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**Major Professor:** Colin Jefcoate

**Degree Objective:** Ph.D. Endocrinology and Reproductive Physiology

**Background:** B.S. Biochemistry, St. Cloud State University, MN. B.S. Biotechnology, St. Cloud State University, MN.

**Current Research Project:**

The effects of maternal dietary intake on progeny are becoming increasingly recognized. Vitamin A (VA) or retinol, the precursor to retinoic acid (RA) has long been known as a critical regulator of the development of neurons, eyes, limbs and cardiovascular system. A maternal Vitamin A deficient (VAD) diet often causes offspring to be born with ocular and facial malformations, CNS defects as well as deficiencies in organ maturation due to RAs large role in organogenesis. Interestingly, when retinol is in excess during gestation, similar defects are seen as in the VAD embryos. This establishes a delicate bipolar threshold where too little or too much retinol can create lifelong toxic effects in the developing offspring.

When VAD is initiated during development, I found a profound effect on liver and adipose development when compared to initiation of VAD later in life. Liver mass is lowered with elevated expression of several collagen genes. Fat mass is also lowered, even when challenged with a high fat diet. This suggests that fetal or neonatal deficiency in VA may severely limit fat pad capacity and, therefore, enhance the risk of systemic lipotoxicity. Circulating levels of cholesterol and triglycerides were low in these developmental VAD mice, suggesting increased oxidation of fat. These mice, whose weight is already low, lose an astonishing amount of weight after a four-hour fast, suggesting a dangerously toxic metabolic phenotype. Recent time points of VAD introduction and reversal suggest a window of development that impacts on liver and fat development that can't be reversed with vitamin A later in life. We suggest that deficient RA in neonatal pups limits ASC progression to pre-adipocytes and thus, inhibits the response to dietary fat. In accordance with the reduced adiposity seen in the developmental VAD mice, a similar phenotype is seen in Cyp1b1 knockout mice. There is a similar fasting weight loss and protective effects between the two groups (low circulating fats, reduced fat deposition in organs) however; the two mechanisms causing this reduced adiposity appear to be different. This facet provides insight in to how dietary influences (fat intake, vitamin A) can affect drug metabolizing cytochrome P450s as well as the overall physiology in these mice.

**Honors:**

NIH T32 Trainee; NIH Ruth L. Kirschstein National Research Service Award NIH T32-HD041921

NIH T32 Trainee; NIH Ruth L. Kirschstein National Research Service Award NIH T32- ES007015



## **Grants Received:**

NIH T32 Trainee; NIH Ruth L. Kirschstein National Research Service Award NIH T32-HD041921 2007-2009.

NIH T32 Trainee; NIH Ruth L. Kirschstein National Research Service Award NIH T32- ES007015. 2010-current.

## **Publications:**

N'jai AU, Larsen MC, Bushkofsky JR, Czuprynski CJ, Jefcoate CR. Acute Disruption of Bone Marrow Hematopoiesis by Benzo(a)pyrene is Selectively Reversed by Ah Receptor Mediated Processes. *Mol Pharmacol.* 2011 Jan 20, 2011 as doi:10.1124/mol.110.070631

## **National Presentations:**

Justin Bushkofsky, Michele Larsen, and Colin Jefcoate. Endogenous Cyp1b1 metabolism in vivo controls endogenous liver PPAR activity without expression in hepatocytes. Cholestasis, Lipid Homeostasis, and Liver Toxicity. Society of Toxicology 2011.

## **Other Presentations:**

Justin Bushkofsky, Michele Larson, Suqing Wang, and Colin Jefcoate. Dietary Effects of Growth and Obesity in Cytochrome P4501b1 Knock-out Mice. ERP Annual Symposium 2008.

Justin Bushkofsky, Colin Jefcoate, Multiple effects of Cyp1b1 deficiency in mouse development. ERP Annual Symposium 2009.

Justin Bushkofsky, Colin Jefcoate. Cross Talk Between Vitamin A and Cytochrome P4501b1 in Early Embryogenesis. ERP Annual Symposium 2010.

ERP Seminar Presentation 9/23/10 "Timing of Vitamin A Deficiency and Effects on Post-natal Development"

METC Seminar presentation 3/3/11 "Effects of maternal vitamin A deficiency on post-natal development"

## **ERP Service:**

ERP Seminar Committee.