

POSTDOCTORAL OPENINGS: Boston University

Epigenetics and Molecular Endocrinology, Molecular Toxicology

POSTDOCTORAL POSITIONS in epigenetics and molecular endocrinology and molecular toxicology, with an interest in utilizing innovative single cell-based next generation sequencing and epigenomic remodeling technologies to study the dysregulation of gene expression and chromatin states in mouse models of liver disease. We seek recent (or upcoming) PhD graduates to fill openings in two NIH-funded research projects. In one project, we are studying the role of long non-coding RNAs in growth hormone regulation of chromatin states and gene expression in mouse models of liver disease; and in a second project we are investigating the persistent disruptive actions of environmental chemicals that activate transcription factors from the nuclear receptor (NR) superfamily, and which can induce developmental and adult disease-associated toxicities. Experience in cell and molecular biology with a strong interest in areas such as genomics, epigenetics, computational biology, NGS technologies, and mouse models is highly desirable.

Send curriculum vitae, brief summary of research experience, interests and accomplishments, and names of three or four references to: Email: djw@bu.edu. *Flexible start date.*

David J. Waxman, Ph.D.

Professor of Cell and Molecular Biology, and Biomedical Engineering, Boston University
Professor of Medicine, Boston University School of Medicine

Mechanisms of growth hormone-regulated sex differences in liver gene expression – This project aims to elucidate global transcriptional and epigenetic networks that dictate the sex-differential expression of more than 1,000 genes in mammalian liver; these sex-differential gene profiles have been linked to clinically relevant sex differences in hepatic drug metabolism, lipid metabolic profiles, and cardiovascular disease risk. We use mouse models and next generation sequencing technologies combined with bioinformatics to elucidate regulatory mechanisms, and we are utilizing CRISPR-based epigenetic remodeling to discover the role of novel long non-coding RNA (lncRNA) genes in the sex-differential regulatory networks. This work is designed to elucidate gene regulatory circuits associated with sex-dependent chromatin states, through which the temporal pattern of pituitary growth hormone secretion either masculinizes (pulsatile hormone stimulation) or, alternatively, feminizes gene expression in the liver (persistent hormone stimulation), with major effects on liver disease susceptibility and development.

Epigenomic actions of environmental chemical exposures – We are studying the genomic and epigenetic actions of environmental chemicals, which can induce developmental and adult disease-associated toxicities in humans and exposed wildlife. For example, prenatal and neonatal exposure to estrogen-like chemicals can induce major structural and functional abnormalities in tissues such as the liver, and thereby increase susceptibility to adult onset of disease, including fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), and hepatocellular carcinoma (HCC). However, the molecular mechanisms that underlie the early developmental lesions and that lead to these developmental and disease-associated defects and adult pathophysiology are poorly understood. We are presently investigating the hypothesis that *in utero* exposure to environmental chemicals alters the expression of epigenetic regulators, including xenochemical-responsive long non-coding RNA (lncRNA) genes that confer life-long changes in expression of key genes controlling tissue development. Our studies primarily use the mouse model, and focus on environmental chemical agonists of transcription factors that belong to the nuclear receptor (NR) superfamily, including CAR, PRX and PPAR, which are also targets of many therapeutic drugs.

For further details about our lab's research program see: <https://www.bu.edu/biology/people/profiles/waxman>

Recent publications:

Widespread dysregulation of long noncoding genes associated with fatty acid metabolism, cell division, and immune response gene networks in xenobiotic-exposed rat liver. Karri K, Waxman DJ. (2020) **Toxicol Sci**, 174:291-310. PMID: 31926019

Impact of 3D genome organization, guided by cohesin and CTCF looping, on sex-biased chromatin interactions and gene expression in mouse liver. Matthews BJ, Waxman DJ. (2020) **Epigenetics and Chromatin**, 13:30. PMID: 32680543

Sex-biased genetic programs in liver metabolism and liver fibrosis are controlled by EZH1 and EZH2.

Lau-Corona D, Bae WK, Hennighausen L, Waxman DJ. (2020) **PLoS Genetics**, 16:e1008796. PMID: 32428001

Genetic factors contributing to extensive variability of sex-specific hepatic gene expression in Diversity Outbred mice. Melia T, Waxman DJ. (2020) **PLoS One**, 15:e0242665. PMID: 33264334

STAT5 regulation of sex-dependent hepatic CpG methylation at distal regulatory elements mapping to sex-biased genes. Hao P, Waxman DJ. (2021) **Mol Cell Bio**, 41:e00166-20. PMID: 33199496