# Edwin J. Squirewell, Ph.D.

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## PERSONAL PROFILE

Experienced scientist with a passion for drug metabolism and toxicology research. Published works on the interactions of tamoxifen metabolites with drug-metabolizing enzymes and studied the role of integrin adhesions in melanoma. Pursuing enzymology, crystallography, and fluorescence studies as part of my postdoctoral training at the University of Florida. Aiming to establish an exciting career within the drug metabolism sector of the pharmaceutical industry.

## EDUCATION

Ph.D. (2014), Pharmacy (Medicinal and Natural Products Chemistry) | University of Iowa | Iowa City, IA
B.S. (2009), Biochemistry | Charleston Southern University | Charleston, SC

## AREAS OF EXPERTISE

- Radiometric enzyme kinetic assays
- Whole-cell assays and cell culture
- Tissue dissection and tumor xenografts
- Proton NMR/ESI/LC-MS
- Protein production and purification
- Rodent handling

## RESEARCH EXPERIENCE

***POSTDOCTORAL ASSOCIATE***

University of Florida | Gainesville, FL — March 2017 – Present

This work examines the dichloroacetate (DCA)-induced inactivation of glutathione transferase zeta 1 (GSTZ1) and aims to determine the mechanism of enzyme protection by chlorine. I lead projects for the native recombinant production and purification of GSTZ haplotypes 1A and 1C. The proteins will be utilized in fluorescence and crystallography studies to observe structural changes in the protein that might occur in the presence of chlorine and DCA. My work also examines the role of kidney, brain, heart, and intestine relative to liver in GSTZ1 expression in juvenile and adult rats treated chronically with DCA.

**Duties**

- Establish purification protocols for native recombinant GSTZ1A and GSTZ1C.
- Design and execute fluorescence-based experiments with recombinant proteins.
- Optimize conditions for crystal formation using the recombinant proteins.
- Perform HPLC-based radiometric enzyme kinetic assays.
- Harvest extrahepatic tissues from rodents for western blot studies.

***POSTDOCTORAL FELLOW***

Mayo Clinic | Rochester, MN — July 2014 – July 2016

My work at Mayo examined the role of focal adhesion kinase and cell adhesion remodeling in melanoma. Melanoma cells were genetically modified and characterized for cell proliferation, migration, and invasion into 3D biomatrix. This was supplemented with a luciferase screening assay to identify human kinases involved in the expression of osteopontin (a protein that is implicated in melanoma metastasis).

**Duties**

- Maintained human and murine cell lines, using antibiotics where appropriate.
- Performed stable and transient transfections with siRNA/lentivirus.
- Designed and executed numerous cell-based assays (e.g., cell proliferation, migration, invasion, and cytotoxicity) and mouse experiments in accordance with project goals.

- Established and managed human tumor xenografts in mice using a variety of tumor implantation techniques (flank, intradermal, subcutaneous, and intracardiac injections).
- Created short-term cell cultures from xenograft implants.
- Experienced with mouse necropsy, tissue dissection, tissue collection, genotyping (embryos and rodent tails), and bioluminescent/fluorescent live mouse imaging (IVIS).
- Experienced with intraperitoneal drug delivery.
- Experienced in use of robotic instrumentation (epMotion, ProteinSimple, BOND-MAX, QiaCube, and IncuCyte).
- Isolated DNA/RNA from cells, tissues, and human melanoma specimens.
- Executed numerous western blot, immunohistochemistry, and flow cytometry studies.
- Trained summer students, technicians, residents, and physicians in the proper use of research equipment.
- Maintained inventory of cell-lines (for accessioning) as well as reagents, kits, and sterile glassware.
- Worked additional hours as needed with frequent weekend responsibilities (e.g., cell culture).

***RESEARCH FELLOW***
University of Iowa | Iowa City, IA August 2009 – May 2014

My PhD examined the role of drug metabolism in the therapeutic action and toxicity of tamoxifen. Tamoxifen metabolites were purchased or synthesized, as appropriate, and characterized to be examined as substrates and/or inhibitors of human cytosolic sulfotransferases 2A1, 1E1, and 1A1*1. A series of steady-state kinetic experiments were performed to obtain $IC_{50}$ values, mode of inhibition, and related kinetic constants ($K_m$, $K_i$, $V_{max}$, and $K_{cat}$) for each metabolite of tamoxifen in the study.

**Duties**
- Established bacterial expression systems for recombinant protein production and purification.
- Designed enzyme kinetic assays that utilized $^{3}H$ and $^{35}S$ radioisotopes.
- Synthesized *N*-oxide, sulfooxy, and sulfamate derivatives of tamoxifen for use in kinetic studies.
- Utilized ESI/LC-MS to elucidate the chemical structures of products formed via the enzyme-catalyzed reactions.
- Analyzed data from liquid scintillation counters, plate readers, proton NMR equipment, and HPLC instrumentation.
- Managed chemical, radiochemical, and compressed gas inventory.

***UNDERGRADUATE RESEARCH ASSISTANT***
Charleston Southern University | Charleston, SC August 2007 – May 2009

Utilized site-directed mutagenesis to elucidate the catalytic mechanism of an enzyme (sialyltransferase) and identify its role in cancer metastasis.

**Duties**
- Cloned, overexpressed, purified, and kinetically characterized recombinant proteins in bacterial and insect cells under the supervision of biochemistry instructor.
- Utilized spectrophotometric coupled HPLC enzyme activity assay for enzyme studies.

## PROFESSIONAL SKILLS
- Excellent computer skills: Microsoft Office, GraphPad, Sigma Plot, ChemDraw, EndNote, Vector NTI.
- Extensive experience writing manuscripts and presenting research data.
- Diverse skill set with an acute ability to perform multiple tasks simultaneously.

## PROFESSIONAL AFFILIATIONS

2013 Member, University of Iowa Holden Comprehensive Cancer Center in Cancer Signaling and Experimental Therapeutics
2012 Member, American Society for Pharmacology and Experimental Therapeutics (ASPET)
2007 Member, American Chemical Society Student Affiliate
2007 Member, Tri Beta Biological Honor Society

## HONORS AND AWARDS

2017 University of Florida Research Supplement to Promote Diversity in Health-Related Research
2014 Mayo Clinic Dermatology Research Fellowship
2012 FASEB/MARC Travel Award to Experimental Biology 2013
2012 Joseph G. Cannon Excellence in Graduate Research Award
2009 University of Iowa Dean's Graduate Research Fellowship
2009 South Carolina Independent Colleges and Universities Faculty/Student Research Grant
2009 Charleston Southern University Chemistry Award

## PUBLICATIONS

- Heim, B. J., **Squirewell, E. J.**, Neu, A., Zocher, G., Sominidi-Damodaran, S., Wyles, S. P., Nikolova, E., Behrendt, N., Saunte, D. M., Lock-Anderson, J., Gaonkar, K. S., Yan, H., Sakaria, J. N., Krendel, M., van Deursen, J., Sprangers, R., Stehle, T., Böttcher, R. T., Lee, J. –H, Ordog, T., Meves, A., "Myosin-1E Interacts with FAK Proline rich Region 1 to Induce Fibronectin-Type Matrix." *Proceedings of the National Academy of Sciences (PNAS).* **114**(15): 3933-3938

- Meves, A., Nikolova, E., Heim, B. J., **Squirewell, E. J.**, Cappel, M.A., Pittelkow, M. R., Otley, C. C., Behrendt, N., Saunte, D. M., Andersen, J. L., Schenck, L. A., Weaver, A. L., Suman, V. J., (2015) "Tumor cell adhesion as a risk factor for sentinel lymph node metastasis in primary cutaneous melanoma." *Journal of Clinical Oncology.* **33**(23): 2509-2515

- **Squirewell, E. J.**, and Duffel, M. W., (2015) "The Effects of Endoxifen and Other Major Metabolites of Tamoxifen on the Sulfation of Estradiol Catalyzed by Human Cytosolic Sulfotransferases hSULT1E1 and hSULT1A1*1." *Drug Metabolism and Disposition*. **43**(6): 843-850

- **Squirewell, E. J**., Qin, X., and Duffel, M. W., (2014) "Endoxifen and Other Metabolites of Tamoxifen Inhibit Human Hydroxysteroid Sulfotransferase 2A1 (hSULT2A1*)." Drug Metabolism and Disposition*. **42**(11): 1843-1850

- **Squirewell, E. J.**, "Interactions of Endoxifen and other Major Metabolites of Tamoxifen with Human Sulfotransferases SULT2A1, SULT1E1, and SULT1A1*1: Implications for the Therapeutic Action and Toxicity of Tamoxifen." PhD (Doctor of Philosophy) thesis, University of Iowa, 2014. http://ir.uiowa.edu/etd/4761.

## PRESENTATIONS

- Parker, V. S., **Squirewell, E. J.**, Lehmler. H. –J., Robertson, L. W., Klingelhutz, A., Duffel, M. W., "Inhibition of Estrogen Sulfotransferase and Adipocyte Differentiation by Hydroxylated Metabolites of Lower Chlorinated Polychlorinated Biphenyls". April 22-27, 2017. Experimental Biology 2017. Chicago, IL

- Parker, V. S., **Squirewell, E. J.**, Lehmler. H. –J., Robertson, L. W., Klingelhutz, A., Duffel, M. W., "Inhibition of Human Steroid Sulfotransferase by Metabolites of Common Airborne Polychlorinated Biphenyls and its Potential for Altering Adipocyte Differentiation". November 8-11, 2016. 43rd

Annual National Organization for the Professional Advancement of Black Chemists and Chemical Engineers (NOBCChE) Conference. Raleigh, NC; and October 9-13, 2016. 9th International PCB Workshop. Kobe, Japan.

- Parker, V. S., **Squirewell, E. J.**, Lehmler. H. –J., Robertson, L. W., Klingelhutz, A., Duffel, M. W., "Steroid Hormone Sulfation Catalyzed by Human Sulfotransferases SULT1E1 and SULT2A1 is Inhibited by Hydroxylated Metabolites of Commonly Observed Airborne Polychlorinated Biphenyls. April 2-6, 2016. American Society for Pharmacology and Experimental Therapeutics (ASPET). San Diego, CA

- Parker, V. S., **Squirewell, E. J.**, Lehmler. H. –J., Robertson, L. W., Klingelhutz, A., Duffel, M. W., "Metabolites of Commonly Occurring Airborne Polychlorinated Biphenyls Inhibit Steroid Hormone Sulfation Catalyzed by Human Cytosolic Sulfotransferase". November 18-20, 2015. National Institute for Environmental Health Sciences Superfund Research Program. San Juan, Puerto Rico.

- Parker, V. S., **Squirewell, E. J.**, Lehmler. H. –J., Robertson, L. W., Klingelhutz, A., Duffel, M. W., "Steroid Hormone Sulfation Catalyzed by Human Sulfotransferases is Inhibited by Metabolites of Commonly Occurring Airborne Polychlorinated Biphenyls". September 21-25, 2015. National Organization for the Professional Advancement of Black Chemists and Chemical Engineers (NOBCChE). Orlando, FL.; and October 29-31, 2015. Society for Advancement of Hispanics/Chicanos and Native Americans in Science (SACNAS), Washington, DC.

- Meves, A., Heim, J. B., **Squirewell, E. J.**, Schneck, L.A., Weaver, A.L., Suman, V.J., "A Method to Identify High-Risk Melanoma." May 16, 2015. Melanoma Patient Education Symposium, Mayo Clinic, Rochester, MN.

- Heim, J. B., **Squirewell, E. J.**, Meves, A., "FAK Tyr-397 Phosphorylation: Roles in Development and Epidermal Homeostasis." May 10-15, 2015. Gordon Research Conference on Fibronectin, Integrins & Related Molecules, Lucca (Barga), Italy.

- Duffel, M. W., Grimm, F. A., **Squirewell, E. J.**, Parker, V. S., Lehmler, H. J., and Robertson, L. W., "Potential Roles for Sulfotransferases and Sulfated Metabolites in PCB-mediated Endocrine Disruption." October 5-9, 2014. 8th International PCB Workshop, Woods Hole, MA.

- Parker, V. S., **Squirewell, E. J.**, Lehmler, H.-J., Robertson, L. W., and Duffel, M. W., "The Inhibition of Human Steroid Sulfotransferases hSULT1E1 and hSULT2A1 by Hydroxylated and Sulfated Metabolites of Polychlorinated Biphenyls." September 23-26, 2014. 41st Annual NOBCChE Conference, New Orleans, LA; and November 12-14, NIEHS Superfund Research Program Annual Meeting, San Jose, CA.

- **Squirewell, E. J.**, and Duffel, M. W., "Interaction of Endoxifen and Other Metabolites of Tamoxifen with Human Hydroxysteroid Sulfotransferase 2A1 hSULT1A1." Holden Comprehensive Cancer Center Scientific Retreat, June 13, 2013, Iowa City, IA.

- **Squirewell, E. J.**, Qin, X., and Duffel, M. W., "Endoxifen and other Metabolites of Tamoxifen Inhibit Human Hydroxysteroid Sulfotransferase hSULT2A1." April 20-24, 2013, Experimental Biology 2013, Boston, MA.

- **Squirewell, E. J.**, and Duffel, M. W., "Interaction of Endoxifen and Other Metabolites of Tamoxifen with Human Hydroxysteroid Sulfotransferase 2A1 hSULT1A1." 51st Annual MIKI Meeting,

(Departments of Medicinal Chemistry at the Universities of Minnesota, Iowa, Kansas, and Illinois) April 12-14, 2013. Minneapolis, MN.

- **Squirewell, E. J.**, Qin, X., and Duffel, M. W., "Endoxifen and Other Metabolites of Tamoxifen Inhibit Human Hydroxysteroid Sulfotransferase hSULT2A1." October 15-16, 2012. 21st Annual CBB Biocatalysis and Bioprocessing Conference, Iowa City, IA.

- **Squirewell, E. J.**, Qin, X., and Duffel, M. W., "Inhibition of Human Hydroxysteroid Sulfotransferase hSULT2A1 by Endoxifen and other Metabolites of Tamoxifen." 50thAnnual MIKI Meeting (Departments of Medicinal Chemistry at the Universities of Minnesota, Iowa, Kansas, and Illinois) April 13-15, 2012. Iowa City, IA.

- **Squirewell, E. J.**, and Burke, E. E., "Mechanistic Studies of Recombinant, Native and Mutant Sialyltransferases from *Pasturella Multocida*." 60th Southeast Regional Meeting of the American Chemical Society, November 12-15, 2008. Greenville, SC.