Date of Preparation: February 2015

Signature

SAROJ P. MATHUPALA, PhD

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EDUCATION

PhD, Biochemistry and Molecular Biology — 1992
Michigan State University, East Lansing, Michigan

BSc (Hon), Chemistry — 1984
University of Colombo, Colombo 7, Sri Lanka

PREGRADUATE AND POSTGRADUATE TRAINING

Postdoctoral Fellow, Biological Chemistry — 1993 - 1998
Johns Hopkins University School of Medicine, Baltimore, Maryland

Graduate Assistant, Biochemistry — 1987 - 1992
Michigan State University, East Lansing, Michigan

Quality Control Chemist — 1979 - 1981
Union Carbide Ceylon Ltd., Colombo, Sri Lanka.

FACULTY APPOINTMENTS

Assistant Professor, Neurosurgery — 1999 - Present
Wayne State University School of Medicine, Detroit, Michigan

Scientific Member, Molecular Therapeutics Program — 2011 - Present
Karmanos Cancer Institute, Detroit, Michigan

Faculty, Cancer Biology Graduate Program — 2011 - Present
Wayne State University School of Medicine, Detroit, Michigan

Graduate Faculty, Dept. Physiology — 2005 - Present
Wayne State University School of Medicine, Detroit, Michigan

Scientific Member, Developmental Therapeutics Program — 2007 - 2011
Karmanos Cancer Institute, Detroit, Michigan

Assistant Lecturer, Chemistry — 1985 - 1986

University of Colombo
Colombo 7, Sri Lanka.

MAJOR PROFESSIONAL SOCIETIES

- α American Association for the Advancement of Science 1992 - Present
- α American Association for Cancer Research 2006 - Present
- α American Society for Microbiology 1987-1992
- α American Society for Biochemistry and Molecular Biology 1992 - Present

HONORS AND AWARDS

Who's Who in America - Marquis 2008 - Present

National Research Service Award in Pathobiology of Cancer 1997 - 1999
National Institute of Health, National Cancer Institute, Bethesda, Maryland
Johns Hopkins University School of Medicine, Baltimore, Maryland

Who's Who in Science and Engineering - Marquis 1995 - Present

Biotechnology Traineeship Award, Molecular Biology Research 1987 - 1989
Michigan Biotechnology Institute, Lansing, Michigan

B.Sc.(Hon) Chemistry Award, First Class Honors (*summa cum laude*) 1984
University of Colombo, Sri Lanka.

SERVICE

Journal/Editorial Activity

- α Editorial Board Member - Scientifica -Biochemistry; Hindawi Publishers, New York 2011 - Present
- α Editorial Board Member – Review Editor, Frontiers Journals – Neuro-Oncology; Frontiers Publishers, Lausanne, Switzerland 2012 - Present

- α Biochimica et Biophysica Acta – Reviewer
- α Current Neuropharmacology – Reviewer
- α PLOS One - Reviewer
- α Cancer Research – Reviewer
- α DNA and Cell Biology – Series Reviewer
- α International Journal of Cellular Biology - Reviewer
- α Journal of Bioenergetics and Biomembranes – Reviewer
- α Journal of Biological Chemistry – Reviewer
- α Current Neuropharmacology - Reviewer
- α Molecular Pharmaceutics -Reviewer
- α Tumor Biology - Reviewer
- α International Journal of Molecular Sciences - Reviewer
- α Experimental Cell Research - Reviewer
- α Carcinogenesis - Reviewer
- α Anti-Cancer Drugs - Reviewer

Other Professionally Related Service

- External Ph.D. Thesis reviewer, Swiss National Science Foundation 2008 - Present
- Karmanos Cancer Institute Developmental Research Committee 2008 - 2011
- Reader, Basic Medical Sciences Master's Program 2008, 2012
- Irvin Reid Honors College Selection Committee 2010
- Neurosurgery Resident Selection Committee 2006 - Present
- Molecular Therapeutics Program Faculty Recruitment Committee 2013, 2015
- MD/PhD Program External Review Committee (NIH site visit) 2011, 2015

Research Grant Reviewer

National Institutes of Health, National Cancer Institute 2012 - 2014
Medical Research Council, UK 2014 - 2015
Skolkovo Foundation, Moscow, Russia 2011 - Present
Netherlands Organization for Scientific Research, The Hague, Netherlands 2010 - Present
Swiss National Science Foundation, Bern, Switzerland 2008 - Present
James & Esther King Biomedical Research Program, Florida Dept. Health 2010 - Present
The Bankhead-Coley Cancer Research Program, Florida Dept. Health 2010 - Present
European Leukodystrophy Association (ELA) Research Foundation, CEDEX 2009 - Present
Walt Disney Memorial Cancer Institute at Florida Hospital 1997 - 1999

TEACHING

Years at Other Colleges and Universities

Assistant Lecturer, Chemistry 1985 - 1986
University of Colombo, Colombo 7, Sri Lanka

Teaching Assistant, Biochemistry, Molecular Biology 1987 - 1992
Michigan State University, East Lansing, Michigan

Postdoctoral Fellow, Bioenergetics and Molecular Medicine 1993 - 1998
Johns Hopkins University School of Medicine, Baltimore, Maryland

Years at Wayne State: (16 Years)

Assistant Professor, Neurosurgery 1999 - Present
Wayne State University School of Medicine, Detroit, Michigan

Courses taught at Wayne State University School of Medicine

- PSL 7660, Advanced Neurophysiology (2004, 2006, 2008, 2010, 2012, 2014)
- CB7240, Cancer Chemotherapy (2015)
- CB7460, Cancer Mechanisms of Neoplasia (2015)
- Elective 8760, Neurosurgery Research (2004, 2005, 2008, 2009, 2010, 2012)
- PSL 999x, Doctoral Dissertation Research (2002-2010)
- PSL 7996, Research Studies, Physiology (2002 - 2010)
- BME 8070, Biomedical Engineering (2012)
- BME 8850, Biomedical Engineering Qualifying Exam (2013)
- PSY4991, Irvin D. Reid Honors College (2009 – 2012)
- CB7700, Cancer Biology Program Journal Club (2012, 2015)

- PYC7890, Neuroscience Journal Club (2013)
- BMS7880, Biomedical Sciences Masters Dissertation Research and Thesis (2012, 2013)

Essays/Theses/Dissertations directed

- Noah Heilbrun, Kalamazoo College, MI (Undergraduate Thesis, 2000-2002); Research Advisor
- Praveen Sateesh (Essay, Wayne State Medical School Summer Internship, 2002), Research Advisor
- Richard Rhiew, M.D. (Ph.D. candidate, Dept. Physiology. Research Advisor, 2002-2004); Research Advisor and *ad hoc* Thesis Advisor
- Chaim Colen, M.D. (Ph.D. candidate, Dept. Physiology. Advisor, 2003-2005); Thesis and Research Advisor
- Chantel Njiwaji (3rd Year Medical Student, Wayne State Univ., Summer elective, 2004); Research Advisor
- Brandon Koch, Rollins College, Fl (Undergraduate Summer Research, 2005-2008); Research Advisor
- Charles Krafchak (4th Year Medical Student, Wayne State Univ., Summer elective, 2008); Research Advisor
- Andrew Lozen (4th Year Medical Student, Wayne State Univ., Summer elective, 2008); Research Advisor
- Todd Francis, M.D. (Ph.D. candidate, Department of Physiology, Advisor, 2006-2010); Thesis and Research Advisor
- Amy Buth (MD/PhD program, 2010-2011) Thesis and Research Advisor
- Bhavika Chepuri (Wayne State Honors College, 2009- 2012) Undergraduate Thesis and Research Advisor
- Elsa Varughese (Wayne State Honors College, 2009- 2012) Undergraduate Thesis and Research Advisor
- Jane Harness, University of Michigan (Undergraduate Summer Research, 2011)
- Michael Monterey (BMS Graduate Program, 2010-2012) Essay and Research Thesis Advisor
- James Caruso, University of Michigan (Undergraduate Honors Thesis, 2010-2012) Thesis and Research Advisor
- Ajal Dave (3rd Year Medical Student, Wayne State Univ., Summer elective, 2012), Research Advisor
- Lidya Neuman (2nd year Biomedical Engineering, Wayne State Univ., Graduate Thesis elective, 2013)
- Pavan Jella (2nd year Biomedical Engineering, Wayne State Univ., Graduate Thesis elective, 2013)
- Bridget Reno (Undergraduate Research, Wayne State, 2012 – 2014) Research Advisor
- Joshua Brady (1st Year Medical Student, Wayne State Univ., Research elective, 2014-15), Research Advisor

Course Curriculum Development
PSL 7660, Advanced Neurophysiology (Metabolism in Malignant Glioma)
CB 7240, Cancer Biology (Tumor Metabolism)
CB 7460, Cancer Biology (Metabolism and Signaling)

GRANT SUPPORT

Induction of Apoptosis in Malignant Glioma by Targeting Glucose Metabolism 2000 - 2002
Individual IRG award, American Cancer Society. (PI). $30,000

Lactate Efflux in Glioblastoma multiforme-A therapeutic Target 2003 - 2006
LEARN Foundation. (PI). $13,000

Lactate Transport as a Therapeutic Target in Glioma 2006 - 2013
NIH R01, National Cancer Institute/National Institutes of Health. (PI). $1,190,000

Metabolic Targeting of Glioma: Clinical and pre-clinical Studies 2015 - 2017
Elsa U. Pardee Foundation.(PI). $155,000/$177,000

Foundation Gifts
Research into using lactate transporters as a therapeutic target against glioblastoma multiforme. 2005 - 2015
exCel Cosmeceuticals, Inc. PI. $38,750

Pharmaceutical Collaborative Agreements (MTA in process)
Pan-Monocarboxylate Transporter Inhibitors: Pre-clinical and Clinical Studies 2015 - 2020
Massachusetts Biomedical Initiatives, (MTA in process) $10,000,000

CLINCIAL TRIALS

Co-PI, Metabolic targeting of Canine Glioma (clinical protocol approved for 2015, trial design in collaboration with Nicholas Szerlip, MD and Elizabeth Dawe, DVM)

PATENT APPLICATIONS

Low-cost media formulation for culture of brain tumor spheroids (neurospheres). **Mathupala, S.P.**, Szerlip, N., Monterey, M. (2014). Wayne State University Disclosure #14-1239

Monocarboxylate transporters as targets in cancer therapy in malignant gliomas. **Mathupala, S.P.** and Sloan, A.E. (2002) Wayne State University Disclosure # O2-618

Arrest of Proliferation of Highly Glycolytic Tumors upon Type II hexokinase down-regulation via an Antisense RNA Approach. Pedersen, P.L. and **Mathupala, S.P.** U.S. Provisional Patent Application Reg. No. 37,518 March 2000. Johns Hopkins University Invention Disclosure #DM-3673.

Mechanism for arresting growth of cancer cells; Tumor Type II Hexokinase Transcription Regulatory Regions. Pedersen, P.L., **Mathupala, S.P.**, and Rempel, A. U.S. Provisional Patent Application Ser. No. 60/001,199 July 1995. Johns Hopkins University Invention Disclosure #DM-9956.

Fusion protein encoding starch-degrading enzymatic activities. Zeikus, J.G. and **Mathupala, S.P.** Application # 08/079,112 June 1993. Michigan State University Invention Disclosure # 92-027.

PUBLICATIONS
Average impact factor per article = 51.16 (Institute of Scientific Information/Thompson-Reuters); 1858 citations/38 articles; Hi-index 22.

Peer-Reviewed Publications

1. **Mathupala SP,** Kiousis S, Szerlip NJ : A lab assembled microcontroller-based sensor module for continuous oxygen measurement in portable hypoxia chambers. PLoS One 11: e0148923, 2016

2. Monterey MD, Szerlip NJ, **Mathupala SP**: Low-cost media formulation for culture of brain tumor spheroids (neurospheres). BioTechniques 55(2): 83-88, 2013

3. Colen CB, Shen Y, Ghoddoussi F, Yu P, Francis TB, Koch BJ, Monterey MD, Galloway MP, Sloan AE, **Mathupala SP:** Metabolic targeting of lactate efflux by malignant glioma inhibits invasiveness and induces necrosis: an in vivo study. Neoplasia 13(7): 620-632, 2011

4. **Mathupala SP**: Metabolic targeting of malignant tumors: small-molecule inhibitors of bioenergentic flux. Recent Pat Anticancer Drug Discoveries 6(1): 6-14, 2011

5. **Mathupala SP**: RNAi expression vector pUC-H1. GenBank Acc. No. FJ687158, National Center for Biotechnology Information. US National Library of Medicine, Bethesda, MD. 2011

6. **Mathupala SP,** Pedersen PL: Voltage dependent anion channel-1 (VDAC-1) as an anti-cancer target. Cancer Biology and Therapy 9(12): 1053-1056, 2010

7. **Mathupala SP,** Ko YH, Pedersen PL. The pivotal roles of mitochondria in cancer: Warburg and beyond and encouraging prospects for effective therapies. Biochimica et Biophysica Acta (BBA) - Bioenergetics 1797(6-7):1225-1230, 2010

8. **Mathupala SP,** Ko YH, Pedersen PL: Hexokinase-2 bound to mitochondria: cancer's stygian link to the "Warburg Effect" and a pivotal target for effective therapy. Seminars in Cancer Biology 19: 17-24, 2009

9. **Mathupala SP**: Delivery of small-interfering RNA (siRNA) to the brain. Expert Opinion on Therapeutic Patents 19: 137-140, 2009

10. **Mathupala SP,** Sloane AE: An agarose-based cloning-ring anchoring method for isolation of viable cell clones. BioTechniques 46: 225-227, 2009
11. **Mathupala SP,** Mittal S, Guthikonda M, Sloan AE: MicroRNA (miRNA) and Malignant Glioma: a Cause and a Cure? DNA and Cell Biology 26: 301-310, 2007

12. Parajuli P, **Mathupala S,** Mittal S, Sloan AE: Dendritic cell-based active specific immunotherapy for malignant glioma. Expert Opinion on Biological Therapy 7: 439-448, 2007

13. **Mathupala SP**, Colen CB, Parajuli P, Sloan AE: Lactate and Malignant Tumors: A Therapeutic Target at the End Stage of Glycolysis. Journal of Bioenergetics and Biomembranes, 34: 73-77, 2007

14. Colen CB, Seraji-Bozorgzad N, Marples B, Galloway MP, Sloan AE, **Mathupala SP**: Metabolic Remodeling of Malignant Glioma for Enhanced Sensitization during Radiotherapy: An in vitro Study. Neurosurgery, 59: 1313-1324, 2006

15. **Mathupala SP**, Guthikonda M, Sloan AE: RNAi Based Approaches to the Treatment of Malignant Glioma. Technology in Cancer Research and Treatment, 5: 261-269, 2006

16. **Mathupala SP**, Ko YH, Pedersen PL: Hexokinase II: Cancer's double-edged sword acting as both facilitator and gatekeeper of malignancy when bound to mitochondria. Oncogene, 25: 4777-86, 2006

17. **Mathupala SP**, Parajuli P, Sloan AE: Silencing of Monocarboxylate Transporters via Small Interfering RNA Inhibits Glycolysis and Induces Cell Death in Malignant Glioma: An in vitro Study. Neurosurgery, 55: 1410-1419, 2004

18. Parajuli P, **Mathupala SP**, Sloan AE: Systemic Comparison of Dendritic Cell based Immunotherapeutic Strategies for malignant gliomas: In vitro induction of cytolytic and NK-like T cells. Neurosurgery, 55: 1194-1204, 2004

19. Goel A, **Mathupala SP**, Pedersen PL: Glucose Metabolism in Cancer: Evidence that demethylation events play a role in activating type II hexokinase gene expression. Journal of Biological Chemistry, 278: 15333-15340, 2003

20. Pedersen PL, **Mathupala SP**, Rempel A, Geschwind JF, Ko YH: Mitochondrial Bound Type II Hexokinase: A key Player in the growth and survival of many Cancers and an Ideal Prospect for Therapeutic Intervention. Biochimica et Biophysica Acta 1555: 14-20, 2002

21. **Mathupala SP**, Sloan AE: "In gel" purified ditags direct synthesis of highly efficient SAGE libraries. BMC Genomics, 3: 20, 2002

22. **Mathupala SP**, Rempel A, Pedersen PL: Glucose Catabolism in Cancer Cells: Identification and characterization of a marked activation response of the Type II hexokinase gene to hypoxia. Journal of Biological Chemistry, 276: 43407-43412, 2001

23. **Mathupala SP**, Heese C, Pedersen PL: Glucose Catabolism in Cancer Cells: The Type II hexokinase Promoter Contains Functionally Active Response Elements for the Tumor Suppressor p53. Journal of Biological Chemistry, 272: 22776-22780, 1997

24. **Mathupala SP**, Rempel A, Pedersen PL: Aberrant Glycolytic Metabolism of Cancer Cells: A Remarkable Coordination of Genetic, Transcriptional, Post-Translational, and Mutational Events that lead to a Critical Role for Type II Hexokinase. Journal of Bioenergetics and Biomembranes, 29: 339-343, 1997

25. Rempel A, **Mathupala SP**, Griffin CA, Hawkins AL, Pedersen PL: Amplification of the Type II Hexokinase Gene in the highly glycolytic hepatoma AS-30D. Cancer Research, 56: 2468-2471, 1996

26. Rempel A, **Mathupala SP**, Pedersen PL: Glucose Catabolism in Cancer Cells: Regulation of the Type II hexokinase promoter by glucose and cyclic. FEBS Letters, 385: 233-237, 1996

27. **Mathupala SP**, Rempel A, Pedersen PL: Glucose catabolism in cancer cells: Isolation, sequence, and activity of the promoter for Type II Hexokinase. Journal of Biological Chemistry, 270: 16918-16925, 1995

28. **Mathupala SP**, Park JH, Zeikus JG: Evidence for α-1,6 and α-1,4 glucosidic bond cleavage in highly branched glycogen by amylopullulanase from Thermoanaerobacter ethanolicus. Biotechnology Letters, 16: 1311-1316, 1994

29. **Mathupala SP**, Zeikus JG: Improved purification and biochemical characterization of extracellular amylopullulanase from Thermoanaerobacter ethanolicus 39E. Applied Microbiology and Biotechnology, 39: 487-493, 1993

30. **Mathupala SP**, Lowe SE, Podkovirov SM, Zeikus JG: Sequencing of the Amylopullulanase (apu) gene of Thermoanaerobacter ethanolicus 39E, and identification of the active site by site-directed mutagenesis. Journal of Biological Chemistry, 268: 16332-16344, 1993

31. Saha BC, Lamed R, Lee CY, **Mathupala SP**, Zeikus JG: Characterization of an endo-acting amylopullulanase from Thermoanaerobacter Strain B6A. Applied and Environmental Microbiology, 56: 881-886, 1990

32. **Mathupala SP**, Saha BC, Zeikus JG: Substrate competition and specificity at the active site of amylopullulanase from Clostridium thermohydrosulfuricum. Biochemical and Biophysical Research Communications, 166: 126-132, 1990

33. Saha BC, **Mathupala SP**, Zeikus JG: Purification and characterization of a highly thermostable pullulanase from Clostridium thermohydrosulfuricum. Biochemical Journal, 252: 343-348, 1988

Book Authorships, Editorships, and Chapters

1. **Mathupala SP**, Mittal S, Guthikonda M, Sloan AE: RNAi based approaches to the treatment of brain tumors In: *RNA Interference Based Therapeutics: Clinical Applications* (Ed. Cho, W.C.S) Springer-Verlag, (2011)

2. **Mathupala SP**, Mittal S, Guthikonda M, Sloan AE: RNA Interference (RNAi) Based Therapies Against Brain Tumors: Potential Clinical Strategies. In: Therapeutic Ribonucleic Acids in Brain Tumors (Eds. Erdmann, V.A., Reifenberger, G., and Barciszewski, J.) Springer-Verlag, Heidelberg, 2009

3. Rempel A, **Mathupala SP**, Pedersen PL: Glucose Catabolism in Cancer Cells: Role and regulation of hexokinase overexpression. In: Monograph on Cell Growth and

Oncogenesis. Eds. Papa, S., Kandue, D., and Tager, J.M. Birkhauser Verlag, Basel, Switzerland, 1998

4. Zeikus JG, **Mathupala SP**, Lee YE, Podkovyrov S, Saha B, Meng M, Bagdasarian M: Thermophilic Enzymes: New Sources, Uses, and Biodesigns. In: American Chemical Society Symposium Series, Thermophilic Enzymes, 110-113. Ladisch, H., and Bosse, A. (Eds.), 1992

5. Saha BC, **Mathupala SP**, Zeikus JG: Comparison of amylopullulanase to alpha-amylase and pullulanase. In: American Chemical Society Symposium Series, Volume 460: Enzymes in Biomass Conversion, 362-371, 1991

6. Saha BC, **Mathupala SP**, Zeikus JG: Novel thermostable saccharidases from thermoanerobes. In: American Chemical Society Symposium Series, Volume 458: Biotechnology of Amylodextrin Oligosaccharides, 86-97, 1991

NCBI (GenBank) Submissions/Publications

1. **Mathupala, S.P.** (2009): RNAi Expression Vector pUC18-H1, complete sequence. Accession # FJ687158
2. **Mathupala, S.P.** (1995): *Rattus norvegicus* type II hexokinase gene, partial cds and promoter region. Accession # U19605
3. **Mathupala, S.P.** (1990): *Clostridium thermohydrosulfuricum* amylopullulanase (apu) gene, complete cds. Accession # M97665
4. **Mathupala, S.P.** (2001): Cloning vector pLXRN, complete sequence. Accession # AF113968
5. **Mathupala, S.P.** (1997): *Rattus norvegicus* mutant type II hexokinase mRNA, complete cds. Accession # AF027179
6. **Mathupala, S.P.** (2009): Rattus norvegicus mutant p53 mRNA, complete cds. Accession # U90328

PRESENTATIONS (select)

Invited Lectures and Grand Rounds

1. Small-molecule activated metabolic gene targets in glioblastoma (Grand Rounds Presentation, Dept. Neurosurgery, Wayne State University) 06/2013
2. Regulation of metabolite transporter expression in response to metabolic flux stimuli in brain tumors (Grand Rounds Presentation, Dept. Neurosurgery, Wayne State University) 10/2012
3. Advances in Brain Tumor Targeting – Metabolic Aspects (Grand Rounds Presentation, Dept. Neurosurgery, Wayne State University) 10/2011
4. Detroit Neurosurgery Symposium, Detroit, MI (invited seminar); Metabolic Targeting of Malignant Glioma (10/ 2010)
5. Neuro-Oncology Imaging via Metabolic Signatures (Grand Rounds Presentation, Dept. Neurosurgery, Wayne State University) 07/2009
6. Metabolic targeting of Malignant Glioma (Grand Rounds Presentation, Dept. Neurosurgery, Wayne State University) 09/2008

7. Case Western Reserve University, Neurological Research Program (invited seminar): Lactate Transport as a Glioma Therapeutic Target. (10/2007)
8. University of Toledo, School of Pharmacy (invited seminar): Metabolic Targeting of Malignant Tumors. (11/2007)
9. Wayne State University, School of Medicine, Department of Neurosurgery: Grand Rounds Seminar: Metabolic Targeting of Glioma. (12/2007).
10. Karmanos Cancer Institute (invited seminar): Therapeutic Targeting of Glycolytic Pathway of Tumors. (03/2008)
11. Wayne State University, School of Medicine, Department of Biochemistry & Molecular Biology (invited seminar): Targeting Aberrant Metabolism in Cancers: Preclinical Research. (03/2009)
12. Wayne State University, School of Medicine, Department of Neurosurgery: Presentations to 2008-2010 Neurosurgery Resident Candidates. (12/2007-12/2013)