. Davis, BM, Encell, LP, **Zielske, SP**, Christians, F, Liu, L, Loeb, LA, and Gerson, SL **1999**. Gene Transfer of Novel O<sup>6</sup>-methylguanine-DNA-methyltransferases (MGMT) Obtained by Directed Evolution Protect Hematopoietic Cells from O<sup>6</sup>-benzylguanine and BCNU. <u>American Society of Hematology Annual Meeting</u>: *Blood* 94(10), abstract 1610.
- 4. Patki, AH, **Zielske, SP**, and Lederman, MM **2000**. S Phase Lymphocytes of HIV-1-Infected Patients Preferentially Undergo Apoptosis. 7th Conference on Retroviruses and Opportunistic Infections, abstract 372, San Francisco, California.
- 5. **Zielske, SP** and Gerson, SL **2000**. Lentiviral Transduction of K562 Cells with P140K MGMT Show Increased Resistance to 1,3-Bis(2-chloroethyl)-1-nitrosourea and O<sup>6</sup>-Benzylguanine. <u>American Society of Gene Therapy Annual Meeting</u>: *Molecular Therapy* 1(5), abstract 212.
- 6. **Zielske, SP** and Gerson, SL **2000**. Drug Resistance of Human Hematopoietic Stem Cells Transduced with MGMT P140K Using a Lentiviral Vector at Low Multiplicity of Infection. American Society of Hematology Annual Meeting: *Blood* 96(11), abstract 923.
- 7. Gerson, SL, Koc, ON, Reese, JS, Davis, BM, Roth, JC, and **Zielske**, **SP 2001**. Repopulating Stem Cells Carrying Chemotherapy Resistance-Inducing Genes. *Clinical Cancer Research* 7(11).
- 8. **Zielske, SP**, Li, Y, Bhakta, S, and Gerson, SL **2001**. The Expression Efficiency of P140K MGMT in Lentiviral Vector Transduced Human Hematopoietic Cells is Sufficient for High Level Drug Resistance and in Vitro Selection. <u>American Society of Hematology Annual Meeting</u>: *Blood* 98(11), abstract 887.
- Gerson, SL; Zielske, SP; Reese, JS; Roth, JC; Volweiller, J 2002. Mutant MGMTs Confer Significant Stem Cell Survival, Enrichment, and Organ Repopulating Advantage. <u>Stem Cell Gene Therapy: Biology and Technology</u>: Blood Cells, Molecules, and Disease.
- 10. **Zielske, SP** and Gerson, SL **2002**. Cytokine Prestimulation is Necessary for High Level Lentiviral Transduction of Human Repopulating Hematopoietic Stem Cells. <u>American Society of Gene Therapy Annual Meeting</u>: *Molecule Therapy* 5(5), abstract 950.
- 11. **Zielske, SP** and Gerson, SL **2002**. HIV vpr Protein in a Lentiviral Vector does not Promote Transduction of Minimally Stimulated Human Hematopoietic Progenitors. <u>American Society of Hematology Annual Meeting</u>: *Blood* 100(11).
- 12. **Zielske, SP**; Reese, JS; Lingas, KT; Donze, J; Gerson, SL **2003**. Human NOD/SCID Repopulating Cells Lentivirus-Transduced with P140K MGMT have a Selective Advantage and are Enriched in Vivo after BG/BCNU Treatment without Pre-transplant Irradiation Conditioning. American Society of Gene Therapy Annual Meeting: *Molecular Therapy* 6(5).
- 13. **Zielske, SP**; Lingas, KT; Arts, EJ; Gerson, SL **2003**. High Level Lentiviral Transduction of Low-dose SDF-1-Exposed Human Hematopoietic Progenitors under Conditions of Reduced Proliferation. <u>American Society of Gene Therapy Annual Meeting</u>: *Molecular Therapy* 6(5).
- 14. **Zielske**, **SP**; Stevenson, M **2005**. Neither Importin 7 nor LEDGFp75 Controls HIV RT-Complex Nuclear Import in Macrophages. <u>12<sup>th</sup></u> Conference on Retroviruses and Opportunistic Infections: # , Boston, Massachusetts.
- 15. **Zielske, SP**; Lawrence, TS. **2006**. Human Mesenchymal Stem Cells Migrate to Colon Cancer Xenografts: Potential Carriers of Cancer Therapeutics. American Society of Gene Therapy Annual Meeting: Molecular Therapy
- 16. Spalding, A; Watson, RL; Zielske, SP; Kim, A; Bommer, G; Fearon, ER; Eldar-Finkelman, H; Lawrence, TS; Ben-Josef, E. 2007. Glycogen synthase kinase 3β Inhibition and β-catenin Activation Contribute to Enhanced Survival After Radiation in Pancreatic Cancer Cells. American Society for Therapeutic Radiation and Oncology Annual Meeting. International Journal of Radiation Oncology Biology Physics 69(3), S608.
- 17. Lee, CJ; Dosch, J; Li, C; **Zielske, SP**; Ljungman, M; Simeone, DM. **2008**. Pancreatic Cancer Stem Cells are Resistant to Ionizing Radiation and the Chemotherapeutic Agent Gemcitabine. Third Annual Academic Surgical Congress. Huntington Beach, California.
- A. C. Spalding, R. L. Watson, M. A. Morgan, S. P. Zielske, G. T. Bommer, G. D. Hammer, E. R. Fearon, T. S. Lawrence, D. L. Livant, E. Ben-Josef. 2008. Pancreatic cancer promotes survival and invasion by GSK3b suppression and b-catenin activation. 2008 Gastrointenstinal Cancers Symposium. Orlando, Florida.
- 19. **S. P. Zielske**, A. C. Spalding, G. Dontu, M. S. Wicha, T. S. Lawrence. **2008**. The radiation sensitivity of breast cancer stem cells. American Association for Cancer Research Annual Meeting. San Diego, California.
- 20. AA Konski, DA Antwih, M Snyder, MC Joiner, **SP Zielske**. **2011**. Potential Relative Biological Effectiveness of High-LET Versus Photon Radiotherapy in Pancreatic Cancer. American Society of Radiation Oncology Annual Meeting. Miami Beach, Florida.
- 21. Antwih, DA, Gabbara, KM, Fasih, A, Ruden, DM, and **Zielske, SP. 2012**. Therapeutic radiation induces an epigenetic DNA methylation response. <u>American Association for Cancer Research Annual Meeting</u>. Chicago, Illinois.
- 22. Fasih, A; Konski, AA; **Zielske, SP**. **2012**. Metformin as a radiosensitizer in pancreatic cancer cells. <u>American Society of Radiation Oncology Annual Meeting</u>. Boston, Massachusetts.
- 23. Fasih, A; Elbaz, HA; Huttemann, M; Konski, AA; **Zielske, SP**. **2013**. The mechanism of metformin induced radiosensitization of pancreatic cancer cells. <u>American Society of Radiation Oncology Annual Meeting</u>. Atlanta, Georgia.

- 24. Antwih, DA; Gabbara, KM; **Zielske, SP**. **2013**. Radiosensitization of breast cancer with DNMT inhibitors. <u>Radiation Research Society Annual Meeting</u>. New Orleans, Louisiana.
- 25. Elbaz, HA; Lee, I; Antwih, DA; Liu, J; Huttemann, M; **Zielske, SP. 2014**. (-)-Epicatechin as a selective radiosensitizer in cancer cells. American Association for the Advancement of Science. Chicago, Illinois.
- 26. Antwih, DA; Gabbara, KM; **Zielske, SP. 2014.** DNMT inhibitors sensitize breast cancer to radiation. <u>16<sup>th</sup> Annual Midwest DNA Repair Symposium</u>. Detroit, Michigan.
- 27. Laney, ME; Antwih, DA; **Zielske, SP. 2014.** Inhibition of DNMT1 radiosensitizes and perturbs cell cycle regulators in breast cancer. Radiation Research Society Annual Meeting. Las Vegas, Nevada.

#### **Awards**

1991: Publication of "Intrinsic Viscosity: Chain Linkage in Polyvinyl Alcohol" in The Best of Gustavus Student Writing.

2007: LUNGevity Foundation - American Cancer Society Postdoctoral Fellowship in Lung Cancer

## References

Wayne Lancaster, Ph.D.

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Relationship: faculty mentor

Theodore S. Lawrence, M.D., Ph.D.

Professor and Chairman

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Relationship: postdoctoral mentor

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Relationship: faculty mentor and collaborator

Douglas Ruden, Ph.D.

Associate Professor and Director of Epigenomics Institute for Environmental Health Sciences

Wayne State University

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Relationship: collaborator

Stanton L. Gerson, M.D. Professor and Director

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