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### **EDUCATION AND TRAINING**

**Postdoctoral Fellow (Mentor: David Allison and Tim Nagy) 2005-2006**

University of Alabama at Birmingham, Birmingham, AL

Project Title: "The energetics of Atypical Antipsychotic Drug-Induced Weight Gain"

**Postdoctoral Fellow (Mentor: David Allison) 2001-2004**

University of Alabama at Birmingham, Birmingham, AL

Project Title: "Atypical Antipsychotic Drug-Induced Weight Gain: Development of an Animal Model"

**Ph.D. in Nutrition (Mentor: Clinton Grubbs) 2001**

University of Alabama at Birmingham, Birmingham, AL

Dissertation: "The Effects of 9-cis-Retinoic Acid and Vitamin D3 on Prevention of MNU-Induced Mammary Cancers in Rats"

**B.S. in Natural Sciences and Mathematics 1996**  
**(Major: Chemistry Minor: Mathematics)**

University of Alabama at Birmingham, Birmingham, AL

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### **HONORS AND AWARDS**

**Ruth L. Kirschstein National Research Service Award (NIH-F32) 2004-2006**

**Career Enhancement Award for Postdoctoral Fellow at UAB 2005**

**Research Development Award for Postdoctoral Fellow at UAB 2004**

**Career Enhancement Award for Postdoctoral Fellow at UAB 2002**

**Cancer Prevention and Control Training Fellow (NCI) 1996-2001**

**William C. Bailey Award for Excellence in Cancer Prevention and Control 1998, 1999 and 2000**

**American Institute of Chemists Award 1995**

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### **RESEARCH INTERESTS**

- Nutrition and Health
- Obesity and Drug-Induced Weight Gain Models
- Pharmacogenetics of Antipsychotic Drug-Induced Weight Gain
- Neurological Pathways Involved with Antipsychotic Drug-Induced Weight Gain
- Chemoprevention of Cancer
- Proteomics of Cancer

## **PROFESSIONAL EXPERIENCE**

### **Research Associate (2007-present)**

- Performed proteomic analysis of mammary tissue from rats using 2D electrophoresis and mass spectrometry.
- Developed protocols to measure protein expression in mammary tissue using 2D difference gel electrophoresis (DIGE).
- Preparing papers for publication on the findings from these initial experiments on mammary tissues.

### **Postdoctoral Fellowship (2001-2006)**

- Developed protocols to investigate atypical antipsychotic drug induced weight gain in mouse models.
- Developed protocols to investigate the energetics involved with atypical antipsychotic drug-induced weight gain in mice using specialized phenotyping techniques
- Mentored undergraduate and graduate students
- Participated in recruiting graduate students at national meetings
- Mentored undergraduate and graduate students at national meetings
- Presented papers at national and international meetings

### **Grants**

- 2004-2006 National Research Service Award (F32)- Energetics of Antipsychotic Drug-Induced Weight Gain (ACTIVE).

### **Journal Reviewer**

*Acta Psychiatrica Scandinavica*

*Behavioural Brain Research*

*Biological Psychiatry*

*International Journal of Neuropsychopharmacology*

*The Journal of Clinical Psychiatry*

*Obesity Reviews*

*Psychiatric Services*

*Schizophrenia Research*

### **Research Experience**

1991-1996 Worked as a student assistant at the University of Alabama at Birmingham investigating the effects of chemopreventive agents such as indole-3-carbinol, 13-cis-retinoic acid, and tamoxifen on prevention of mammary and bladder cancers. Rats and mice were used in these studies. The following techniques and skills were required to carry out these experiments:

1. Preparation of diets that contained the chemopreventive agents required careful calculations to insure that each animal received the proper treatment concentration.
2. Body weights were measured weekly to monitor for possible toxicity of the agents.
3. Oral gavage, intraperitoneal injections and subcutaneous injections were performed to administer the agents.
4. Palpation and careful evaluation of tumors were performed weekly.
5. Food intake analysis and metabolic cage isolations were often used.
6. Complete necropsies were conducted at the end of each study and tumors were removed.
7. Tumors were analyzed to determine malignancy.
8. Data were plotted and analyzed using various statistical methods with SigmaStat.

1996-1997 I worked for 6 months in the Chemoprevention Center at the University of Alabama at Birmingham continuing to test chemopreventive agents in animal models. After completing my undergraduate degree in chemistry, I decided to apply for Graduate School and pursue a Ph. D. in Nutrition Sciences at the University of Alabama at Birmingham. For one year, I focused my attention on my coursework and did not work on a major project in the lab. After completing lab rotations in my second year of graduate studies, I decided to focus my research in the field of chemoprevention of mammary cancer.

- 1997-2001 During my dissertation level research, I investigated the effects of 9-cis-retinoic acid (9-cis-RA) on the methyl-nitrosourea (MNU)-induced mammary cancer model in female Sprague-Dawley rats. I also investigated the effects of 9-cis-RA in combination with vitamin D3 and 4-hydroxyphenylretinamide (4-HPR) in this animal model. I designed a technique for separating epithelial cells from fat cells in rat mammary tissue and I analyzed these cells for mRNA expression levels of retinoic acid receptors. I was involved with a study investigating the effects of high doses of 4-HPR and 13-cis-RA on retinoic acid receptor mRNA expression levels in mouse tissues. Following the completion of my dissertation, I accepted a postdoctoral position in Nutrition Sciences, Division of Energy Metabolism, where I currently work with Drs. David Allison and Tim Nagy.
- 2001-2006 Developed an animal model of atypical antipsychotic drug-induced weight gain (obesity) and investigated the energetics involved with this process. These medications induce weight gain in almost every patient treated with the drugs. I have completed studies investigating weight gain in mice that are being fed olanzapine, ziprasidone, quetiapine, and clozapine in peanut butter tablets. This model can be used to monitor antipsychotic drug-induced weight gain and related metabolic disturbances. After 3 years of work to get the model established, the manuscript describing the antipsychotic drug-induced weight gain in mice is now published in the *International Journal of Obesity* (March, 2005). Another manuscript related to the model was published in the *International Journal of Obesity* (April, 2006) titled "No effect of dietary fat on short-term weight gain in mice treated with atypical antipsychotics". I received an Individual (F32) National Research Service Award (NRSA) from NIH-NIDDK in December 2004 to continue the current project looking at the "energetics" involved with antipsychotic drug induced weight gain in rodent models. I completed my F32 work in December of 2006 and accepted a Research Associate position in the department of Pharmacology at the University of Alabama at Birmingham.
- 2007- Currently working on a project (CNGI) investigating the effects of nutrients on the prevention of cancer in animal models. Specifically, we are evaluating the mammary gland proteome using tissues from female rats and the prostate proteome in male rats. In order to measure the expression of proteins, we conduct a series of assays. We run 2D gel electrophoresis (specifically DIGE) and identify specific proteins using mass spectrometry. Our first manuscript was recently submitted to the *Journal of Proteomics* (2007).

## **PUBLICATIONS AND PRESENTATIONS**

### **Abstracts**

**Cope, M.B.**, DiCostanzo, C., Kesterson, R.A., Allison, D.B., and Nagy, T.R. Effect of modest food restriction on olanzapine-induced weight gain in mice. Submitted to Obesity Society Annual Meeting, 2006.

DiCostanzo, C., **Cope, M.B.**, Kesterson, R.A., and Nagy, T.R. Atypical Antipsychotics Have Variable Effects on Activity and Core Body Temperature in The Female Rat. Submitted to Obesity Society Annual Meeting, 2006.

Kump, D., Jamison, W., Jumbo-Lucioni, P., **Cope, M.B.**, Nagy, T.R., and Kesterson, R.A. Atypical Antipsychotic-Induced Gene Changes in the Mouse Hypothalamus. Submitted to Obesity Society Annual Meeting, 2006.

**Cope, M.B.**, Jumbo-Lucioni, P., Kesterson, R.A., Johnson, M.S., Allison, D.B., and Nagy, T.R. Effect of a high-fat diet on atypical antipsychotic-drug induced weight gain in mice. *Obesity Research* 13: A172, 665-P, 2005.

**Cope, M.B.**, Jumbo-Lucioni, P., Walton, G., Kesterson, R.A., Allison, D.B., and Nagy, T.R. Antipsychotic Drug-Induced Weight Gain: Dose Response of Three Atypical-Antipsychotic Drugs in Female Mice. *Obesity Research* 13: A171, 660-P, 2005.

**Cope, M.B.**, Nagy T.R., Chen, L., Page, G., Kesterson, R.A., and Allison, D.B. Identification of differentially expressed genes in mouse hypothalamus after olanzapine treatment using cDNA microarray. *Obesity Research* 12: A177, 694-P, 2004.

Walton, G., **Cope, M.B.**, Johnson, M.S., Allison, D.B. and Nagy, T.R. Effects of Antipsychotic Drugs on Body Composition in Mice. *Obesity Research* 12: A131, 509-P, 2004.

**Cope M.B.**, Nagy TR, and Allison DB. The effects of quetiapine (Seroquel) on food intake and body weight in mice. *Pharmacotherapy* 23:123 Abs.231, 2003.

**Cope, M.B.**, Walton, G., Fernandez, J.R., Nagy, T.R., and Allison, D.B. Effect of risperidone on body weight in C57BL/6J mice. *Obesity Research* 11: A70, 283-P, 2003.

**Cope, M.B.**, Fernandez, J.R., Nagy, T.R., and Allison, D.B. Atypical Antipsychotic-Induced Weight Gain in Mice After Oral Administration of Agents. *Obesity Research* 11: A75, 303-P, 2003.

Page, G., **Cope, M.B.**, Chen, L., Allison, D.B., Kesterson, R.A., Jamison, W.L., and Ercil, E.N. Olanzapine-induced changes in gene expression in the hypothalamus associated with weight gain: a cDNA microarray analysis study. *Obesity Research* 11: A47, 186-P, 2003.

**Cope, M.B.**, Nagy, T.R., Fernandez, J and Allison, D.B. Effects of Ziprasidone on Body Weight in C57BL/6J Mice. *FASEB* 17(5): A1043, 652.1, 2003.

**Cope, M.B.**, Nagy, T.R., Fernandez, J and Allison, D.B. Effects of Olanzapine on Body Weight in C57BL/6J Mice. *International Journal of Obesity* 26(1):S157, 597, 2002.

**Cope, M.B.**, Davis, B., Nagy, T.R. and Allison, D.B. Extraction and Purification of Olanzapine from Zyprexa Tablets. *FASEB* 16: A568, 442.16, 2002.

Grubbs, C.J., Steele, V.E., Eto, I., **Cope, M.B.** and Lubet, R.A. Dose Levels of Tamoxifen and 9-cis-Retinoic Acid Alone or in Combination Required to Achieve Chemopreventive and Chemotherapeutic Activity. *Proceedings of the American Association for Cancer Research*, 42: 309, March 2001.

Johanning, G.L., Wilborn, T.W., **Cope, M.B.**, Grubbs, C.J., Steele, V.E., Kelloff, G.J., and Lubet, R.A. Effect of High Doses of Retinoids on RAR- $\beta$  mRNA Expression in Female Mice. *Proceedings of the American Association for Cancer Research*, 41: 54, March 2000.

**Cope, M.B.**, Steele, V.E., Lubet, R.L., Kelloff, G.J., Johanning, G.L., Wilborn, T.W., Anderson, A.S. and Grubbs, C.J. Prevention of Mammary Cancers by 9-cis-Retinoic Acid (9-cis-RA) and 4-Hydroxyphenylretinamide (4-HPR) Either Alone or in Combination. *Proceedings of the American Association for Cancer Research*, 41: 56, March 2000.

**Cope, M.B.**, Eto, I, Anderson, A.S., Hill, D.L., Wilborn, T.W., Weiss, H. and Grubbs, C.J. Prevention of Methylnitrosourea (MNU)-Induced Mammary Cancers by 9-cis-Retinoic Acid (9-cis-RA) and Vitamin D3 Given Either Alone or in Combination. Comprehensive Cancer Center Retreat. 2000-William C. Bailey Award, University of Alabama at Birmingham.

**Cope, M.B.**, Steele, V.E., Lubet, R.L., Anderson, A.S., Johanning, G.L., Wilborn, T., Kelloff, G.J., and Grubbs, C.J. The Efficacy of 9-Cis-Retinoic Acid (9-cis-RA) and 4-Hydroxyphenylretinamide (4-HPR) Alone and Combined in the Prevention of Chemically-Induced Mammary Cancers. Comprehensive Cancer Center Retreat. 1999-William C. Bailey Award, University of Alabama at Birmingham.

Grubbs, C.J., Steele, V.E., Bowden, C.R., Hill, D.L., **Cope, M.B.**, Anderson, A.S., Kelloff, G.J., and Lubet, R.A. Efficacy of an Aromatase Inhibitor and an Estrogen Receptor Modulator Either Alone or in Combination in the Prevention of Mammary Cancer. *Proceedings of the American Association for Cancer Research*, 40: 651, March 1999.

**Cope, M.B.**, Hill, D.L. and Grubbs, C.J. Efficacy of Dehydroepiandrosterone (DHEA) and 4-Hydroxyphenylretinamide (4-HPR) Alone and in Combination in the Prevention of Chemically-Induced Mammary Cancers. Comprehensive Cancer Center Retreat. 1998-William C. Bailey Award, University of Alabama at Birmingham.

### Research Papers

**Cope, M.B.** and Allison, D.B. Critical Review of the World Health Organization's (WHO) 2007 report on "Evidence of the Long-Term Effects of Breastfeeding: Systematic Reviews and Meta-Analysis" with respect to obesity. (In preparation for submission to *Obesity Reviews*, 2008).

**Cope, M.B.**, Kesterson, R.A., DiCostanza, K., Allison, D.B., and Nagy, T.R. Motor activity levels and body temperature effects in risperidone treated mice. (In preparation for submission to *Physiology &*

*Behavior, 2008)*

**Cope, M.B.**, Page, G., Nagy, T.R., Chen, L., Kesterson, R.A., and Allison, D.B. Olanzapine-Induced Changes in Gene Expression in the Hypothalamus of Mice: A cDNA Microarray Analysis Study (In preparation for submission to *Obesity Research, 2008*).

**Cope, M.B.**, Walton, R.G., Allison, D.B., Chua, S., Nagy, T.R. Phenotyping of 5-HT<sub>2C</sub> receptor transgenic and 5-HT<sub>2C</sub> receptor knockout mice. (In preparation for *International Journal of Body Composition Research, 2008*).

Huffman, D.M., Cope, M.B., Johnson, M.S., Desmond, R.A. and Nagy, T.R. Effect of Acute Exercise on Liver SIRT1 Expression in Trained and Untrained Mice (Submitted to *Experimental Gerontology, 2007*)

**Cope, M.B.** and Allison, D.B. Obesity Person Population. *Obesity* 2006; 14(4):156S-159S.

**Cope, M.B.**, Jumbo-Lucioni, P., Kesterson, R.A., Walton, R.G., Allison, D.B., and Nagy, T.R. No Effect of Dietary Fat on Short-term Weight Gain in Mice Treated with Atypical Antipsychotics. *Int J Obes*, 2007; 31(6): 1014-22.

**Cope, M.B.**, Nagy, T.R., Fernandez, J, Geary, N.D., Casey D.E. and Allison, D.B. Antipsychotic-Induced Weight Gain: Development of an Animal Model. *Int J Obes Relat Metab Disord*. 2005 Jun; 29(6):607-14.

**Cope, M.B.**, Steele, V.E., Hill, D.L., Eto, I., Kelloff, G.J., Grubbs, C.J. and Lubet, R.A. Prevention of Mammary Cancers by 9-cis-Retinoic Acid (9-cis-RA) and 4-Hydroxyphenylretinamide (4-HPR) Either Alone or in Combination. *Oncology Reports, 11, 465-469, 2004*.

**Cope, M.B.**, Lubet, R.A., Eto, I., Steele, V.E., Hill, D.L. and Grubbs, C.J. Prevention of Methylnitrosourea (MNU)-Induced Mammary Cancers by 9-cis-Retinoic Acid (9-cis-RA) and Vitamin D3 Given Either Alone or in Combination. *Oncology Reports, 9(3), 533-537, 2002*

Johanning, G.L., **Cope, M.B.**, Wilborn, T.W., Grubbs, C.J., and Lubet, R.A. Effect of High Retinoid Doses on RAR- $\beta$  mRNA Expression in Female B6D2F1 Mice. *Anticancer Research, 21(3), 1691-1695, 2001*.

#### **Book Chapter**

**Cope, M.B.**, Fernandez, J., and Allison, D.B. Genetic Influences on Energy Balance. Handbook of Eating Disorders and Obesity. Wiley Inc. (Sept./Oct., 2003).

#### **Invited Review**

**Cope M.B.**, Erdman J.W., Allison D.B. The potential role of soyfoods in weight and adiposity reduction: an evidence-based review. *Obesity Reviews* 2007 (OnlineEarly Articles). <http://dx.doi.org/10.1111/j.1467-789X.2007.00390.x>

#### **Seminars Presented**

**Cope, M.B.** Chemoprevention of MNU-Induced Mammary Cancer with 9-cisRA and/or Vitamin D3 in a Rat Model-Presented at the September, 2001 Cancer Trainee Seminar Series.

**Cope, M.B.** A Mouse Model of Antipsychotic Induced Weight Gain-Presented at the January, 2003 Department of Nutrition Sciences Seminar Series.

**Cope, M.B.** Risperidone: Past, Present and Future...2006 Department of Nutrition Sciences, Division Meeting, January, 2006.

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## **MENTORING AND TEACHING EXPERIENCE**

### **Mentoring Experience**

McNair Scholar Summer Student 2000 (student: Venus Childress)

NASA Summer High School Student Training 2003 (student: LaQuinta Maddox)  
SACNAS annual meeting 2004, 2005 (Participated in mentoring session)  
MANNRS annual meeting 2005 (Recruited Students)

### **Teaching Experience**

Course: Body Composition and Energy Expenditure, Spring-2006, University of Alabama at Birmingham  
Lecture Title: Use of Indirect Calorimetry to Determine Energy Expenditure

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### **MEMBERSHIPS-SCIENTIFIC SOCIETIES**

American Chemical Society  
American Association for Cancer Research  
North American Association For the Study of Obesity

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### **DESCRIPTION OF DISSERTATION**

Chemopreventive agents inhibit the process of carcinogenesis by either blocking initiation or by inhibiting promotion and progression following carcinogenic insult. The class of compounds called retinoids includes all vitamin A derivatives, natural or synthetic. One of the naturally occurring retinoids is 9-cis-retinoic acid (9-cis-RA). 9-cis-RA was shown to be an effective inhibitor of cancer formation in the mammary gland of young rats (50 days of age when carcinogen was administered). The biochemical mechanism(s) involved, however, are not understood. At the beginning of this effort, it was unclear how 9-cis-RA, at various dose levels or in combination with other chemopreventive agents, affected cancer incidence in the methylnitrosourea (MNU)-induced mammary cancer model of young and older rats (100 days of age when carcinogen was administered).

In an initial study, conducted with older animals that received a range of 9-cis-RA dose levels that began seven days prior to MNU injection, a dose dependent response was found within the groups. Another study demonstrated that, to achieve a strong chemopreventive effect, 9-cis-RA had to be administered continuously; removing 9-cis-RA after 10 weeks allowed tumor growth to occur. Both of these studies were investigating the effects of 9-cis-RA as an inhibitor of initiation. Overall, the animals had significant reductions in mammary cancer incidence when administered 9-cis-RA one week prior to carcinogen treatment.

To investigate the effects of 9-cis-RA combined with 4-hydroxyphenylretinamide (4-HPR), animals were administered agents in the diet, starting at 53 days of age (three days following MNU injection). The combination caused significant reductions in cancer incidence and number per animal. This study showed that both 9-cis-RA and 4-HPR inhibited initiation of carcinogenesis and the combination of 9-cis-RA with 4-HPR was more effective. Older animals (administered agents in the diet at 93 days of age) showed an even greater effect when treated with the combination of 4-HPR and 9-cis-RA.

Another study was designed to determine if the combination of vitamin D3 with 9-cis-RA would inhibit mammary carcinogenesis in young rats. The two groups of animals fed vitamin D3 alone had no reductions in mammary cancer compared to controls. When combined with 9-cis-RA, however, both dose levels of vitamin D3 inhibited mammary cancer to a greater extent than 9-cis-RA alone. This study introduced the possibility that the nuclear receptors, retinoic x receptor and vitamin D receptor, may require binding by the respective ligands, 9-cis-RA and vitamin D3, in order for the chemopreventive effect to occur.

A final study was conducted in an attempt to understand the mechanism(s) in which 9-cis-RA may decrease mammary cancers. The diets of animals were supplemented with 9-cis-RA for either 3 days or 4 weeks, and various parameters were evaluated. Mammary epithelial cells were isolated from the animals, and the total RNA was extracted. mRNA expression for the retinoid nuclear receptor, RAR $\beta$ , was measured in the epithelial cells; no differences in expression were found among the groups. Theoretically, RAR $\beta$  expression decreases during the carcinogenic process and 9-cis-RA may cause an increase in its expression leading to decreased cancer formation. Morphologic evaluation of the mammary glands showed no increased differentiation in rats treated with 9-cis-RA.

In conclusion, these studies showed that 9-cis-RA, at various dose levels, alone and in combination with other chemopreventive agents, strongly inhibited MNU-induced mammary cancer. Additional studies are needed to determine the mechanism(s) involved in this effect.