BIOGRAPHICAL SKETCH

NAME: **David J. Waxman**

eRA COMMONS USER NAME: David_Waxman

POSITION TITLE: Professor of Cell & Molecular Biology, Prof. of Medicine, Prof. of Biomed. Engineering

EDUCATION/TRAINING:

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Queens College, CUNY, Flushing, NY	B.A.	06/1975	Chemistry
Harvard University, Cambridge, Massachusetts	A.M.	06/1976	Chemistry
Harvard University, Cambridge, Massachusetts	Ph.D.	06/1980	Biochem & Molec Biology
Mass. Institute of Technology, Cambridge, MA	Postdoctoral	06/1983	Enzymology

A. Positions and Honors

Academic Appointments:
Assistant Professor **(1983-1986)** and Associate Professor of Biological Chemistry & Molecular Pharmacology **(1987-1993)**, Dana-Farber Cancer Institute and Harvard Medical School
Professor of Cell and Molecular Biology, Department of Biology, Boston University (**1994-present**)
Professor of Medicine, Dept. of Medicine, Boston University School of Medicine **(1998-present)**
Professor of Biomedical Engineering, Boston University College of Engineering **(2014-present)**

Other Professions Positions and Appointments:
Academic: Visiting Scientist, Dept. of Biophysics, Weizmann Institute 1980; External Research Consultant, Division of Hepatic Diseases, NYU Medical Center 1986-1987; Program in Cell and Developmental Biology, Harvard Medical School 1983-1990; Biophysics Program, Harvard Univ. 1984-1988; Program in Biomolecular Pharmacology, Boston Univ. School of Medicine 1996-present; Program in Bioinformatics, Boston Univ. 1998-present; Visiting Scientist, Cancer Genomics Program, MIT-Whitehead Inst. Genome Center, 2000-2001.

Assoc. Director for Basic Research, Boston University Cancer Center, Boston University, 2009-2015
Deputy Director, Superfund Basic Research Program at Boston University, 1999-2005
Chairman, Scientific Advisory Committee, Environ. Health Science Ctr. at Wayne State Univ. 1998-2009
International Advisory Board, International Symposium on Microsomes and Drug Oxidations, 1996-present
Scientific Advisory Boards: Oxford BioMedica PLC, 1998-2009; Metabasis Therapeutics, 2001-2009.
Associate Managing Editor 1990-1994 and **Associate Executive Editor** 1995-1997, *Biochim Biophys Acta*
Member, NIH Physical Biochemistry Study Section 1991-1994

Other Advisory Boards and Committees: AACR Program Committee 1994; Board of Scientific Counselors, NIEHS, Intramural Review Committee 1997, 2013, 2014; Scientific Advisory Committee, Brain Tumor Gene Therapy Program, Mass. General Hospital 1998; Scientific Advisory Board, International Microsomes & Drug Oxidations Conference Series, International Advisory Board, 1998-present; New England Drug Metabolism Discussion Group, Steering Committee and Founding Member, 1999-present; NIH Site Visit Committees and Special Emphasis Review Panels: 1987-1994, 1996, 1997, 2001, 2003, 2008, 2010, 2011, 2015, 2016; Endoc Soc, Abstract Committee, 2001-2005, 2013-present; Univ. Kansas, NIH COBRE Award Review Panel, 2001-2002; GH-IGF1 Int'l Sympos 2004, Abstract Review Committee; Univ. Rhode Island, External Advisory Committee, NIH COBRE, 2007; Int'l Scientific Advisory Board, Joint MDO/ European ISSX Meeting, 2012; Charles A. King Trust Postdoctoral Fellowship, Scientific Review Committee, 2012-2017; BU/Pfizer Centers for Therapeutic Innovation Steering Committee, 2012-present; Scientific Advisory Committee, MDO 2014.

Journal Editorial Boards: *Molec Pharmacol,* 1992-present; *Biochem J,* 1992-2008; *Pharmacology,* 1992-2009; *Drug Metabolism Dispos,* 1994-2011; *J Biol Chem*, 1996-2000; *Xenobiotica*, 1997-present; *J Pharmacy Pharmaceut Sci,* 1997-2010; *Cancer Gene Therapy*, 1999-2013; *Molec Endocrinol*, 2000-2003, 2013-2016; *Molec Cancer Therap*, 2001-2017; *Biochem Pharmacol*, 2002-2004; *Endocrinology*, 2002-2005, 2008-2011, and 2016-2017; *Canc Therapy,* 2003-2007; *Lett Drug Design Discovery,* 2004-present; *Medical Hypothesis and Research*, 2004-present; *Arch Biochem Biophys,* 2004-2006; *Medicinal Chemistry,* 2005-2014; *PPAR*

Research, 2006-present; *Open Drug Metabolism,* 2007-2012; *Open Toxicology Journal*, 2007-2013; *BioMed Res Int'l/Pharmacology*, 2008-present; *Clin Pharmacol: Advances and Applications*, 2009-present; *Hepatic Medicine: Evidence and Research*, 2009-present; *Frontiers in Drug Metabolism and Transport*, 2010-present; *BMC Molecular Cancer*, 2010-present; *JAK-STAT Journal*, 2011-present; *Am J Cancer Research*, 2011-present; *J Canc Ther Res*, 2011-present; *Res J Endocrinol Metab*, 2013-present.

Society Memberships: Endocrine Society, Amer Assoc Cancer Research, Amer Soc Biochem & Molec Biol, Int'l Society for Study of Xenobiotics (ISSX), Amer Soc Pharmacol Exper Therapeutics, Growth Hormone Research Society, American Soc Gene Therapy, Amer Soc Microbiology

Honors and Awards: New York State Regents Scholar, 1972-1975; Konkol Chemistry Prize, Queens College, CUNY, 1975; Summa Cum Laude, Queens College, CUNY, 1975; Phi Beta Kappa, 1975; Damon Runyon-Walter Winchell Cancer Fund Fellowship, 1980-1981; NIH NRSA Postdoctoral Fellowship Award, 1981-1983; Research Corporation Award, 1983; Rita Allen Foundation Scholar Award, Harvard Medical School nominee and Awardee finalist, 1988; Burroughs-Wellcome Endocrine Toxicology Symposium Lectureship, 1993; Howard Hughes Medical Institute-sponsored Senior Faculty Appointment, Boston University, 1994-1998; Thompson-ISI Twenty Year Highly Cited Researcher in Pharmacology, 1985-2004; Top 100 Cited Researchers in Pharmacology & Toxicology: 2006 Citation Rank, 13 of top 100; Humboldt and Free University of Berlin: Molecular Endocrinology Lectureship, 2009; 10th Annual Nancy Bucher Lecture, BU School of Med, 2016; Brodie Award in Drug Metabolism, American Soc Pharmacology and Experimental Therapeutics, 2018.

Invited Speaker *(through 2017):* 146 speaking invitations at national and international conferences and symposia, and 130 departmental seminar series invitations.

Publications: *267 peer-reviewed primary journal articles, 8 issued patents, 83 journal review articles and book chapters, 322 meeting abstracts.* ***Total citations****: 36,148 lifetime citations; 6,529 citations since 2013.* ***H-index*** *89, i10-index 294; 75 publications cited >100 times each (Google Scholar)*

C. Contribution to Science: Publications: http://www.ncbi.nlm.nih.gov/pubmed/?term=waxman+dj

Overview: My laboratory has made seminal contributions to the biochemistry, cancer pharmacology and therapeutics, and gene-based regulation of hepatic cytochrome P450 drug and steroid-metabolizing enzymes over the past 35 years. Our work led to fundamental discoveries on the molecular basis of sex-differences in the expression and endocrine regulation of liver drug-metabolizing enzymes, and on the actions of nuclear receptors that are central to the endocrine actions, toxicology and carcinogenesis of many xenobiotics. I also pioneered research in the field of cancer gene therapy using prodrug-activating P450 enzymes, exemplified with cyclophosphamide. My laboratory's most recent work in this area has led to important advances with translational potential on the impact of drug scheduling on the efficacy of cytotoxic cancer chemotherapeutic drugs, their interactions with anti-angiogenic agents, and their stimulatory effects on the immune system.

Our current research efforts are directed in three areas: **1)** genomic and epigenetic actions of growth hormone (GH), which underlie sex differences in liver gene expression and confer clinically significant sex differences in the metabolism of many drugs, steroids and lipids, as well as responses to hepatic stresses and the occurrence of hepatocellular carcinoma; **2)** receptor-based mechanisms by which environmental chemical exposures impart long-term effects on development and adult disease susceptibility; **3)** the impact of cancer chemotherapeutic drug scheduling on the tumor microenvironment, in particular anti-tumor immune responses.

Select Publications (Highlights)

1) GH and STAT5 regulation of liver sex-differences

Waxman DJ*, Dannan GA, Guengerich FP. Regulation of rat hepatic cytochrome P450. Age-dependent expression, hormonal imprinting, and xenobiotic inducibility of sex-specific isoenzymes. (1985) Biochemistry 24: 4409-4417.* Citations: ***644***

Udy GB, Towers RP, Snell RG, Wilkins RJ, Park SH, Ram PA, ***Waxman DJ****, Davey HW*. Requirement of STAT5b for sexual dimorphism of body growth rates and liver gene expression. (1997) Proceedings of the National Academy of Sciences, USA 94: 7239-7244. (*correspondence);* Citations: ***966***

Waxman DJ*, Holloway MG. Sex differences in the expression of hepatic drug metabolizing enzymes. (2009) Molecular Pharmacology 76: 215-228.* Citations: ***412***

Zhang Y, Laz EV, ***Waxman DJ****. Dynamic, sex-differential STAT5 and BCL6 binding to sex-biased, growth hormone-regulated genes in adult mouse liver. (2012) Molec Cellular Biology 32: 880-896.* Citations: ***74***

2) Sex-specific liver chromatin states

Ling G, Sugathan A, Mazor T, Fraenkel E, ***Waxman DJ****. Unbiased, genome-wide in vivo mapping of transcriptional regulatory elements reveals sex differences in chromatin structure associated with sex-specific liver gene expression. (2010) Molecular Cellular Biology 30: 5531-5544.* Citations: ***53***

Sugathan A, ***Waxman DJ****. Genome-wide analysis of chromatin states reveals distinct mechanisms of sex-dependent gene regulation in male and female mouse liver. (2013) Molecular Cellular Biology 33: 3594-3610.* Citations: ***43***

Melia T, Hao P, Yilmaz F, ***Waxman DJ****. Hepatic long intergenic noncoding RNAs: high promoter conservation and dynamic, sex-dependent transcriptional regulation by growth hormone*. (2016) *Molecular Cellular Biology 36: 50-69*.

Lau-Corona D, Suvorov A, ***Waxman DJ****. Feminization of male mouse liver by persistent growth hormone stimulation: Activation of sex-biased transcriptional networks and dynamic changes in chromatin states. (2017) Molecular Cellular Biology. [Epub ahead of print] PMID: 28694329.*

3) Xenobiotic-responsive nuclear receptors in pharmacology and toxicology

Xie W, Radominska-Pandya A, Shi Y, Simon CM, Nelson MC, Ong ES, ***Waxman DJ****, Evans RM. An essential role for nuclear receptors SXR/PXR in detoxification of cholestatic bile acids. (2001) Proceedings of the National Academy of Sciences, USA 98:3375-3380.* Citations*:* ***691***

Hurst CH, ***Waxman DJ****. Activation of PPARα and PPARγ by environmental phthalate monoesters. (2003) Toxicological Sciences 74: 297-308.* Citations: ***330***

Ngan CH, Beglov D, Rudnitskaya AN, Kozakov D, ***Waxman DJ****, Vajda S. The structural basis of pregnane X receptor binding promiscuity. (2009) Biochemistry 48: 11572-11581.* Citations: ***58***

Lodato NJ, Melia T, Rampersaud A, ***Waxman DJ****. Sex-differential responses of tumor promotion-associated genes and dysregulation of novel long noncoding RNAs in constitutive androstane receptor-activated mouse liver. (2017) Toxicological Sciences. 159: 25-41.*

4) P450 bioactivation of anti-cancer prodrugs cyclophosphamide and ifosfamide

Chang TKH, Weber GF, Crespi CL, ***Waxman DJ****. Differential activation of cyclophosphamide and ifosfamide by cytochrome P450 2B and cytochrome P450 3A in human liver microsomes. (1993) Cancer Research 53: 5629-5637.* Citations: ***587***

Roy P, Yu LJ, Crespi CL, ***Waxman DJ****. Development of a substrate-activity based approach to identify the major human liver P450 catalysts of cyclophosphamide and ifosfamide activation based on cDNA-expressed activities and liver microsomal P450 profiles. (1999) Drug Metab. and Disposition 27: 655-666.* Citations: ***307***

5) Metabolism-based strategies to increase efficacy of anti-cancer drugs

Waxman DJ*, Schwartz PS. Harnessing apoptosis for improved anticancer gene therapy. (2003) Cancer Research 63: 8563-8572.* Citations: ***139***

Ma J, ***Waxman DJ****. Combination of antiangiogenesis with chemotherapy for more effective cancer treatment. (2008) Molecular Cancer Therapeutics 7: 3670-3684.* Citations: ***244***

Doloff JC, ***Waxman DJ****. VEGF receptor inhibitors block the ability of metronomically dosed cyclophosphamide to activate innate immunity-induced tumor regression. (2012) Cancer Research* 72: 1103-1115. Citations: ***71***

Wu J, ***Waxman DJ****. Metronomic cyclophosphamide eradicates large implanted GL261 gliomas by activating antitumor Cd8+ T cell responses and immune memory. (2015) OncoImmunology*, 4: e1005521. Citations: ***29***

Citation summary statistics ***(Google Scholar)***

	All	Since 2013
Citations	36,167	6,536
h-index	89	38
i10-index	294	139

BIBLIOGRAPHY

(I) ORIGINAL JOURNAL ARTICLES: *(DJW PhD publications: 1-13; DJW Postdoctoral publications: 14-20)*

1. Waxman DJ, Strominger JL. Cleavage of a COOH-terminal hydrophobic region from D-alanine carboxypeptidase, a penicillin-sensitive bacterial membrane enzyme: characterization of active, water-soluble fragments. (1979) J Biol Chem 254, 4863-4875.

2. Waxman DJ, Strominger JL. Cephalosporin-sensitive penicillin-binding proteins of Staphylococcus aureus and Bacillus subtilis active in the conversion of [^{14}C]penicillin G to [^{14}C]phenylacetylglycine. (1979) J Biol Chem 254, 12056-12061.

3. Yocum RR, Waxman DJ, Rasmussen JR, Strominger JL. Mechanism of penicillin action: pencillin and substrate bind covalently to the same active site serine of two bacterial D-alanine carboxypeptidases. (1979) Proc Natl Acad Sci 76, 2730-2734.

4. Waxman DJ, Yocum RR, Strominger JL. Penicillins and cephalosporins are active site-directed acylating agents: evidence in support of the substrate analog hypothesis. (1980) Phil Trans R Soc Lond B289, 257-271.

5. Waxman DJ, Strominger JL. Sequence of active site peptides from the penicillin-sensitive D-alanine carboxypeptidase of Bacillus subtilis: mechanism of pencillin action and sequence homology to β-lactamases. (1980) J Biol Chem 255, 3964-3976.

6. Waxman DJ, Yu W, Strominger JL. Linear, uncrosslinked peptidoglycan secreted by penicillin-treated Bacillus subtilis: characterization as a substrate for penicillin-sensitive D-alanine carboxypeptidase. (1980) J Biol Chem 255, 11577-11587.

7. Waxman DJ. Structural studies of penicillin-sensitivie D-alanine carboxypeptidase. (1980) Ph.D. Dissertation, Harvard University.

8. Moews PC, Knox JR, Waxman DJ, Strominger JL. Comparison of predicted secondary structures of β-lactamases and penicillin-sensitive D-alanine carboxypeptidases. (1981) Int J Prot Pept Res 17, 211-218.

9. Waxman DJ, Strominger JL. Limited proteolysis of the penicillin-sensitive D-alanine carboxypeptidase purified from Bacillus subtilis membranes. Active, water-soluble fragments generated by cleavage of a COOH-terminal membrane anchor. (1981) J Biol Chem 256, 2059-2066.

10. Waxman DJ, Strominger JL. Primary structure of the COOH-terminal membranous segment of a penicillin-sensitive enzyme purified from two bacilli. (1981) J Biol Chem 256, 2067-2077.

11. Waxman DJ, Lindgren DM, Strominger JL. High-molecular weight penicillin-binding proteins from membranes of bacilli. (1981) J Bacteriol 148, 950-955.

12. Yocum RR, Amanuma H, O'Brien TA, Waxman DJ, Strominger JL. Penicillin is an active site inihibitor for four genera of bacteria. (1982) J Bacteriol 149, 1150-1153.

13. Waxman DJ, Amanuma H, Strominger JL. Amino acid sequence homologies between Escherichia coli penicillin-binding protein 5 and class A β-lactamases. (1982) FEBS Lett 139, 159-163.

14. Light DR, Waxman DJ, Walsh C. Studies on the chirality of sulfoxidation catalyzed by bacterial flavoenzyme cyclohexanone monooxygenase and hog liver flavin adenine dinucleotide-containing monooxygenase. (1982) Biochemistry 21, 2490-2498.

15. Waxman DJ, Light DR, Walsh C. Chiral sulfoxidations catalyzed by rat liver cytochromes P-450. (1982) Biochemistry 21, 2499-2507.

16. Waxman DJ, Walsh C. Phenobarbital-induced rat liver cytochrome P-450. Purification and characterization of two closely related isozymic forms. (1982) J Biol Chem 257, 10446-10457.

17. Waxman DJ, Walsh C. Catalytic and structural properties of two new cytochrome P-450 isozymes from phenobarbital-induced rat liver: comparison to the major induced isozymic form. (1982) In: Hietanen E, et al., eds. Cytochrome P-450. Biochemistry, biophysics and environmental implications. New York: Elsevier/Biomedical Press, 311-316.

18. Waxman DJ, Ko A, Walsh C. Testosterone hydroxylations catalyzed by purified rat liver cytochrome P-450 isozymes. (1982) In: Hietanen E, et al., eds. Cytochrome P-450. Biochemistry, biophysics and environmental implications. New York: Elsevier/Biomedical Press, 381-386

19. Waxman DJ, Walsh C. Cytochrome P-450 isozyme 1 from phenobarbital-induced rat liver: Purification, characterization and interactions with metyrapone and cytochrome b_5. (1983) Biochemistry 22, 4846-4855.

20. Waxman DJ, Ko A, Walsh C. Regioselectivity and stereoselectivity of androgen hydroxylations catalyzed by cytochrome P-450 isozymes purified from phenobarbital-induced rat liver. (1983) J Biol Chem 258, 11937-11947.

21. Waxman DJ. Rat hepatic cytochrome P-450 isoenzyme 2c: identification as a male-specific, developmentally-induced steroid 16α-hydroxylase and comparison to a female-specific cytochrome P-450 isoenzyme. (1984) J Biol Chem 259, 15481-15490.

22. Tauber AI, Wright J, Higson FK, Edelman SA, Waxman DJ. Purification and characterization of the human neutrophil NADH-cytochrome b_5 reductase. (1985) Blood 66, 673-678.

23. Waxman DJ, Dannan GA, Guengerich FP. Regulation of rat hepatic cytochrome P-450: age-dependent expression, hormonal imprinting and xenobiotic inducibility of sex-specific isoenzymes. (1985) Biochemistry 24, 4409-4417.

24. Frey AB, Waxman DJ, Kreibich G. The structure of phenobarbital-inducible rat liver cytochrome P-450 isoenzyme PB-4: production and characterization of site-specific antibodies. (1985) J Biol Chem 260, 15253-15265.

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33. Dannan GA, Guengerich FP, Waxman DJ. Hormonal regulation of rat liver microsomal enzymes: role of gonadal steroids in programming, maintenance and suppression of Δ^4-steroid 5α-reductase, flavin-containing monooxygenase and sex-specific cytochromes P-450. (1986) J Biol Chem 261, 10728-10735.

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35. Clarke L, Rosowsky A, Waxman DJ. Inhibition of human liver folylpolyglutamate synthetase by non γ-glutamylatable folate analogs. (1987) Molec Pharmacol 31, 122-127.

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