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US PERMANENT RESIDENCE APPLICATION USCIS No. 026-620-507 (PENDING)

EMPLOYMENT AUTHORIZATION PERMIT No. SRC 1490389231

ORIGINAL CITIZENSHIP, MEXICAN

MILITARY SERVICE, BASIC INSTRUCTION IN 1976. CLASS OF 1957, No. 199112446, MEXICO

6TH BATTALION OF THE 16TH INFANTRY BRIGADE, MOVING TO 1ST RESERVE IN 1977

FLUENT IN ENGLISH AND SPANISH

PREPARATION: MARCH 2016

PROFILE

I independently obtained M.D. and Ph.D. degrees, the last with major in Biochemistry. I also obtained the specialty in Medical Genetics in Mexico. I am highly proficient in the biomedical applications of magnetic resonance (MR) technology working in this field for more than 20 years. I am highly knowledgeable in creating and managing research projects involving humans and experimental animals as subjects of research from conception to completion including multi-institutional trials and have been successful in obtaining peer-reviewed funding. I also have ample teaching experience in the fields of Biochemistry and the biomedical applications of MR technology and have trained young professionals in my trade.

My overall research goal aims to increase the ever-expanding applications of MR technology to the noninvasive study of live tissues and organs. MR technology has shown the capability to assess numerous subcellular variables in live systems at the morphologic, functional, and metabolic levels. Given this, my present specific goal seeks to test MR-visible variables in tissues and organs as a means to help resolving the critical need for reliable information to optimize treatment assignment and follow-up. The main aim of this goal is to demonstrate if initial abnormalities in variables measured by MR technology and their changes in serial studies correlate with response to treatment. If this goal is reached, then MR visible subcellular variables with correlative power can function as predictive biomarkers of response aiding with the risk assignment of treatment. These parameters can also be used as prognostic biomarkers to determine treatment success.

Recent contributions of my research have been the substantiation of the correlation and thus the prediction of therapy outcome in patients with lymphomas by the pretreatment tumor measurement of phosphoethanolamine and phosphocholine determined by phosphorus MR spectroscopic imaging. Preliminary results of my research have also suggested the power to predict treatment outcome by three methods. (1) The choline tumor value determined by hydrogen MR spectroscopic imaging. (2) The apparent diffusion of water of cancer cells by diffusion-weighted MR imaging. (3) The kinetic parameters of the incorporation of gadolinium-tagged compounds into cancer cells by dynamic contrast-enhanced imaging.

Given my general goal and these achievements, my current five aims follow. (1) Elucidate the mechanism(s) by which higher tumor levels of phosphocholine and phosphoethanolamine correlate with lack of response to therapy in DLBCL using experimental animals. (2) Assess the power to predictive treatment outcome of multivariate analyses that incorporate variables determined by MR technology (phosphocholine, phosphoethanolamine, total choline, apparent diffusion of water, and the kinetic variables of gadolinium incorporation) and non-MR procedures (i.e., cell of origin by gene expression profiling and tumor incorporation of ¹⁸F-fluorodeoxyglucose by positron emission tomography). (3) Extend the potential value of MR variables to predict treatment outcome in other types of cancer and other diseases where MR technology can assess alteration of subcellular parameters. (4) Increase the sensitivity and speed of MR data acquisition by applying current technical MR advances (i.e., higher magnetic field strengths, echo-planar encoding for MRSI). (5) Improve the post-acquisition processing and analysis of MR data by using advanced mathematical algorithms (i.e., principal component analysis).

EDUCATION

- 1975-1981 DOCTOR OF MEDICINE, NATIONAL UNIVERSITY OF MEXICO, MEXICO CITY, MEXICO.
Comprehensive exam, May of 1981.
License Certification by the National Secretariat of Health under registration number DGP-759011, Mexican Government, Mexico, 1981.
- 1981-1983 MASTER IN SCIENCES (BIOCHEMISTRY), NATIONAL UNIVERSITY OF MEXICO, MEXICO CITY, MEXICO.
Thesis: "Effect of the Intracellular Redox Potentials on Rat Liver Metabolism". Oral exam taken on 1987.
- 1985-1988 DOCTOR OF PHILOSOPHY (BIOCHEMISTRY), NATIONAL UNIVERSITY OF MEXICO, MEXICO CITY, MEXICO.
Thesis: "Application of MR Spectroscopy to the Study of Intermediary Metabolism In Vivo". Oral exam taken on 1989.

POSTGRADUATE TRAINING & FELLOWSHIP APPOINTMENTS

- 1982-1985 INTERNATIONAL POSTDOCTORAL RESEARCH FELLOW, DEPARTMENT OF MOLECULAR BIOPHYSICS & BIOCHEMISTRY, YALE UNIVERSITY, CONNECTICUT, USA.
Research topic: noninvasive applications of ^{13}C , ^1H , and ^{31}P nuclear magnetic resonance to the study of intermediary metabolism in perfused mouse liver and *in situ* (exposed) rat liver.

SPECIALTY CERTIFICATIONS

- 1990 BOARD-CERTIFIED IN MEDICAL GENETICS, NATIONAL BOARD OF HUMAN GENETICS, MEXICO.
LICENSE: NATIONAL, BOARD REGISTRY CNEGH-129 (MEXICO).

FACULTY APPOINTMENTS

- 1981-1982 RESEARCH SCIENTIST, DEPARTMENT OF BIOCHEMISTRY, SCHOOL OF MEDICINE, NATIONAL UNIVERSITY OF MEXICO, MEXICO.
Studying the ethanol effect on the malate-aspartate shuttle in rat liver extracts using spectrofluorometry and spectrophotometry.
- 1984-1985 VISITING RESEARCHER, CHEMISTRY DEPARTMENT, WEIZMANN INSTITUTE OF SCIENCE. REHOBOTH, ISRAEL.
Two-month visit to set-up a magnetic resonance-compatible perfusion system for living tissues to study the effect of hormones in isolated rat ovaries by ^{31}P nuclear magnetic resonance.
- 1991-1997 ASSOCIATE RESEARCH SCIENTIST, DEPARTMENT OF NMR & MEDICAL SPECTROSCOPY, FOX CHASE CANCER CENTER, PHILADELPHIA, PA USA.
- 1997-2001 STAFF SCIENTIST, DEPARTMENT OF NMR & MEDICAL SPECTROSCOPY, FOX CHASE CANCER CENTER, PHILADELPHIA, PA USA.
Principal investigator and co-investigator in research programs using noninvasive ^1H and ^{31}P magnetic resonance spectroscopy to study humans and preclinical models of cancer.
- 2001 STAFF SCIENTIST, DEPARTMENT OF RADIOLOGY, COLLEGE OF PHYSICIANS & SURGEONS, COLUMBIA UNIVERSITY MEDICAL CENTER, NEW YORK, NY USA.
- 2001-2010 SENIOR ASSOCIATE RESEARCH SCIENTIST, DEPARTMENT OF RADIOLOGY, COLLEGE OF PHYSICIANS & SURGEONS, COLUMBIA UNIVERSITY MEDICAL CENTER, NEW YORK, NY USA.
- 2010-2014 ASSOCIATE PROFESSOR OF RADIOLOGY (PHYSICS), COLLEGE OF PHYSICIANS & SURGEONS, COLUMBIA UNIVERSITY MEDICAL CENTER, USA.
Principal investigator and co-investigator in research programs using MR technology to study human tissues noninvasively working at the Hatch MR Research Center.
- 2011-TO DATE ADJUNCT ASSOCIATE PROFESSOR OF RADIOLOGY, UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM, PENNSYLVANIA, USA.
Adjunct investigator in research programs using MR technology to study human tissues noninvasively.

HOSPITAL APPOINTMENTS

- 1990-1991 DIRECTOR, CLINICAL & LABORATORY SERVICES FOR INBORN ERRORS OF METABOLISM, MEDICAL GENETICS SERVICE, GENERAL HOSPITAL OF MEXICO CITY, MEXICO CITY, MEXICO.
Setting-up a new section dedicated to the study of patients with possible Inborn Errors of Metabolism.
- 1986-1990 DIRECTOR, CLINICAL & LABORATORY SERVICES FOR INBORN ERRORS OF METABOLISM, DEPARTMENT OF GENETICS OF NUTRITION, NATIONAL INSTITUTE OF PEDIATRICS, MEXICO CITY, MEXICO.
As an Associate Research Scientist of the Institute of Biomedical Investigations (National University of Mexico, Mexico City, Mexico), I was assigned to direct this clinical service where patients with possible Inborn Errors of Metabolism were screened, diagnosed, and followed up. I coordinated the work of four technicians versed on several analytical techniques and implemented new analytical methods of biofluids including NMR. I also trained medical residents in Pediatrics, and mentored college students.
- 1980-1981 UNDERGRADUATE INTERNSHIP, GENERAL HOSPITAL OF MEXICO CITY, MEXICO.

AWARDS & HONORS

- 1980 HONORS DIPLOMA FOR OUTSTANDING PERFORMANCE DURING INTERNSHIP, GENERAL HOSPITAL OF MEXICO CITY, MEXICO.
- 1986 REPATRIATION AWARD, MEXICAN FOUNDATION FOR HEALTH, MEXICAN GOVERNMENT, MEXICO.
Lump sum of \$5,000 USD to pay relocation costs after international postdoctoral research fellowship.
- 1990 ANNUAL SCIENTIFIC AWARD, MEXICAN ASSOCIATION OF HUMAN GENETICS, MEXICO.
Awarded to the work "MR Imaging Applications to the Study of Human Genetics" presented in the Annual Meeting of the association, Xalapa Veracruz, Mexico.
- 2000 FIRST PLACE POSTER AWARD, EUROPEAN SOCIETY FOR MAGNETIC RESONANCE IN MEDICINE AND BIOLOGY.
Awarded to the work "Investigation of the predictive value of phosphoethanolamine and phosphocholine

measured by *in vivo* ³¹P MR spectroscopy in non-Hodgkin's lymphoma patients in a multi-institutional setting" presented in the Annual Meeting of the Society, Paris (France).

- 2007 CLINICAL & TRANSLATIONAL SCIENCE PILOT AWARD, HERBERT IRVING COMPREHENSIVE CANCER CENTER, COLUMBIA UNIVERSITY MEDICAL CENTER, NEW YORK, NY USA.
Award received to study patients with prostate cancer to obtain preliminary MRI and ¹H-MRS data to demonstrate feasibility to carry out the study.
- 2008 CLINICAL & TRANSLATIONAL SCIENCE PILOT AWARD, HERBERT IRVING COMPREHENSIVE CANCER CENTER, COLUMBIA UNIVERSITY MEDICAL CENTER, NEW YORK, NY USA.
Award received to study patients with lymphoma under novel therapies to obtain preliminary data to demonstrate better early and objective predictive measures of treatment response to new drugs. The pilot data acquired with this award was used to support a formal grant application to the National Cancer Institute (NIH), which was awarded under registration number R21CA152858.
- 2010 MOLECULAR IMAGING AWARD, RADIOLOGICAL SOCIETY OF NORTH AMERICA, ILLINOIS, USA.
Recipient of the Molecular Imaging Award for best abstract submitted in the Molecular Imaging field entitled "*In vivo* ³¹P MRSI of non-Hodgkin's Lymphoma: improving the prediction of therapeutic response of the International Prognostic Index based on pretreatment measurements" presented during the 2010 annual meeting of the Society.
- 2014 HERBERT M. STAUFFER AWARD, ASSOCIATION OF UNIVERSITY RADIOLOGISTS OF THE RADIOLOGICAL SOCIETY OF NORTH AMERICA, ILLINOIS, USA.
Recipient of the Herbert M. Stauffer Award for Best Basic Science Paper for the publication entitled "Noninvasive phosphorus magnetic resonance spectroscopy imaging predicts outcome to first-line chemotherapy in newly diagnosed patients with diffuse large B-cell lymphoma", published on the September 2013 issue of the journal Academic Radiology.

PROFESSIONAL ORGANIZATIONS & SOCIETIES

- 1984-TO DATE INTERNATIONAL SOCIETY OF MAGNETIC RESONANCE IN MEDICINE, SAN FRANCISCO, CALIFORNIA, USA.
- 1986-TO DATE NATIONAL BIOCHEMICAL SOCIETY, MEXICO CITY DF, MEXICO.
- 1987-TO DATE NATIONAL SOCIETY OF PHYSIOLOGICAL SCIENCES, MEXICO CITY DF, MEXICO.
- 1988-TO DATE NATIONAL ASSOCIATION OF HUMAN GENETICS, MEXICO CITY DF, MEXICO.
- 2003-2014 H. IRVING COMPREHENSIVE CANCER CENTER, COLUMBIA UNIVERSITY, NEW YORK CITY, NEW YORK, USA.
- 2014-TO DATE AMERICAN ASSOCIATION OF CANCER RESEARCH, PHILADELPHIA, PENNSYLVANIA, USA.

ACADEMIC COMMITTEES

- 1980-1982 COORDINATOR, UNDERGRADUATE EXAMINATIONS COMMITTEE, DEPARTMENT OF BIOCHEMISTRY, SCHOOL OF MEDICINE, NATIONAL UNIVERSITY OF MEXICO, MEXICO.
- 1982-1990 MEMBER, EDITORIAL COMMITTEE OF THE THEMATIC OBJECTIVES FOR THE BIOCHEMISTRY UNDERGRADUATE COURSE, DEPARTMENT OF BIOCHEMISTRY, SCHOOL OF MEDICINE, NATIONAL UNIVERSITY OF MEXICO.
Developing the thematic objectives of the undergraduate course of Biochemistry. The first edition of the objectives booklet was released in 1982 and reprinted annually from 1983 to 1985. A second edition with revisions was published in 1986 and reprinted annually from 1987 to 1990.

MAJOR TEACHING & CLINICAL RESPONSIBILITIES

- 1976-1979 TEACHING ASSISTANT, UNDERGRADUATE BIOCHEMISTRY, DEPARTMENT OF BIOCHEMISTRY, SCHOOL OF MEDICINE, NATIONAL UNIVERSITY OF MEXICO.
- 1978-1979 TEACHING ASSISTANT, UNDERGRADUATE MODULE OF BIOCHEMISTRY & PHYSIOLOGY, NATIONAL SCHOOL OF UNDERGRADUATE STUDIES "ZARAGOZA", NATIONAL UNIVERSITY OF MEXICO, MEXICO.
- 1980-1982 COURSE LECTURER, UNDERGRADUATE BIOCHEMISTRY, DEPARTMENT OF BIOCHEMISTRY, SCHOOL OF MEDICINE, NATIONAL UNIVERSITY OF MEXICO, MEXICO.
- 1985-1990 COURSE LECTURER, UNDERGRADUATE BIOCHEMISTRY, DEPARTMENT OF BIOCHEMISTRY, SCHOOL OF MEDICINE, NATIONAL UNIVERSITY OF MEXICO, MEXICO.
- 1988 COURSE LECTURER FOR PHD CANDIDATES: "SELECTED TOPICS ON METABOLIC REGULATION AND INTEGRATION IN MAMMALS", INSTITUTE OF BIOMEDICAL INVESTIGATIONS, NATIONAL UNIVERSITY OF MEXICO, MEXICO.
- 1988-1989 COURSE LECTURER: "NORMAL AND PATHOLOGIC GROWTH & DEVELOPMENT", INSTITUTE OF BIOMEDICAL INVESTIGATIONS, NATIONAL UNIVERSITY OF MEXICO, MEXICO.
Coordinating the module "Physiology & Pathology of the Intermediary Metabolism" given to the residents of the specialty in Pediatrics of the National Institute of Pediatrics.

- 1989-1990 UNDERGRADUATE THESIS ADVISOR FOR MS. MARIA T. CABRAL-MEDINA, INSTITUTE FOR BIOMEDICAL INVESTIGATIONS, NATIONAL UNIVERSITY OF MEXICO, MEXICO.
Candidate for the Bachelor's Degree in Biology in the School of Sciences. Thesis: "Cystic Fibrosis: Recent Advances".
- 1989-1991 UNDERGRADUATE THESIS ADVISOR FOR MS. LEDA C. TORRES-MALDONADO, INSTITUTE FOR BIOMEDICAL INVESTIGATIONS, NATIONAL UNIVERSITY OF MEXICO, MEXICO.
Candidate for the Bachelor's Degree in Biology in the School of Sciences. Thesis: "Two-Year Retrospective Study of the Metabolic Screening in the National Institute of Pediatrics".
- 1999-2000 RESEARCH MENTOR TO MR. FRANK BERARDOCCO, DEPARTMENT OF NMR & MEDICAL SPECTROSCOPY, FOX CHASE CANCER CENTER, PHILADELPHIA, PENNSYLVANIA USA.
Research apprenticeship for Mr. F. Berardocco who was on the gifted program for high-school students of Philadelphia. Project: Advanced Post-Processing of ³¹P MRS signals in Lymphoma Patients. First prize winner of the 1998 Wistar Institute research award for high-school students.
- 2004-2014 COURSE LECTURER, "BIOMEDICAL ENGINEERING METHODS", DEPARTMENT OF RADIOLOGY, COLUMBIA UNIVERSITY MEDICAL CENTER, NEW YORK, USA.
Coordinating the module "Magnetic Resonance Imaging and Spectroscopy" given to the senior year of undergraduate students in the Department of Biomedical Engineering.
- 2009 RESEARCH MENTOR TO MR. DEREK BIEDERMAN, DEPARTMENT OF RADIOLOGY, COLUMBIA UNIVERSITY MEDICAL CENTER, NEW YORK, USA.
NIH-Sponsored Summer Research Apprenticeship for Mr. D. Biederman, a college student at Columbia University. Project "Searching for Metabolic Predictors of Treatment Response in Cancer: Retrospective Analysis of *In Vivo* ³¹P MR Spectroscopy Data of Lymphoma Patients".
- 2011-2013 ASSOCIATE RESEARCH POSTGRADUATE ADVISOR TO DR. HAMED MOJAHED, DEPARTMENT OF RADIOLOGY, COLUMBIA UNIVERSITY MEDICAL CENTER, NEW YORK, USA.
Candidate for the Degree of Doctor of Philosophy (Biomedical Engineering) in the Graduate School of Arts & Sciences of Columbia University. Thesis: Sequence Development and Expansion of Zero J-Modulation Echo-Planar Chemical Shift Imaging in Three Dimensions (3D-ZJEPSI).
- 2012 RESEARCH MENTOR TO MR. RAYMOND TANG, DEPARTMENT OF RADIOLOGY, COLUMBIA UNIVERSITY MEDICAL CENTER, NEW YORK, USA.
Summer Research Apprenticeship for Mr. R. Tang, who was on a gifted program for high-school students. Project "Muscle Activation Assessed by ³¹P MR spectroscopic imaging in human subjects under exercise regimen".

LECTURES BY INVITATION

- 1982 ETHANOL: CATABOLISM AND METABOLIC EFFECTS.
Symposium presented during the ordinary session of March 17, 1982 of the National Academy of Medicine of Mexico, Mexico City, Mexico.
- 2002 APPLICATION OF MR SPECTROSCOPY TO THE DIAGNOSIS OF MITOCHONDRIAL DISEASE.
Workshop for Laboratory Standards, part of the Mitochondrial Medicine Symposium "Streams of Energy" of the United Mitochondrial Disease Foundation, Dallas, Texas, USA.
- 2004 SPECTROSCOPIC EVALUATION OF NEUROMETABOLIC & NEURODEGENERATIVE DISEASES.
Workshop for Laboratory Standards, part of the Mitochondrial Medicine Symposium "Streams of Energy" of the United Mitochondrial Disease Foundation, Pittsburgh, Pennsylvania, USA.
- 2006 PREDICTING TREATMENT RESPONSE IN NON-HODGKIN'S LYMPHOMA – A MULTI-INSTITUTIONAL MRS STUDY.
Workshop "Data Processing for MR Spectroscopy & Imaging" of the International Society of Magnetic Resonance in Medicine, Warrenton, Virginia, USA.
- 2012 MR TECHNOLOGY IN CANCER.
Seminar Series on Magnetic Resonance Imaging of the Irving Institute for Clinical and Translational Research. Columbia University New York, New York, USA.

CONSULTATIVE ACTIVITIES

- 1995-2001 SCIENTIFIC CONSULTANT, BARNETT CENTER FOR MITOCHONDRIAL CYTOPATHIES.
To apply novel MR techniques to study patients with Mitochondrial Disease. In collaboration with the Department of Neurology of the St. Christopher's Hospital for Children. Philadelphia PA, USA.
- 1999-2001 SCIENTIFIC CONSULTANT, SCIGRO, INC.
To develop novel contrast agents for MR Imaging. Malvern, Pennsylvania, USA.
- 1999-2006 SCIENTIFIC CONSULTANT, ADVANCED IMAGING RESEARCH, INC.
To develop and test novel radiofrequency probes for in vivo MR applications. Cleveland, Ohio, USA.

2007-2009 SCIENTIFIC CONSULTANT, WANG NMR, INC. & JUPITER NMR, INC.
To develop high-field magnets with a very homogeneous but small field of view for in vivo breast and prostate cancer research. Livermore California, USA.

ROLES IN SCIENTIFIC ORGANIZATIONS

- 1990-1991 SECRETARY, GOVERNING BOARD OF THE MEXICAN ASSOCIATION OF HUMAN GENETICS.
Scientific and administrative support to accomplish the academic activities (i.e., scientific sessions, annual meetings) of the Association.
- 1994 SCIENTIFIC SESSION CHAIR, ANNUAL MEETING OF THE SOCIETY OF MAGNETIC RESONANCE.
Coordinate oral presentations during the session. Dallas, Texas USA.
- 2003-TO DATE ABSTRACT REVIEWER, INTERNATIONAL SOCIETY OF MAGNETIC RESONANCE IN MEDICINE.
Review of abstracts submitted to be presented in the annual meetings of the Society.
- 2008-TO DATE SCIENTIFIC MANUSCRIPT REVIEWER, MAGNETIC RESONANCE IMAGING JOURNAL.
Scientific reviewer (peer-review) for manuscripts submitted for publication in the journal.
- 2010-TO DATE SCIENTIFIC MANUSCRIPT REVIEWER, NMR IN BIOMEDICINE JOURNAL.
Scientific reviewer (peer-review) for manuscripts submitted for publication in the journal.
- 2011-TO DATE SCIENTIFIC MANUSCRIPT REVIEWER, ACADEMIC RADIOLOGY JOURNAL.
Scientific reviewer (peer-review) for manuscripts submitted for publication in the journal.
- 2012-TO DATE SCIENTIFIC MANUSCRIPT REVIEWER, CLINICAL CANCER RESEARCH JOURNAL.
Scientific reviewer (peer-review) for manuscripts submitted for publication in the journal.

BIBLIOGRAPHY

RESEARCH PUBLICATIONS, PEER-REVIEWED

1. Pina-Garza E, Garcia-Sainz A, Chagoya de Sanchez V, Arias-Mendoza F: [Ethanol: catabolism and metabolic effects]. *Gac Med Mex* 119:1-14, 1983 (PMID 6884680).
2. Rothman D, Arias-Mendoza F, Shulman G, Shulman R: A pulse sequence for simplifying hydrogen NMR spectra of biological tissues. *J Magn Reson* 60:430-436, 1984 (PMID).
3. Bendall MR, de Hollander JA, Arias-Mendoza F, Rothman DL, Behar KL, Shulman RG: Application of multipulse NMR to observe ¹³C-labeled metabolites in biological systems. *Magn Reson Med* 2:56-64, 1985 (PMID 3831677).
4. Jue T, Arias-Mendoza F, Gonnella NC, Shulman GI, Shulman RG: A ¹H NMR technique for observing metabolite signals in the spectrum of perfused liver. *Proc Natl Acad Sci USA* 82:5246-5249, 1985 (PMID 3860859).
5. Haseltine FP, Arias-Mendoza F, Kaye AM, Degani H: ³¹P NMR studies of adenosine-stimulated ATP synthesis in perfused luteinized ovaries. *Magn Reson Med* 3:796-800, 1986 (PMID 3784895).
6. Stromski ME, Arias-Mendoza F, Alger JR, Shulman RG: Hepatic gluconeogenesis from alanine: ¹³C nuclear magnetic resonance methodology for *in vivo* studies. *Magn Reson Med* 3:24-32, 1986 (PMID 3959887).
7. Arias-Mendoza F, Pina E: A sensitive multienzymatic assay for the measurement of pyruvate, dihydroxyacetone phosphate, oxaloacetate, and acetoacetate in clear extracts from biological samples. *Prep Biochem* 21:211-214, 1991 (PMID 1780273).
8. Arias-Mendoza F, Pina E: A simple method to fix and extract ATP from rat liver samples. *Prep Biochem* 21:205-209, 1991 (PMID 1780272).
9. McNamara R, Arias-Mendoza F, Brown TR: Investigation of broad resonances in ³¹P NMR spectra of the human brain *in vivo*. *NMR Biomed* 7:237-242, 1994 (PMID 7848814).
10. Hu J, Javaid T, Arias-Mendoza F, Liu Z, McNamara R, Brown TR: A fast, reliable, automatic shimming procedure using 1H chemical-shift-imaging spectroscopy. *J Magn Reson B* 108:213-219, 1995 (PMID 7670755).
11. Arias-Mendoza F, Javaid T, Stoyanova R, Brown TR, Gonen O: Heteronuclear multivoxel spectroscopy of in vivo human brain: two-dimensional proton interleaved with three-dimensional 1H-decoupled phosphorus chemical shift imaging. *NMR Biomed* 9:105-113, 1996 (PMID 8892396).
12. Gonen O, Arias-Mendoza F, Goelman G: 3D localized *in vivo* ¹H spectroscopy of human brain by using a hybrid of 1D-Hadamard with 2D-chemical shift imaging. *Magn Reson Med* 37:644-650, 1997 (PMID 9126937).
13. Ochs MF, Stoyanova RS, Arias-Mendoza F, Brown TR: A new method for spectral decomposition using a bilinear Bayesian approach. *J Magn Reson* 137:161-176, 1999 (PMID 10053145).
14. Franks S, Smith M, Arias-Mendoza F, Shaller C, Padavic-Shaller K, Kappler F, Zhang Y, Negendank W, Brown T: Phosphomonoester concentrations differ between chronic lymphocytic leukemia cells and normal human lymphocytes. *Leuk Res* 26:919, 2002 (PMID 12163053).
15. Shukla-Dave A, Poptani H, Loevner LA, Mancuso A, Serrai H, Rosenthal DI, Kilger AM, Nelson DS, Zakian KL, Arias-Mendoza F, Rijpkema M, Koutcher JA, Brown TR, Heerschap A, Glickson JD: Prediction of treatment response of head and neck cancers with P-31 MR spectroscopy from pretreatment relative phosphomonoester levels. *Acad Radiol* 9:688-694, 2002 (PMID 12061743).

16. Arias-Mendoza F, Brown TR: In vivo measurement of phosphorous markers of disease. *Dis Markers* 19:49-68, 2003-2004 (PMID 15096705).
17. Arias-Mendoza F: In vivo magnetic resonance spectroscopy in the evaluation of mitochondrial disorders. *Mitochondrion* 4:491-501, 2004 (PMID 16120408).
18. Arias-Mendoza F, Smith MR, Brown TR: Predicting treatment response in non-Hodgkin's lymphoma from the pretreatment tumor content of phosphoethanolamine plus phosphocholine. *Acad Radiol* 11:368-376, 2004 (PMID 15109009).
19. Arias-Mendoza F, Zakian K, Schwartz A, Howe FA, Koutcher JA, Leach MO, Griffiths JR, Heerschap A, Glickson JD, Nelson SJ, Evelhoch JL, Charles HC, Brown TR: Methodological standardization for a multi-institutional in vivo trial of localized (31)P MR spectroscopy in human cancer research. In vitro and normal volunteer studies. *NMR Biomed* 17:382, 2004 (PMID 15386624).
20. Robinson JN, Cleary-Goldman J, Arias-Mendoza F, Cruz-Lobo J, Tempany C, Mulkern RV, Feinberg BB, Brown TR: Detection of fetal lactate with two-dimensional-localized proton magnetic resonance spectroscopy. *Obstet Gynecol* 104:1208-1210, 2004 (PMID 15516455).
21. Arias-Mendoza F, Payne GS, Zakian KL, Schwarz AJ, Stubbs M, Stoyanova R, Ballon D, Howe FA, Koutcher JA, Leach MO, Griffiths JR, Heerschap A, Glickson JD, Nelson SJ, Evelhoch JL, Charles HC, Brown TR: In vivo ³¹P MR spectral patterns and reproducibility in cancer patients studied in a multi-institutional trial. *NMR Biomed* 19:504-512, 2006 (PMID 16763965).
22. Coon AL, Arias-Mendoza F, Colby GP, Cruz-Lobo J, Mocco J, Mack WJ, Komotar RJ, Brown TR, Connolly ES, Jr.: Correlation of cerebral metabolites with functional outcome in experimental primate stroke using in vivo ¹H-magnetic resonance spectroscopy. *AJNR Am J Neuroradiol* 27:1053-1058, 2006 (PMID 16687542).
23. Freda PU, Shen W, Reyes-Vidal CM, Geer EB, Arias-Mendoza F, Gallagher D, Heymsfield SB: Skeletal muscle mass in acromegaly assessed by magnetic resonance imaging and dual-photon x-ray absorptiometry. *J Clin Endocrinol Metab* 94:2880-2886, 2009 (PMID 19491226).
24. Sonabend AM, Stuart RM, Yun J, Yanagihara T, Mohajed H, Dashnaw S, Bruce SS, Brown T, Romanov A, Sebastian M, Arias-Mendoza F, Bagiella E, Canoll P, Bruce JN: Prolonged intracerebral convection-enhanced delivery of topotecan with a subcutaneously implantable infusion pump. *Neuro-Oncology* 13:886-893, 2011 (PMID 21750007).
25. Lee S-C, Arias-Mendoza F, Poptani H, Delikatny EJ, Wasik M, Marzec M, Schuster SJ, Nasta SD, Svoboda J, O'Connor OA, Smith MR, Glickson JD: Prediction and early detection of response by NMR spectroscopy and imaging. *PET Clin* 7:119-126, 2012 (PMID 22737093).
26. Arias-Mendoza F, Payne GS, Zakian K, Stubbs M, O'Connor OA, Mojahed H, Smith MR, Schwarz AJ, Shukla-Dave A, Howe F, Poptani H, Lee SC, Pettengel R, Schuster SJ, Cunningham D, Heerschap A, Glickson JD, Griffiths JR, Koutcher JA, Leach MO, Brown TR: Noninvasive Phosphorus Magnetic Resonance Spectroscopic Imaging Predicts Outcome to First-line Chemotherapy in Newly Diagnosed Patients with Diffuse Large B-Cell Lymphoma. *Acad Radiol* 20:1122-1129, 2013 (PMID 23931426).
27. Garcia-Diaz B, Garone C, Barca E, Mojahed H, Gutierrez P, Pizzorno G, Tanji K, Arias-Mendoza F, Quinzii CM, Hirano M: Deoxynucleoside stress exacerbates the phenotype of a mouse model of mitochondrial neurogastrointestinal encephalopathy. *Brain* 137:1337-1349, 2014 (PMID 24727567).
28. Reyes-Vidal C, Mojahed H, Shen W, Jin Z, Arias-Mendoza F, Fernandez JC, Gallagher D, Bruce JN, Post KD, Freda PU: Adipose tissue redistribution and ectopic lipid deposition in active Acromegaly and effects of surgical treatment. *J Clin Endocrinol Metab* 100:2946-55, 2015 (PMID 26037515).

CONTRIBUTIONS TO PEER-REVIEWED PUBLICATIONS BUT NOT BY AUTHORSHIP.

1. Negendank WG, Sauter R, Brown TR, Evelhoch JL, Falini A, Gotsis ED, Heerschap A, Kamada K, Lee BC, Mengeot MM, Moser E, Padavic-Shaller KA, Sanders JA, Spraggins TA, Stillman AE, Terwey B, Vogl TJ, Wicklow K, Zimmerman RA, (Arias-Mendoza F, Fox Chase Cancer Center participant: see appendix): Proton magnetic resonance spectroscopy in patients with glial tumors: a multicenter study. *J Neurosurg* 84:449-458, 1996 (PMID 8609557).
2. Griffiths JR, Tate AR, Howe FA, Stubbs M, and the group on MRS Applications to Cancer: Magnetic Resonance Spectroscopy of cancer-practicalities of multi-centre trials and early results in non-Hodgkin's lymphoma. *Eur J Cancer* 38:2085-2093, 2002 (PMID 12387834).

RESEARCH PUBLICATIONS, SUBMITTED OR IN PREPARATION.

1. Arias-Mendoza F, Konchanin LM, Selak MA, Kaye AM, Brown TR: Familial creatine deficiency with a myopathic component: near-absent signals in the ¹H-decoupled ³¹P MR spectra of the calf muscles. (in preparation), 0000 (PMID 000).
2. Arias-Mendoza F, Payne G, Zakian K, Stubbs M, O'Connor OA, Mojahed H, Smith MR, Schwartz LH, Shukla-Dave A, Howe FA, Poptani H, Lee S-C, Pettengel R, Schuster SJ, Cunningham D, Heerschap A, Glickson JD, Griffiths JR, Koutcher J, Leach MO, Brown TR: The effect of rituximab as part of the first-line treatment of diffuse large B-cell lymphoma in the prediction of response to treatment by ³¹P magnetic resonance spectroscopic imaging. (in preparation), 0000 (PMID 000).

3. Arias-Mendoza F, Payne G, Zakian K, Stubbs M, O'Connor OA, Mojahed H, Smith MR, Schwartz LH, Shukla-Dave A, Howe FA, Poptani H, Lee S-C, Pettengel R, Schuster SJ, Cunningham D, Heerschap A, Glickson JD, Griffiths JR, Koutcher J, Leach MO, Brown TR: Correlation of ¹H and ³¹P MR spectroscopic imaging to aid in the prediction of response to treatment in non-Hodgkin lymphoma. (in preparation), 0000 (PMID 000).
4. Arias-Mendoza F, Siegel AA, Persigehl T, Mojahed H, Schwartz LH: Comprehensive MR study for the evaluation of the patient with hepatocellular carcinoma. (in preparation), 0000 (PMID 000).
5. Arias-Mendoza F, Stoyanova R, Smith MR, Brown TR: Application of principal component analysis to study spectral patterns in ³¹P MR spectra of non-Hodgkin's lymphoma *in vivo*. (in preparation), 0000 (PMID 000).
6. Mojahed H, Arias-Mendoza F, Persigehl T, Brown TR: Localized proton MR spectroscopy using 3D zero J-modulation echo planar chemical shift imaging (3D ZJ-EPSI). *NMR Biomed* (accepted), 0000 (PMID).
7. Mojahed H, Persigehl T, O'Connor OA, Sawas A, Schwartz LH, Brown TR, Arias-Mendoza F: Non-Hodgkin lymphoma refractory to previous treatments: a diffusion weighted MR imaging approach. (in preparation), 0000 (PMID 000).

REVIEWS, CHAPTERS, EDITORIALS & PUBLICATIONS BY INVITATION.

1. Garcia M, Villalobos-Molina R, Arias-Mendoza F: Thematic Objectives for the Course in Biochemistry, (ed First in 1982, republished from 1983 to 1985. Second edition in 1987, republished from 1988 to 1990). University City, Mexico, National University of Mexico, School of Medicine, Department of Biochemistry, 1982-1990.
2. Arias-Mendoza F: Application of NMR spectroscopy to the study of hepatic metabolism *in vivo* [Spanish], in Jimenez S, Carabez A, et al (eds): *Mensaje Bioquimico*. Mexico City, School of Medicine, National University of Mexico, 1987, pp 36-64.
3. Arias-Mendoza F, Jimenez-Sanchez G: Inborn errors of metabolism [Spanish], in Loredano-Abdala A (ed): *Medicina Interna Pediatrica*. Mexico City, McGraw-Hill/Nueva Interamericana, 1990, pp 320-357.
4. Arias-Mendoza F, Elkashef A, Stoyanova R, Gold J, Wyatt RJ, Brown TR: Coenzyme Q₁₀ effect on cognitive functions and bioenergetics in schizophrenia: a brain-localized ³¹P MR spectroscopy study, in Oudkerk M, Edelman RR (eds): *High power gradient MR-imaging, advances in MRI II*. Berlin, Vienna, Blackwell Wissenschafts-Verlag, GmbH, 1997, pp 257-262.
5. Stoyanova R, Arias-Mendoza F, Brown TR: Making multidimensional spectroscopy practical: application of principal component analysis to CSI data, in Oudkerk M, Edelman RR (eds): *High power gradient MR-imaging, advances in MRI II*. Berlin, Vienna, Blackwell Wissenschafts-Verlag GmbH, 1997, pp 253-256.
6. Arias-Mendoza F: Metabolic Measurements: A discussion of the efforts to improve current methods of defining prognostic variables in non-Hodgkin lymphoma by zeroing in at a subcellular level., *International Innovation*, 138:87-90, 2014.
7. Juliá-Sapé M, Arias-Mendoza F, Griffiths JR: Clinical Trials of MRS Methods, *eMagRes* 4:779–788 2015 DOI 10.1002/9780470034590.emrstm1474.

SELECTED CONFERENCE PRESENTATIONS (FROM 2011).

1. Arias-Mendoza F, Brown TR: *In vivo* phosphorus MR spectroscopy demonstrates the heterogeneous composition in sarcomas, Annual Meeting of the International Society of Magnetic Resonance in Medicine. Montreal, Canada, 2011.
2. Arias-Mendoza F, Brown TR: Heterogeneous distribution of ³¹P MR signals in sarcomas., Proceedings of the Annual Meeting of the International Society of Magnetic Resonance in Medicine. Montreal, Quebec Canada, 2011.
3. Arias-Mendoza F, Lackman R, Brown TR: Noninvasive evaluation of malignant foci in sarcomas by *in vivo* 31P-MRS, Annual Meeting of the Radiological Society of North America. Chicago, IL, USA, 2011.
4. Mojahed H, Persigehl T, O'Connor OA, Sawas A, Brown TR, Arias-Mendoza F: Diffusion-weighted imaging (DWI) of non-Hodgkin's lymphoma (NHL) patients refractory to previous treatment(s): preliminary results., Annual Meeting of the International Society of Magnetic Resonance in Medicine. Montreal, Canada, 2011.
5. Mojahed H, Persigehl T, O'Connor OA, Sawas A, Brown TR, Arias-Mendoza F: Non-invasive differentiation between malignant and normal lymph nodes in non-Hodgkin's lymphoma patients (NHL) refractory to previous treatment(s): still a challenge, Experimental NMR Conference (ENC). Asilomar, CA, USA, 2011.
6. Persigehl T, Mui L, Mojahed H, Siegel A, Arias-Mendoza F, Schwartz L: Evaluation of the diagnostic quality of a comprehensive liver MRI protocol combining cross-sectional and pharmacokinetic DCE-MRI, 1H MRS and 31P MRS., Annual Meeting of the Radiological Society of North America. Chicago, IL, USA, 2011.
7. Arias-Mendoza F, Mojahed H, Sawas A, O'Connor OA: Predictive and Diagnostic Capabilities of Noninvasive MR Technology in Non-Hodgkin's Lymphoma Patients, 54th American Society of Hematology Annual Meeting and Exposition (accepted). Atlanta GA, USA, 2012.
8. Arias-Mendoza F, Payne GS, Zakian KL, Stubbs M, O'Connor OA, Mojahed H, Smith MR, Schwartz AJ, Shukla-Dave A, Howe FA, Poptani H, Lee S-C, Pettengel R, Schuster SJ, Cunningham D, Heerschap A, Glickson JD, Griffiths JR, Koutcher JA, Leach MO, Brown TR: The Addition of Rituximab to First-Line Chemotherapy for Newly-Diagnosed Diffuse Large B-Cell Lymphoma Does Not Modify the Prediction of Therapy Outcome by

Phosphorus MR Spectroscopy, Annual Meeting of the International Society of Magnetic Resonance in Medicine. Melbourne, Australia, 2012.

9. Mohajed H, Read C, Dresner A, Brown TR, Freda PU, Arias-Mendoza F: Assessment of Bone Marrow and Muscle Lipids in Acromegaly using 1H Magnetic Resonance Spectroscopy, Annual Meeting of the International Society of Magnetic Resonance in Medicine. Melbourne, Australia, 2012.
10. Persigehl T, Mui L, Mojahed H, Siegel A, Arias-Mendoza F, Schwartz L: Evaluation of the diagnostic quality of a comprehensive liver MRI protocol combining cross-sectional and pharmacokinetic DCE-MRI, and 1H and 31P MRS. (German), Experimentelle Radiologie. Kiel, Germany, 2012.
11. Persigehl T, Mui L, Mojahed H, Siegel A, Arias-Mendoza F, Schwartz L: Evaluation of the diagnostic quality of a comprehensive liver MRI protocol combining cross-sectional and pharmacokinetic DCE-MRI, 1H MRS and 31P MRS. (German), Annual Meeting of the German Radiological Society. Hamburg, Germany, 2012.
12. Mojahed H, Arias-Mendoza F, Brown TR: 3D Zero J-modulation echo planar chemical shift imaging (3D ZJ-EPSI), Proceedings of the International Society of Magnetic Resonance in Medicine. Salt Lake City UT, USA, 2013.
13. Mojahed H, Sawas A, O'Connor OA, Arias-Mendoza F: Prognostic value of diffusion weighted MR imaging in recurrent lymphomas, 12th International Conference on Malignant Lymphoma Lugano, Switzerland, 2013.
14. Arias-Mendoza F, Mojahed H, Sawas A, O'Connor OA: Correlation of the apparent diffusion coefficient of water assessed by diffusion-weighted MR imaging with treatment outcome in refractory non-Hodgkin lymphoma patients, Annual Meeting of the American Association of Cancer Research. San Diego, CA, USA, 2014.
15. Mojahed H, Arias-Mendoza F, Brown TR: Method of transforming brain spectroscopic waterline data into standard brain space (analyzing functional MR spectroscopy in FSL), Annual Meeting of the International Society of Magnetic Resonance in Medicine. Milan, Italy, 2014.
16. Mojahed H, Sawas A, O'Connor OA, Arias-Mendoza F: Correlation of the apparent diffusion coefficient of water assessed by diffusion-weighted MR imaging with treatment outcome in refractory non-Hodgkin lymphoma patients, Annual Meeting of the American Society of Hematology. New Orleans, LA, USA, 2014.

FERNANDO ARIAS-MENDOZA, M.D., PH.D.

GRANT SUPPORT

PAST GRANT SUPPORT

IN VIVO MURINE LIVER METABOLISM STUDIES BY NMR AT 9.4 TESLA

09/01/82-08/30/85 TG (International) Principal Investigator (Trainee) 12 mo/yr (100%) PUIC-UNAM-1982-02 (PI: Arias-Mendoza, F)
National University of Mexico \$11,900
International training program to assess liver metabolism on the isolated (perfused) live mouse liver by ^{13}C , ^{31}P and ^1H MRS at 9.4 Tesla. Department of Molecular Biochemistry & Biophysics, Yale University. This grant was one of the only two given in 1982 by the National University of Mexico.

IN SITU MURINE LIVER METABOLISM STUDIES BY NMR IN A LARGE BORE MAGNET AT 2.0 TESLA

09/01/83-08/30/85 TG (International) Principal Investigator (Trainee) 12 mo/yr (100%) 1F05TW03346 (PI: Arias-Mendoza, F)
Fogarty International Center, NIH \$20,000
Public Health Service International Research Fellow training program to assess liver metabolism on *in situ*, exposed rat livers using noninvasive ^{13}C , ^{31}P , and ^1H MR spectroscopy using one of the first whole-animal 2.0 Tesla MR spectrometers. Molecular Biophysics & Biochemistry Department, Yale University.

CLINICAL STUDIES ON INBORN ERRORS OF METABOLISM

06/01/88-05/31/90 FG (Mexico) Principal Investigator 3.0 mo/yr (25%) NSR-AIMF570214 (PI: Arias-Mendoza, F)
Natl. System of Research (Mexico) \$10,000
Competing research grant award to study biological samples of children with Inborn Errors of Metabolism using different screening and diagnostic techniques, including MR spectroscopy.

PREDICTING HUMAN TUMOR RESPONSE BY ^{31}P MR SPECTROSCOPY

05/18/95-05/31/06 Cooperative R01 Co-Leader from 1999 2.4 mo/yr (20%) U01CA0062556 (PI: Brown, TR)
NCI (NIH) ca. \$125,000
To test if tumor variables obtained using ^{31}P MRS predicted sensitivity or resistance of human cancer to treatment. The final results suggested that the pretreatment value of phosphomonoesters normalized to nucleotide triphosphates (PME/NTP) could predict response to treatment in non-Hodgkin's lymphomas.

NMR STUDIES OF HUMAN CANCER

07/01/97-03/31/05 P01 PI Project II; Co-Investigator Project I 3.0 mo/yr (25%) 5P01CA41078 (PI: Brown, TR)
NCI (NIH) ca. \$600,000
Program Project Grant with the major goals to combine *in vivo*, *ex vivo*, and *in vitro*, methodological strategies with emphasis on MRS to study cancer metabolism in humans in a multidisciplinary fashion.

DUAL-TUNED PROBE FOR MRI/MRS OF THE HUMAN BRAIN

06/01/98-05/30/99 R43 Consultant Fixed salary 1R43NS037273 (PI: Srinivasan, R)
NINDS (NIH) ca. \$175,000
The aim of this proposal was to build a dual-tuned ($^{31}\text{P}/^1\text{H}$) probe for the study of human brain using MRI and multinuclear spectroscopic imaging with similar fields of views for all nuclei.

DUAL-TUNED PROBE FOR MRI/MRS OF THE HUMAN BRAIN

06/01/00-05/30/02 R44 Consultant Fixed salary 1R44NS037273 (PI: Srinivasan, R)
NINDS (NIH) ca. \$175,000
The aim of this proposal was the continuation of research program 1R43NS037273 to build dual-tuned coils.

MITOCHONDRIAL ENCEPHALOMYOPATHIES & MENTAL RETARDATION

12/01/04-02/28/15 P01 Co-Investigator 1.2 mo/yr (10%) 5P01HD032062-17 (Di Mauro/De Vivo)
NICHD (NIH) \$847,115
This program focused on mitochondrial encephalomyopathies and mental retardation. In Project 1, patients were enrolled for long-term evaluation as part of a natural history study, which include MR imaging and spectroscopy of the brain and muscle.

IN VIVO ^{31}P & ^1H MR SPECTROSCOPY STUDIES OF NON-HODGKIN'S LYMPHOMAS

05/01/07-02/28/14 Cooperative R01 Principal Investigator from 2010 5R01CA118559-04 (PI: Brown, T/ Arias-Mendoza, F)
NCI (NIH) \$1,222,428
Cooperative program with the aim to corroborate if the tumor PME/NTP value measured by ^{31}P MR spectroscopy is correlated with treatment outcome in an independent, larger cancer patient cohort. We also seek to extend these findings by investigating absolute choline levels by ^1H MRS and to follow up on initial indications that the significance of the correlation between PME/NTP and treatment outcome is widely applicable to other forms of lymphoma.

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|--|---------|------------------------|-----------------|---------------------------------|--|--|
| <u>LEPTIN IN HUMAN ENERGY & NEUROENDOCRINE HOMEOSTASIS</u> | | | | | | 5R01DK64773-08 (PI: Liebel, R) |
| 05/01/08-09/30/13 | R01 | Co-Investigator | 0.5 mo/yr (4%) | NIDDKD (NIH) | | \$259,216 |
| The major goal of this project was to characterize the effects of maintenance of reduced body weight on systemic energetics and on specific neuroendocrine and autonomic axes related to energy metabolism. The protocol examined the effects on these parameters of administration of exogenous leptin. | | | | | | |
| <u>NEW APPROACHES TO THE EVALUATION AND TREATMENT OF ACROMEGALY</u> | | | | | | R01DK064720 (PI: Freda, P) |
| 07/01/09-06/30/14 | R01 | Co-Investigator | 1.2 mo/yr (10%) | NIDDKD (NIH) | | \$166,727 |
| The major goal of this project was to integrally study patients with acromegaly. We are utilizing modern biochemical and imaging methods including whole body MRI and ¹ H MRSI of the liver and muscle prior and after therapy in a uniquely large ongoing prospective acromegaly patient cohort. | | | | | | |
| <u>PREDICTING OUTCOME OF EXPERIMENTAL THERAPY IN LYMPHOMAS BY ³¹P & ¹H MR SPECTROSCOPY</u> | | | | | | 5R21CA152858-02 (PI: Arias-Mendoza, F) |
| 07/01/10-05/31/13 | R21 | Principal Investigator | 3.6 mo/yr (30%) | NCI (NIH) | | \$105,488 |
| The aim of this proposal was to demonstrate if ³¹ P and ¹ H MR Spectroscopy could provide early and objective predictive measures of treatment response in recurrent patients afflicted with non-Hodgkin's lymphoma, who will be treated with non-standard, experimental therapy. | | | | | | |
| <u>MOLECULAR PATHOGENESIS AND TREATMENT OF MNGIE</u> | | | | | | 5R01HD056103-02 (PI: Hirano, M) |
| 04/01/10-01/31/15 | R01 | Co-Investigator | 0.5 mo/yr (4%) | NICHHD (NIH) | | \$260,077 |
| The major goal of this project was to characterize a mouse model of mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) including <i>in vivo</i> MR imaging and MR spectroscopy of the mouse brain. | | | | | | |
| <u>MAGNETIC RESONANCE SPECTROSCOPY (MRS) TO ASSESS PROGRESSION OF ALZHEIMER DISEASE</u> | | | | | | PG004259 (PI: Honig, L) |
| 06/01/12-11/30/13 | PG | Co-Investigator | 0.12 mo/yr (1%) | Alzheimer's Drug Discovery Fund | | \$83,499 |
| The aim of this project was to study in a group of patients with Alzheimer Disease the anterior cingulate cortex, the premotor cortex, the occipital cortex, and the parietal subcortical white matter to assess slope of temporal decline of N-acetyl aspartate, choline, myoinositol, and creatine measured by MRS. | | | | | | |
| <u>CHRONIC CONVECTION-ENHANCED DELIVERY (CED) OF TOPOTECAN FOR GLIOBLASTOMA</u> | | | | | | 1R01CA161404-01A1 (PI: Bruce, J) |
| 07/01/12-04/30/17 | R01 | Co-Investigator | 0.6 mo/yr (5%) | NCI (NIH) | | \$624,087 |
| The aim of this proposal was to critically test an innovative implantable catheter and pump system for delivering chemotherapy (topotecan) directly into the tumor for over extended time periods to avoid the side effects associated with standard oral or intravenous delivery. | | | | | | |
| <u>SARC SARCOMA SPORE, QUANTITATIVE IMAGING BIOMARKERS FOR ASSESSING RESPONSE TO THERAPY</u> | | | | | | 1U54CA168512-01 (PI: Pollock R/Schwartz, LH) |
| 07/01/12-06/30/17 | P50/U54 | Co-Investigator | 0.6 mo/yr (5%) | NCI (NIH) | | \$2,300,000 |
| The goal was to develop imaging biomarkers of apoptosis, angiogenesis, and hypoxia that will predict therapeutic efficacy in sarcoma to test that functional and molecular imaging of these tumor characteristics will enable early identification of therapeutic efficacy of molecular agents that target these processes. | | | | | | |
| <u>PHASE II CLINICAL TRIAL OF PERIFOSINE PLUS TEMSIROLIMUS FOR RECURRENT GLIOBLASTOMA WITH TISSUE AND IMAGING CORRELATES OF RESPONSE</u> | | | | | | JMDF (PI, Lassman, A) |
| 01/01/13-12/31/15 | PG | Co-Investigator | 0.6 mo/yr (5%) | JS McDonell Foundation | | \$449,148 |
| The program aimed to recruit patients with glioblastoma multiforme refractory to standard initial therapy (radiotherapy and temozolomide), who were included on a phase II trial to demonstrate efficacy of perifosine plus temsirolimus. Three methods were being used to assess the efficacy of this treatment: clinical outcomes (aim 1), molecular analyses (aim 2), and advanced imaging analyses (aim 3). | | | | | | |
| PENDING/SUBMITTED GRANT SUPPORT | | | | | | |
| <u>CLINICAL APPLICATIONS OF BIOMARKERS MEASURED BY MR TECHNOLOGY IN SARCOMAS</u> | | | | | | 1R01CA163733 (PI: Arias-Mendoza, F) |
| TBA | R01 | Principal Investigator | 3.6 mo/yr (30%) | NCI, NIH | | \$481,791 |
| Grant proposal to be submitted for its second review to NCI. The goal of this proposal is to extend previous results where we proved that <i>in vivo</i> phosphorus magnetic resonance spectroscopic imaging (MRSI) provides metabolic signatures that predict treatment outcomes to standard treatment in lymphomas into sarcoma patients undergoing standard neoadjuvant chemo- and radiotherapy. Thus, the central aim of this proposal is to determine if the metabolic profiles determined noninvasively by <i>in vivo</i> ³¹ P and ¹ H MRS prior to standard neoadjuvant therapy initiation in the three most common histological forms of sarcoma are an independent <i>a priori</i> predictor of tumor therapy outcome. Achieving this aim would set the stage for a clinical trial to evaluate the feasibility of using MRSI criteria to help guide the use of more aggressive and novel therapies. | | | | | | |

DEVELOPMENT OF MULTIPLATFORM MULTIVARIATE MODELS TO PREDICT TREATMENT OUTCOME IN NEWLY
DIAGNOSED DIFFUSE LARGE B-CELL LYMPHOMA

1R21CA191778 (PI: Arias-Mendoza, F)

TBA

R21

Principal Investigator

3.6 mo/yr (30%)

NCI, NIH

\$250,000

Exploratory grant application to be submitted for its second review to NCI. Given that we have been able to accurately determine presence of malignant foci and predict therapy outcome in DLBCL patients using noninvasive ³¹P MRSI, our aim here is to demonstrate if additional subcellular markers to create multivariate models based on our ³¹P MRSI results derives into a more precise prediction of treatment outcome in DLBCL patients. For this, we will prospectively accrue DLBCL patients scheduled to receive first-line therapy assessing the following markers: (1) PME/NTP, total choline, and the apparent diffusion constant of water; (2) IPI, immunohistochemistry, fluorescent *in situ* hybridization, and the specific uptake value of ¹⁸F-fluorodeoxyglucose determined by positron emission tomography from standard of care tests; and (3) cell of origin phenotypes by gene expression profiling.

INTERIM MR SPECTROSCOPIC IMAGING & POSITRON EMISSION TOMOGRAPHY TO NORM TREATMENT IN DLBCL

1R21CA185801 (PI: Arias-Mendoza, F)

TBA

R21

Principal Investigator

2.4 mo/yr (20%)

NCI (NIH)

\$250,000

Exploratory grant application to be submitted for its second review to NCI. Given our results where high levels of phosphomonoesters (phospholipid-related intermediates) determined by noninvasive MR spectroscopic imaging (MRSI) are present in foci of malignancy in DLBCL and other tumors, we seek to demonstrate if the use of an interim (during treatment) MRSI exam could be of use instead of an interim biopsy to increase the positive predictive value of the uptake of ¹⁸F-deoxyglucose (FDG) during treatment (interim) by positron emission tomography (i-PET) to risk-assign treatment in lymphoma patients.

BRAIN METABOLOMICS USING ZERO J-MODULATION ECHO PLANAR MR SPECTROSCOPIC IMAGING

1R21NS087536 (PI: Arias-Mendoza, F)

TBA

R21

Principal Investigator

1.2 mo/yr (10%)

NINDS (NIH)

\$250,000

Exploratory grant application to be submitted for its second review. This program seeks to development, optimize, and standardize a robust acquisition sequence, which combines echo-planar imaging (EPI) and chemical shift imaging (CSI) algorithms to obtain spectra in a three dimensional matrix of volumes at high speed and high resolution. In addition, the echo time in the sequence has also been reduced to obtain spectral data without J-modulation. The performance of this sequence has already been tested in aqueous solutions. Brain of healthy volunteers will be the target of study in the present program.