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Name: Edmund A. Mroz, Jr.

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460 West 12th Avenue
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Education

1970 B.A. magna cum laude	Chemistry, Yale University
1971 A.M.	Physiology, Harvard University
1978 Ph.D.	Physiology, Harvard University Thesis adviser: Susan E. Leeman, Ph.D.

Postdoctoral Training

1978-1980	Research Fellow in Physiology, Harvard Medical School
1980-1982	Research Associate in Physiology, Harvard Medical School Lab PI: Claude P. Lechene, M.D.

Faculty Academic Appointments

1982-1994	Assistant Professor of Physiology in the Department of Otology and Laryngology, Harvard Medical School
1994-2015	Associate Professor of Physiology in the Department of Otology and Laryngology, Harvard Medical School
2015-present	Research Associate Professor Department of Otolaryngology – Head and Neck Surgery The Ohio State University

Appointments at Hospitals

1982-2004	Research Associate in Otolaryngology Massachusetts Eye and Ear Infirmary, Boston, MA
2006-2011	Research Fellow in Surgery Massachusetts General Hospital, Boston, MA
2011-2012	Research Scientist Department of Surgery (Surgical Oncology) Massachusetts General Hospital, Boston, MA
2012-2015	Senior Research Scientist Department of Surgery (Surgical Oncology) Massachusetts General Hospital, Boston, MA

Other Professional Positions

1971-1973	Biological Sciences Assistant, U.S. Army Medical Research and Nutrition Laboratory, Denver CO.
1973-1975	Teaching Fellow in Physiology, Harvard Medical School

Major Administrative Leadership Positions

Local:

1981-1995	Director of laboratory exercises on respiratory physiology for first-year HMS students
1984-1988	Originator, course director, "Forces, flows and feedback in physiology," Harvard Medical School
1989-1991	Organizer, course director, "Principles of mammalian physiology," Harvard Medical School
1991-1995	Co-organizer, co-course director, "Human physiology: classical and contemporary approaches," Harvard Medical School
1994	Co-course organizer, "Molecular Biology of the Auditory System," Harvard Medical School
1996-2003	Course director, "Human physiology: classical and contemporary approaches," Harvard Medical School
1999-2003	Course director, "The Auditory Periphery," Harvard/MIT Division of Health Sciences and Technology

Committee Service

Local:

1988-2002	Resident Selection Committee, Department of Otology and Laryngology, Harvard Medical School
1992-1997	Student Tracking Committee, HST graduate program in Speech and Hearing Science
2000-2005	Chair, Animal Care Committee, Mass. Eye and Ear Infirmary

Professional Societies

1989-2006	Association for Research in Otolaryngology; member of Program Committee for 1990 Midwinter Meeting

Grant Review Activities

1990, 1991, 1995	Communicative Disorders Review Committee, National Institute on Deafness and Other Communication Disorders, National Institutes of Health; ad hoc consultant
1991, 1997, 1998	Hearing Research Study Section, Division of Research Grants, National Institutes of Health; ad hoc consultant

Report of Funded and Unfunded Projects

Funding Information

Past

1978-1980	Nephron handling of hormones and enzymes NIH F32 AM005894 Individual NRSA
1980-1982	Pancreatic enzymes in individual granules and cells (C. Lechene, PI) NIH R01 AM026488 Investigator
1983-1992	Cochlea—hair cell transmitters under Program Project: Basic and Clinical Studies of the Auditory System NIH P01 NS013126 Project PI
1984-1990	Identification of hair cell transmitters (W. Sewell, PI) NIH R01 NS019097 Investigator
1990-2003	Pharmacological analysis of ionic balance in hair cells NIH R01 DC000033 PI
1990-2003	Pharmacology of neurotransmitters in hair-cell organs (W. Sewell, PI) NIH R01 DC000767 Investigator
1992-1997	Inner Ear: Ion homeostasis in the sensory epithelium under Program Project: Basic and Clinical Studies of the Auditory System NIH P01 DC000119 Project PI
1997-2002	Inner Ear: Cell networks in normal & damaged cochleas (J. Adams, PI) under Program Project: Basic and Clinical Studies of the Auditory System NIH P01 DC000119 Investigator
1997-1999	Spatial dynamics of protein turnover in stereocilia (C. Lechene, PI)

NIH R21 DC003463
Investigator

1999-2003 National resource for imaging mass spectrometry (C. Lechene, PI)
NIH P20 EB001974
Investigator

2000-2003 Spatial dynamics of protein turnover in cochlea (C. Lechene, PI)
NIH R01 DC004179
Investigator

2009-2012 Smoking's impact on epigenetic regulation of p16 (J Rocco, PI)
Flight Attendant Medical Research Institute
Investigator

Current

2011- Bcl-2 as a Biomarker for Prognosis and Therapy of Head and Neck Cancer (J. Rocco, PI)
NIH R01 DE022087, and Supplement -03S1
Investigator
Goal: parent project, to evaluate the relations of Bcl2 expression, Bcl2-related apoptotic function, HPV status, and TP53 mutation to outcome in oropharyngeal squamous cell carcinoma; supplement, to incorporate analysis of intra-tumor genomic heterogeneity into the parent project, using the MATH measure of heterogeneity developed by Mroz and Rocco. Role: collaborate with J. W. Rocco in formulating the project, experimental design, conduct of experiments, supervision of students, and preparing oral and written publications of results; primary responsibility for data analysis.

Current Unfunded Projects

2003- Control of the INK/ARF locus (J. Rocco, PI)
Goal: to decipher the mechanisms that regulate the expression of the two products of this single tumor suppressor gene. Role: collaborate with J. W. Rocco in formulating the project, experimental design, conduct of experiments, supervision of students, and preparing oral and written publications of results.

Report of Local Teaching and Training

Medical/Dental/DMS/HST Courses:

Years	Course Name	Role	Students:		Prep.	Contact
			type	no./yr.	Hr./year	Hr./year
1973	Physiology (HST)	Conference instructor	medical/ Ph.D.	10	40	20
1974-1975 1981-1991	Medical Physiology	Conference instructor	medical/ dental	10	40	40
1981-1995	Medical Physiology; later Metabolism and Function of Human Organ Systems	Director, respiratory lab	medical /dental	150	40	10
1982-1995	Medical Physiology; later Metabolism and Function of Human Organ Systems	Lecturer	medical /dental	150	30	10
1985	Topics in Physiology	Lecturer	Ph.D.	10	24	6
1984-1988	Forces, flows, and feedback in physiology	Originator, sole lecturer	Ph.D.	6	120	40
1989-1991	Principles of mammalian physiology	Originator, main lecturer	Ph.D.	6	120	40
1991-1995	Metabolism and Function of Human Organ Systems	“Expert resource” faculty	medical /dental	150	6	3
1991-1995	Human physiology: classical and contemporary approaches	Co-organizer, Co-director and lecturer	Ph.D.	12	80	40
1996-2003	Human physiology: classical and contemporary approaches	Director, sole lecturer	Ph.D.	6	100	50
1992-2003	Anatomy of speech and hearing	Lecturer	Ph.D.	8	4	2
1994	Molecular Biology of the Auditory System	Co-organizer, lecturer	Ph.D.	8	20	20
1999-2003	The Auditory Periphery (HST 721)	Course director, lecturer	Ph.D.	10	40	60

Graduate Medical Courses:

Years	Course Name	Role	Students:		Prep.	Contact
			type	no./yr.	Hr./year	Hr./year
1983-1986; 1996-2003	Otolaryngology Basic Sciences	Lecturer	resident/ fellow	12	6	2

Local Invited Teaching Presentations:

Years	Course Name	Role	Students:		Prep.	Contact
			type	no./yr.	Hr./year	Hr./year
1974,1975	Health Sciences (Harvard Summer School)	Lecturer	under-graduate	50	20	3
1979	Math tutorial (MARC program)	Instructor, tutor; helped design	under-graduate	10	120	60
1987,1989, 1993	Auditory Physiology (MIT)	Lecturer	Ph.D.	8	8	2

Formally Supervised Trainee:

Ph.D. Thesis Supervisor of Diane Ronan (1995-2003). Thesis: "Sodium entry pathways in isolated goldfish hair cells," Harvard-MIT Division of Health Sciences and Technology, Program in Speech and Hearing Bioscience and Technology, 2003. Diane (Ronan) Williams is now a Lecturer in the School of Public Health and Health Systems, University of Waterloo, Waterloo, ON, Canada.

Recent Local Invited Presentations:

2013 Measuring intra-tumor heterogeneity and its relation to outcome.
Radiation Oncology lunchtime seminars, Mass. General Hospital

Report of Regional, National and International Invited Teaching and Presentations

1987 Invited talk at Symposium on "New Techniques for Otolaryngology Research," Association for Research in Otolaryngology. Title: "Methods for biochemical and pharmacological analysis of isolated auditory cells."

1994 Invited "Overview" paper at Symposium on "Homeostatic Mechanisms of the Inner Ear," Association for Research in Otolaryngology. Title: "Unique demands placed on ion-transport processes of cells in the inner ear."

Report of Technological and Other Scientific Innovations

Use of secondary-ion imaging mass spectroscopy to quantify subcellular protein turnover rates.

1996-2003. With C.P. Lechene (Brigham and Women's Hospital, BWH), I originated the concept of using heavy-nitrogen labeling combined with secondary-ion imaging mass spectroscopy to quantify subcellular protein turnover rates, and I began studies based on this technology to examine protein turnover rates in hair-cell stereocilia and in other inner-ear structures. My efforts were instrumental in the establishment of a National Biotechnology Resource for this technology at BWH in 2000, which has resulted in a dozen papers by others applying this technology to biology, including one on the question I initially identified about stereociliary protein turnover (Zhang DS et al., Nature. 2012 Jan 15;481:520-4).

System and method for using genetic data to determine intra-tumor heterogeneity.

International patent application PCT/US2013/063044, filed by Mass. General Hospital October 2, 2013.
Working with J.W. Rocco, I developed a method to use results of next-generation sequencing (NGS) of tumor and matched normal DNA to measure intra-tumor heterogeneity, differences among cancer cells within a tumor that have long been suspected to influence outcome of cancer therapy. High heterogeneity by this measure was related to worse outcome in an initial single-institution cohort of head and neck cancer patients, particularly among those receiving chemoradiotherapy (*Cancer* 2013). We have subsequently validated this result in a larger multi-institutional data set from The Cancer Genome Atlas (*PLOS Medicine* 2015). With such NGS expected soon to enter clinical oncology practice, this heterogeneity measure should provide a straightforward way to incorporate information about intra-tumor heterogeneity into design of clinical trials and ultimately into clinical practice, in head and neck cancer and in other cancers.

Report of Education of Patients and Service to the Community

Educational Material for Patients and the Lay Community:

1999 Reviewed and extensively revised illustrations and captions for "How the Body Works" chapter in *The Harvard Medical School Family Health Guide*, (A. Komaroff, ed.), Harvard Medical Publications.

Report of Scholarship

Publications:

Peer-Reviewed Publications in print or other media

Research investigations

Sullivan FJ, **Mroz** EA, Miller RE. Electronic calibration for indocyanine dye-dilution curves. Am Heart J 1973; 85: 506-510.

Sullivan FJ, **Mroz** EA, Miller RE. The precision of a special-purpose analog computer for cardiac output determination. Ann Surg 1975; 181: 232-238.

Mroz EA, Brownstein MJ, Leeman SE. Evidence for substance P in the habenulo-interpeduncular tract. Brain Research 1976; 113: 597-599.

Brownstein MJ, **Mroz** EA, Kizer JS, Palkovits M, Leeman SE. Regional distribution of substance P in the brain of the rat. Brain Research 1976; 116: 299-305.

Schenker C, **Mroz** EA, Leeman SE. Release of substance P from isolated nerve endings. Nature 1976; 264: 790-792.

Mroz EA, Brownstein MJ, Leeman SE. Evidence for substance P in the striatonigral tract. Brain Research 1977; 125: 305-311.

Brownstein MJ, **Mroz** EA, Tappaz ML, Leeman SE. On the origin of substance P and glutamic acid decarboxylase in the substantia nigra. Brain Research 1977; 135: 315-323.

Gamse R, **Mroz** EA, Leeman SE, Lembeck F. The intestine as source of immunoreactive substance P in plasma of the cat. Naunyn-Schmiedeberg's Arch Pharmacol 1978; 305: 17-21.

Palkovits M, **Mroz** EA, Brownstein MJ, Leeman SE. Descending substance P-containing pathway: a component of the ansa lenticularis. Brain Research 1978; 156: 124-128.

Guyenet PG, **Mroz** EA, Aghajanian GK, Leeman SE. Iontophoretic ejection of substance P from glass micropipets--correlation with time-course of neuronal excitation in vivo. Neuropharmacology 1979; 18: 553-558.

Nutt JG, **Mroz** EA, Leeman SE, Williams AC, Engel WK, Chase TN. Substance P in human cerebrospinal fluid: reductions in peripheral neuropathy and autonomic dysfunction. Neurology 1980; 30: 1280-1285.

Mroz EA, Lechene C. Fluorescence analysis of picoliter samples. Analyt Biochem 1980;

102: 90-96.

Graber ML, Bengele HH, **Mroz** E, Lechene C, Alexander EA. Acute metabolic acidosis augments collecting duct acidification rate in the rat. Am J Physiol 1981; 241: F669-F676.

Mroz EA, Roman RJ, Lechene C. Fluorescence assay for picomole quantities of ammonia. Kidney International 1982; 21: 524-527.

Mroz EA, Lechene, C. An NADH-coupled assay for femtogram or nanogram quantities of chymotrypsin. Analyt Biochem 1983; 128: 181-185.

Leese, HJ, Biggers, JD, **Mroz**, EA, Lechene, C. Nucleotides in a single mammalian ovum or preimplantation embryo. Analyt Biochem 1984; 140: 443-448.

Mroz EA, Lechene C. Pancreatic zymogen granules differ markedly in protein composition. Science 1986; 232: 871-873.

Adams JC, **Mroz** EA, Sewell WF. A possible neurotransmitter role for CGRP in a hair-cell sensory organ. Brain Research 1987; 419: 347-351.

Sweeney TK, **Mroz** EA, Sewell WF. Isolation and culture of auditory cells from the goldfish (*Carassius auratus*). Hearing Research 1987; 28: 153-160.

Sewell WF, **Mroz** EA. Neuroactive substances in inner ear extracts. J Neuroscience 1987; 7: 2465-2475.

Mroz EA, Sewell WF. Pharmacological alterations of the activity of afferent fibers innervating hair cells. Hearing Research 1989; 38: 141-162.

Sewell WF, **Mroz** EA. Purification of a low-molecular-weight excitatory substance from the inner ears of goldfish. Hearing Research 1990; 50:127-137.

Mroz EA, Nissim KR, Lechene C. Electron-probe analysis of isolated goldfish hair cells: implications for preparing healthy cells. Hearing Research 1993; 70:9-21.

Mroz EA, Nissim KR, Lechene C. Rapid resting ion fluxes in goldfish hair cells are balanced by (Na^+,K^+)-ATPase. Hearing Research 1993; 70:22-30.

Sewell WF, **Mroz** EA. Flavin-adenine dinucleotide is a major endogenous fluorophore in hair cells of the inner ear. Hearing Research 1993; 70: 131-138.

Mroz EA, Lechene C. Calcium and magnesium transport by isolated goldfish hair cells. Hearing Research 1993; 70: 139-145.

Mroz EA, Lechene C. Extracellular *N*-methyl-D-glucamine leads to loss of hair-cell sodium, potassium, and chloride. Hearing Research 1993; 70: 146-150.

Sewell WF, **Mroz** EA, Evans JE. Extracts of retina and brain that excite afferent fibers innervating hair cells contain a compound related to hydroxyphenylglycine-N-carbamoyl. Synapse 2005; 58: 129-40.

Mroz EA, Baird AH, Michaud WA, Rocco JW. COOH-terminal binding protein regulates expression of the p16INK4A tumor suppressor and senescence in primary human cells. Cancer Res 2008; 68: 6049-53.

Michaud WA*, Nichols AC*, **Mroz** EA*, Faquin WC, Clark JR, Begum S, Westra WH, Wada H, Busse PM, Ellisen LW, Rocco JW. Bcl-2 blocks cisplatin-induced apoptosis and predicts poor outcome following chemoradiation treatment in advanced oropharyngeal squamous-cell carcinoma. Clin Cancer Res 2009; 15: 1645-54. *co-first authors

Nichols AC, Faquin WC, Westra WH, **Mroz** EA, Begum S, Clark JR, Rocco JW. HPV-16 infection predicts treatment outcome in oropharyngeal squamous cell carcinoma. Otolaryngol Head Neck Surg 2009; 140: 228-34.

Nichols AC, Finkelstein DM, Faquin WC, Westra WH, **Mroz** EA, Kneuertz P, Begum S, Michaud WA, Busse PM, Clark JR, Rocco JW. Bcl2 and HPV16 as predictors of outcome following concurrent chemoradiation for advanced oropharyngeal cancer. Clin Cancer Res 2010; 16: 2138-2146.

Mroz EA, Rocco JW. MATH, a novel measure of intratumor genetic heterogeneity, is high in poor-outcome classes of head and neck squamous cell carcinoma. Oral Oncol 2013; 49: 211-5.

Mroz EA, Tward AD, Pickering CR, Myers JN, Ferris RL, Rocco JW. High intratumor genetic heterogeneity is related to worse outcome in patients with head and neck squamous cell carcinoma. Cancer 2013; 119: 3034-42.

Mroz EA, Tward AD, Hammon RJ, Ren Y, Rocco JW. Intra-tumor Genetic Heterogeneity and Mortality in Head and Neck Cancer: Analysis of Data from The Cancer Genome Atlas. PLOS Medicine Feb. 10, 2015; DOI: 10.1371/journal.pmed.1001786

Other peer-reviewed publications

Leeman SE, **Mroz** EA. Substance P. Life Sci 1974; 15: 2033-2044.

Mroz EA, Leeman SE. Substance P. Vitamins and Hormones 1977; 35: 209-281.

Mroz, EA. Possible role of carbamates in neurotoxicity and neurotransmitter inactivation. Science 1989; 243: 1613.

Mroz, EA, Rocco JW. RNA interference: natural, experimental, and clinical roles in cancer

biology. Head Neck 2006; 28: 1132-41.

Mroz EA, Rocco JW. Functional p53 status as a biomarker for chemotherapy response in oral-cavity cancer. J Clin Oncol 2010; 28: 715-7.

Mroz EA, Forastiere AA, Rocco JW. Implications of the oropharyngeal cancer epidemic**.** J Clin Oncol. 2011; 29: 4222-3.

Mroz EA, Rocco JW. Gene expression analysis as a tool in early-stage oral cancer management. J Clin Oncol. 2012; 30: 4053-5.

Bonilla-Velez J, **Mroz** EA, Hammon RJ, Rocco JW. Impact of human papillomavirus on oropharyngeal cancer biology and response to therapy: implications for treatment. Otolaryngol Clin North Am**.** 2013; 46:521-43.

Non-peer reviewed scientific or medical publications/materials in print or other media

Proceedings of meetings or other non-peer reviewed research publications

Mroz EA, Brownstein MJ, Leeman SE. Distribution of substance P in the rat brain: evidence for the existence of substance P-containing tracts. In: von Euler US, Pernow B, eds. Substance P. New York: Raven, 1977: 147-154.

Losay J, **Mroz** EA, Tregear GW, Leeman SE, Gamble WJ. Action of substance P on the coronary blood flow in the isolated dog heart. In: von Euler US, Pernow B, eds. Substance P. New York: Raven, 1977: 287-293.

Reviews, chapters, monographs and editorials

Leeman SE, **Mroz** EA, Carraway RE. Substance P and neurotensin. In: Gainer H, ed. Peptides in Neurobiology. New York: Plenum, 1977: 99-144.

Mroz EA, Leeman SE. Substance P. In: Jaffe BM, Behrman HR, eds. Methods of Hormone Radioimmunoassay, second edition. New York: Academic, 1978: 121-137.

Professional Educational Materials or Reports, in print or other media

1975-1995 "Camel" for HMS first-year Medical Physiology course. Wrote discussion questions on respiratory physiology in 1975; reviewed and revised annually through 1995. Prepared and annually revised detailed lecture notes for my lectures (1982-1995); depending on year, topics included respiratory mechanics, respiratory gas exchange, control of ventilation, acid-base regulation, renal concentrating mechanisms, renal acid-base handling.

1984-2003 Handouts on selected topics covered in graduate physiology courses: units of

measurement, forces and flows in physiology, equations commonly used in physiology, solute and ion transport, respiratory mechanics and flow limitation, acid-base chemistry in physiology.

1984-2003 Problem sets/discussion questions (approximately biweekly during the semester) for graduate physiology courses.

1996-2003 Notes and bibliography on "Cochlear homeostasis" for HMS/MEEI Basic Sciences course in Otolaryngology.

1997-1998 Overview, "Getting started in physiology," written for students in Markey/MBS program taking "Human physiology: classical and contemporary approaches".

1997-1998 Detailed notes to accompany assigned textbook readings, for students in Markey/MBS program taking "Human physiology: classical and contemporary approaches".

Thesis:
Mroz EA. Substance P: radioimmunoassay, regional distribution in the brain of the rat, and quantitation of iontophoretic application [dissertation]. Cambridge (MA): Harvard University; 1978.

Abstracts, Poster Presentations and Exhibits Presented at Professional Meetings (last 4 years):

Mroz EA, Michaud W, Ryan J, Deschler D, Emerick K, Lin D, Faquin W, Busse, P, Chan A, Clark J, Rothenberg S, Wirth L, Letai A, Rocco JW. BH3 profiling to predict outcome in oropharyngeal cancer. MGH Clinical Research Day, Boston MA, October 2011. (Named best abstract from the Department of Surgery.)

Mroz EA, Michaud W, Ryan J, Letai A, Rocco JW. Directly measuring mitochondrial apoptotic priming in human oropharyngeal cancer. Cell Death Meeting, Cold Spring Harbor NY, October 2011.

Mroz EA, Rocco JW. MATH, a novel measure of intratumor genetic heterogeneity, is high in poor-outcome classes of head and neck squamous cell carcinoma. MGH Clinical Research Day, Boston MA, October 2012.

Mroz EA, Tward A, Pickering C, Myers J, Ferris R, Rocco JW. Higher intra-tumor genetic heterogeneity is related to worse outcome in head and neck squamous cell carcinoma. MGH Clinical Research Day, Boston MA, October 2013.

Rocco JW, Tward AD, Ren Y, Hammon RJ, **Mroz EA**. Mutant-Allele Tumor Heterogeneity (MATH) Adds to Human Papillomavirus (HPV) Status in Predicting Outcome in Head and Neck Squamous Cell Carcinoma. Multidisciplinary Head and Neck Cancer Symposium. Scottsdale AZ, February 2014. (Featured in Meeting highlights and Meeting Press conference)