

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/david-j-waxman/>

Recent publications:

Plasma growth hormone pulses induce male-biased pulsatile chromatin opening and epigenetic regulation in adult mouse liver. Rampersaud A, Connerney J, Waxman DJ. **Elife**. 2023 12:RP91367. doi: 10.7554/eLife.91367. PMID: 38091606

Dysregulation of murine long noncoding single-cell transcriptome in nonalcoholic steatohepatitis and liver fibrosis. Karri K, Waxman DJ. **RNA**. 2023 (7):977-1006. PMID: 37015806

Sex matters in liver fat regulation. Waxman DJ, Kineman RD. **Science**. 2022 378(6617):252-253. doi: 10.1126/science.ade7614. PMID: 36264790

Interplay Between GH-regulated, Sex-biased Liver Transcriptome and Hepatic Zonation Revealed by Single-Nucleus RNA Sequencing. Goldfarb CN, Karri K, Pyatkov M, Waxman DJ. **Endocrinology**. 2022 163(7):bqac059. doi: 10.1210/endo/bqac059. PMID: 35512247

Constitutively Active STAT5b Feminizes Mouse Liver Gene Expression. Lau-Corona D, Ma H, Vergato C, Sarmiento-Cabral A, Del Rio-Moreno M, Kineman RD, Waxman DJ. **Endocrinology**. 2022 163(5):bqac046. doi: 10.1210/endo/bqac046. PMID: 35396838