

**PUBLICATIONS, ABSTRACTS AND FUNDING GENERATED BY
THE P50 ICMIC PROGRAM**

(08/01/03-12/20/06)

RESEARCH COMPONENTS

ZAVER M. BHUJWALLA, PH.D.

Research Component #1 - Combined Anti-Angiogenic Therapy and siRNA Targeting of Choline Kinase

Publications

Glunde, K., Jie, C., and Bhujwalla, Z. M. (2004) Molecular basis of the aberrant choline phospholipid metabolism of breast cancer cells. *Cancer Res.* 64, 4270-4276.

Mori, N., Delsite, R., Natarajan, K., Kulawiec, M., Bhujwalla, Z. M. and Singh, K.K. (2004) Loss of p53 function in colon cancer cells results in increased phosphocholine and total choline. *Molecular Imaging* 3, 319-323.

Glunde, K., Raman, V., Mori, N., and Bhujwalla, Z. M. (2005) RNA interference-mediated choline kinase suppression in breast cancer cells induces differentiation and reduces proliferation. *Cancer Res.* 65, 11034-11043.

Glunde, K., Ackerstaff, E., Mori, N., Jacobs, M. A., and Bhujwalla, Z. M. (2006) Choline phospholipid metabolism in cancer: consequences for molecular pharmaceutical interventions. *Molecular Pharmaceutics* 3, 496-506.

Book chapters and review articles

Bhujwalla, Z. M., Ackerstaff, E., Artemov, D., Glunde, K., Pathak, A. P., Raman, V., and Solaiyappan, M. (2005) *In vivo* cellular and molecular imaging of cancer. In: *Biomedical Magnetic Resonance Proceedings of the International Workshop*. Edited by Jagannathan, N. R., Jaypee Brothers Medical Publishers (P) Ltd., New Delhi, pages 247-256.

Bhujwalla, Z. M., Glunde, K., Ackerstaff, E., Pathak, A. P., Gimi, B., and Artemov, D. (2006) Molecular Imaging in Cancer Therapies of the Future. In: *In vivo* MR Techniques in Drug Discovery and Development. Edited by Beckmann, N., CRC Press, Boca Raton, FL.

Jacobs, M. A., Glunde, K., Gimi, B., Pathak, A. P., Ackerstaff, E., Artemov, D., and Bhujwalla, Z. M. (2006) MR Molecular and Functional Imaging of Cancer. In: *Molecular and Cellular MR Imaging*. CRC Press, Boca Raton, FL (in press)

Glunde, K., Foss, C. A., Bhujwalla, Z. M. (2007) Molecular Imaging in Cancer. In: *Biomedical Information Technology*. Elsevier, Burlington, MA (in press)

Ackerstaff, E., Glunde, K., and Bhujwalla, Z. M. (2003) Choline Phospholipid Metabolism: A target in cancer cells? *J. Cell Biochem.* 90, 525-53.

Pathak, A. P., Gimi, B., Glunde, K., Ackerstaff, E., Artemov, D., and Bhujwalla, Z. M. (2004) Molecular and functional imaging of cancer: Advances in MRI and MRS. *Methods Enzymol.* 386, 3-60.

Gimi, B., Pathak, A. P., Ackerstaff, E., Glunde, K., Artemov, D., and Bhujwalla, Z. M. (2005) Molecular imaging of cancer: Applications of MR methods. *IEEE Trans. Med. Imaging* 93, 784-799.

Glunde, K., Jacobs, M. A., Bhujwalla, Z. M. (2006) Choline Metabolism in Cancer: Implications for Diagnosis and Therapy. *Expert Rev. Mol. Diagn.* 6, 821-829.

Glunde, K. and Serkova, N. J. (2006) Profiling of Choline Metabolites in Cancer. *Pharmacogenomics* 7, 1109-1123.

Raman, V., Pathak, A. P., Glunde, K., Artemov, D., and Bhujwalla, Z. M. (2006) Magnetic resonance imaging of transgenic mouse models of cancer. *NMR Biomed.* (in press)

Glunde, K., Pathak, A. P., and Bhujwalla, Z. M. (2006) Molecular-Functional Imaging of Cancer: To Image and Imagine. *Trend Mol. Med.* (in press)

Abstracts

Raman, V., Mori, N., Mironchik, Y., Glunde, K., and Bhujwalla, Z. M. (2003) Gene expression inhibition of choline kinase in breast cancer cells using RNA interference detected by ¹H NMR spectroscopy. Eleventh Scientific Meeting of the International Society of Magnetic Resonance in Medicine, Toronto, Ontario, Canada.

Mori, N., Glunde, K., and Bhujwalla, Z. M. (2003) Effect of choline kinase inhibition using hemicholinium-3 on choline phospholipid metabolism of human mammary epithelial cells. Eleventh Scientific Meeting of the International Society of Magnetic Resonance in Medicine, Toronto, Ontario, Canada.

Mori, N., Glunde, K., and Bhujwalla, Z. M. (2003) Impact of choline kinase inhibition on choline phospholipid metabolism in human mammary epithelial cells. The Second Annual Meeting of the Society for Molecular Imaging, San Francisco, CA, USA.

Glunde, K., Raman, V., Mori, N., Mironchik, Y., and Bhujwalla, Z. M. (2003) Choline kinase downregulation in breast cancer cells using RNA interference detected by ¹H NMR spectroscopy. The Second Annual Meeting of the Society for Molecular Imaging, San Francisco, CA, USA.

Glunde, K., Jie, C., and Bhujwalla, Z. M. (2003) Molecular Alterations underlying differences in choline phospholipid metabolism of nonmalignant versus malignant human mammary epithelial cells. The Second Annual Meeting of the Society for Molecular Imaging, San Francisco, CA, USA.

Glunde, K., Raman, V., Mori, N., Mironchik, Y., and Bhujwalla, Z. M. (2004) Choline kinase knock-down in breast cancer cells using RNA interference is associated with an increase in intracellular lipid droplets and triacylglycerides. Twelfth Scientific Meeting of the International Society of Magnetic Resonance in Medicine, Kyoto, Japan.

Glunde, K., Raman, V., and Bhujwalla, Z. M. (2004) Correlation between choline kinase mRNA and ¹H MRS-detectable choline metabolite levels in stable choline kinase knock-down clones of a human breast cancer cell line. Twelfth Scientific Meeting of the International Society of Magnetic Resonance in Medicine, Kyoto, Japan.

Mori, N., Glunde, K., Raman, V., and Bhujwala, Z. M. (2004) Vascular endothelial growth factor overexpression increases phosphocholine levels in a human breast cancer model. Twelfth Scientific Meeting of the International Society of Magnetic Resonance in Medicine, Kyoto, Japan.

Bhujwala, Z. B., Solaiyappan, M., Pathak, A. P., Ackerstaff, E., and Raman, V., Glunde, K., Artemov, D. (2004) Characterizing tumors with multi-modality imaging. The Third Annual Meeting of the Society for Molecular Imaging, St. Louis, MO, USA.

Mori, N., Glunde, K., Raman, V., and Bhujwala, Z. M. (2004) Effect of vascular endothelial growth factor (VEGF) overexpression on choline phospholipid metabolism in a human breast cancer model. The Third Annual Meeting of the Society for Molecular Imaging, St. Louis, MO, USA.

Glunde, K., Raman, V., Mori, N., Wildes, F., and Bhujwala, Z. M. (2004) RNA interference-mediated choline kinase knock-down in human breast cancer cells monitored by magnetic resonance spectroscopy. The Third Annual Meeting of the Society for Molecular Imaging, St. Louis, MO, USA.

Glunde, K., Mori, N., Raman, V., and Bhujwala, Z. M. (2004) Choline kinase knock-down in human breast cancer xenografts monitored by ³¹P MR spectroscopy. The Third Annual Meeting of the Society for Molecular Imaging, St. Louis, MO, USA.

Glunde, K., Mori, N., Raman, V., and Bhujwala, Z. M. (2004) Choline Kinase knock-down in human breast cancer xenografts monitored by ³¹P MR Spectroscopy. ISMRM Workshop on Advances in Experimental and Clinical MR in Cancer Research, Manchester, England, UK.

Glunde, K., Mori, N., Raman, V., and Bhujwala, Z. M. (2005) Phosphorus MR spectroscopic changes mediated by choline kinase knock-down in a human breast tumor model. XXI International Conference on Magnetic Resonance in Biological Systems (ICMRBS), Hyderabad, India.

Glunde, K., Raman, V., Mori, N., and Bhujwala, Z. M. (2005) Choline kinase knock-down in human breast cancer xenografts monitored by ³¹P MR spectroscopy. Thirteenth Scientific Meeting of the International Society of Magnetic Resonance in Medicine, Miami Beach, Florida, USA.

Glunde, K., Raman, V., Solaiyappan, M., Pathak, A. P., Artemov, D., and Bhujwala, Z. M. (2005) Hypoxia increases cellular phosphocholine and total choline levels in human prostate cancer cells. Thirteenth Scientific Meeting of the International Society of Magnetic Resonance in Medicine, Miami Beach, Florida, USA.

Mori, N., Glunde, K., and Bhujwala, Z. M. (2005) Tumor microenvironment alters choline phospholipid metabolite levels. Thirteenth Scientific Meeting of the International Society of Magnetic Resonance in Medicine, Miami Beach, Florida, USA.

Glunde, K., Raman, V., Solaiyappan, M., Pathak, A. P., Artemov, D., and Bhujwala, Z. M. (2005) Hypoxia-driven increase in cellular phosphocholine and total choline levels in human prostate cancer cells. The Fourth Annual Meeting of the Society for Molecular Imaging, Cologne, Germany.

Mori, N., Glunde, K., Takagi, T., Raman, V., and Bhujwala, Z. M. (2006) Inhibition of choline kinase expression by siRNA enhances treatment of breast cancer cells with 5-Fluorouracil. 97th annual meeting of the American Association for Cancer Research (AACR), Washington, DC, USA.

Glunde, K., Raman, V., and Bhujwala, Z. M. (2006) Hypoxia regulates phosphocholine and total choline concentrations in human prostate cancer. Fourteenth Scientific Meeting of the International Society of Magnetic Resonance in Medicine, Seattle, Washington, USA.

Glunde, K., Artemov, D., Raman, V., and Bhujwala, Z. M. (2006) Choline kinase suppression increases tumor lipid content and vascular volume in a human breast cancer model. Fourteenth Scientific Meeting of the International Society of Magnetic Resonance in Medicine, Seattle, Washington, USA.

Mori, N., Glunde, K., Takagi, T., Raman, V., and Bhujwala, Z. M. (2006) Choline kinase downregulation by siRNA reduces phosphocholine and total choline, and enhances treatment of breast cancer cells with 5-fluorouracil. Fourteenth Scientific Meeting of the International Society of Magnetic Resonance in Medicine, Seattle, Washington, USA.

Shah, T., Glunde, K., Winnard Jr, P. T., Raman, V., Bhujwala, Z. M. (2006) Role of hypoxia in regulating choline kinase in human prostate cancer cells. Fifth Scientific Annual Meeting of the Society for Molecular Imaging, Waikoloa Village, Hawaii, USA.

Glunde, K., Mori, N., Takagi, T., Raman, V., and Bhujwala, Z. M. (2006) siRNA-mediated choline kinase suppression sensitizes breast cancer cells to 5-fluorouracil treatment. ISMRM Workshop on Frontiers in Metabolic, Molecular, and Clinical Imaging, Pocono Manor, PA, USA.

Glunde, K., Artemov, D., Raman, V., and Bhujwala, Z. M. (2006) Increased tumor lipid content and vascular volume following choline kinase suppression in a human breast cancer model. ISMRM Workshop on Frontiers in Metabolic, Molecular, and Clinical Imaging, Pocono Manor, PA, USA.

GREGG SEMENZA, M.D., PH.D.

Research Component #2 - Imaging the Role of HIF-1 in Breast Cancer Progression

Publications

Stoeltzing, O., McCarty, M. F., Wey, J. S., Fan, F., Liu, W., Belcheva, A., Bucana, C. D., Semenza, G. L. and Ellis, L. M. Role of hypoxia-inducible factor 1a in gastric cancer cell growth, angiogenesis and vessel maturation. *Journal of the National Cancer Institute*, 96: 946-956, 2004.

Zagzag, D., Krishnamachary, B., Yee, H., Okuyama, H., Chiriboga, L., Ali, M. A., Melamed, J., Semenza, G. L. Stromal cell-derived factor-1a and CXCR4 expression in hemangioblastoma and clear cell-renal cell carcinoma: von Hippel-Lindau loss-of-function induces expression of a ligand and its receptor. *Cancer Research*, 65: 1-11, 2005.

Krishnamachary, B., Zagzag, D., Nagasawa, H., Rainey, K., Okuyama, H., Baek, J. H., Semenza, G. L. Hypoxia-inducible factor-1 dependent repression of e-cadherin in von Hippel-Lindau tumor suppressor-null renal cell carcinoma mediated by TCF3, ZFH1A and ZFH1b. *Cancer Research*, 66: 2725-2731, 2006.

venu RAMAN, PH.D.

Research Component #3 - Imaging and Targeting Hypoxia in Solid Tumors

Publications

Winnard, P. Jr. and Raman, V. Real time non-invasive imaging of receptor-ligand interactions *In vivo*. (2003) *Journal of Cellular Biochemistry* 90:454-463.

Winnard, P. Jr., Mironchik, Y. and Raman, V. Robust expression of transgenes in MCF-7 breast cancer cells is expression vector-dependent. (2004) *BioTechniques* 37:370-374.

Winnard, P. Jr., Kluth, B. J. and Raman, V. Non-invasive optical tracking of red fluorescent protein expressing cancer cells in a model of metastatic breast cancer. (2006) *Neoplasia* 8:796-806.

Raman, V., Artemov, D., Pathak, A. P., Winnard, P. Jr., McNutt, S., Yudina, A., Bogdanov, A. Jr. and Bhujwala, Z. M. Characterizing vascular parameters in hypoxic regions: A combined MR and optical imaging study of a human prostate cancer model. (2006) *Cancer Research* 66:9929-9936.

Abstracts

Winnard, P., Mironchik, Y., Wildes, F., Bhujwala, Z. M. and Raman, V. Engineering a cell surface expressed receptor for targeted molecular imaging. Proceedings of the 3rd annual meeting of the society for molecular imaging, St. Louis, September 9-12, 2004.

Winnard, P., Mironchik, Y., Wildes, F., Bhujwala, Z. M. and Raman, V. Engineering a Novel Receptor for Molecular Imaging. Proceedings of the Twelfth Scientific Meeting and Exhibition of the ISMRM, Kyoto, Japan, May 15-21, 2004.

Winnard, P., Kluth, J. and Raman, V. Non-invasive optical tracking of metastatic progression of live animals. The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Fellow Research Day, May, 2006.

Winnard, P., Kluth, J. and Raman, V. Non-invasive Optical Tracking of Red Fluorescent Protein Expressing Cancer Cells in a Model of Metastatic Breast Cancer, 5th Annual Mtg Society of Molecular Imaging, Hawaii, 2006.

Funding resulting from this support

FAMRI 6/1/2006 - 5/31/2009

Activation of DDX3 by benzo[a]pyrene diol epoxide, a component of secondhand tobacco smoke, in human breast cells: a potential mechanism for neoplastic transformation-

DMITRI ARTEMOV, PH.D.

Research Component #4 - Molecular and Functional Imaging of the HER-2/*neu* Receptor

Publications

W. Zhu, B. Okollie, D. Artemov "Controlled Internalization of Her-2/*neu* Receptors by Cross-linking for Targeted Delivery", Submitted to *Cancer Research*, 2006.

Book chapters and reviews

Artemov, D., Bhujwala, Z. M. and Bulte, J. W. M. Magnetic Resonance Imaging of cell surface receptors using targeted contrast agents. *Current Pharmaceutical Biotechnology*, 5, 441-450, 2004.

Artemov, D. and Bhujwala, Z. M. Novel Imaging Agents for Molecular MR Imaging of Cancer. *Drug Discovery Handbook*, by Shayne C. Gad. John Wiley & Sons, Inc., pp 1309-1341, 2005.
Artemov, D. MRI: Overview and Applications. *The handbook of genomic medicine*, 2006 (in press).

Abstracts

ISMRM 12th Meeting, Kyoto, Japan (2004) D. Artemov "Advances in Molecular imaging for Oncology" Invited talk for the Study Group MR of Cancer.

The 3rd Meeting of the Society for Molecular Imaging, St. Louis, MO (2004) #358 D. Artemov, C. Foss, B. Okollie, Z.M. Bhujwala "MR Molecular Imaging of Her-2/neu Receptors Using Multi-component targeted Contrast Agent".

ISMRM 13-th Meeting, Miami Beach, Florida (2005)#2595 D. Artemov, B. Okollie, C. Foss, Z.M. Bhujwala "Multicomponent T1 Targeted Contrast Agent for MR Imaging of Her-2/neu Receptors".

RSNA 91st Meeting, Chicago
D. Artemov, "MR Imaging", categorical Course.

ISMRM 14th Meeting, Seattle, Washington (2006) #1744 W. Zhu, B. Okollie, Z.M. Bhujwala, D. Artemov "A Dendrimer based contrast agent for MR imaging of Her-2/neu Receptors by a Three-step Pretargeting Approach".

ISMRM 14th Meeting, Seattle, Washington (2006) #1843 W. Zhu, B. Okollie, Z.M. Bhujwala, D. Artemov "Controlled Internalization and Recycling of Her-2/*neu* by Cross-linking with an Avidin/streptavidin-biotin system for MR Enhancement".

The 5th Meeting of the Society for Molecular imaging, Hawaii (2006) #246 W. Zhu, B. Okollie, Z.M. Bhujwala, D. Artemov "Enhancing Targeted Delivery to Her-2/neu Receptor by Internalization Induced by Cross-linking".
232d National Meeting of American Chemical Society, San Francisco, CA

ISMRM Workshop on MR of Cancer (2006) D. Artemov "Developing of Imaging Probes for Molecular Magnetic Resonance Imaging", Invited talk for Recent Advances in Molecular Imaging session.

Funding resulting from this support

R01CA125552 (Artemov, D., PI) (Pending under review)
Specific tumor targeting, therapy and imaging using EGF receptors

DEVELOPMENTAL PROJECTS

PETER VANZIJL, PH.D.

Pilot Project #1 (2003 – 2005) Receptor Imaging Using Non-Paramagnetic MRI Contrast Agents

Publications

A.A. Gilad, M.T. McMahon, P. Walczak, P.T. Winnard Jr., V Raman, H.W.M. van Laarhoven, C.M. Skoglund, J.W.M. Bulte, & P.C.M. van Zijl, "Artificial reporter gene providing MRI contrast based on proton exchange", *Nature Biotech.*, in press

Abstracts

Gilad AA, McMahon, Walczak, P, MT Winnard PT, Raman V, Bulte, JW, van Zijl PC. Artificial Reporter Gene Providing MRI Contrast *In vivo* Based on Chemical Exchange. Proc. ISMRM 2006. P 100.

Gilad AA, McMahon MT, Walczak, P, Winnard PT, Raman V, Bulte, JW, van Zijl PC. Artificial reporter gene providing frequency selective contrast for magnetic resonance imaging (MRI) in xenografted 9l glioma. Proc Amer Assoc Cancer Res 2006;47:2754.

Gilad AA, McMahon MT, Walczak, P, Winnard PT, Raman V, Bulte, JW, van Zijl PC. Artificial reporter gene for MRI providing frequency-selective contrast. SMI 2005 4(3) p.13.

Gilad AA, McMahon, MT Winnard PT, Raman V, Bulte, JW, van Zijl PC. MRI reporter gene providing contrast based on chemical exchange saturation transfer (CEST) Proc. ISMRM 2005. P.363.

Funding resulting from this support

R21 EB005252 (P.I. J.W.M. Bulte) 10/01/05-09/30/09 1.20 calendar NIH/NIBIB \$250,000
Developing a CEST reporter gene
This grant aims to develop an artificial MRI reporter gene based on amide-rich proteins

CHI V. DANG, M.D., PH.D.

Pilot Project #2 (2003-ongoing) Imaging Studies of C-Myc Regulation of Tumor Metabolism

Publications

Gao, P., Zhang, H., Dinavahi, R., Li, F., Raman, V., Bhujwalla, Z. M., Felsher, D., Cheng, L., Pevsner, J., Lee, L., Semenza, G. L., and Dang, C. V. HIF-1-dependent Anti-tumorigenic Effects of Anti-oxidants *In vivo*, *Nature Medicine* (submitted), 2006.

MARTIN POMPER, M.D., PH.D.

Pilot Project #3 (2003 – 2005) New Imaging Agents for Prostate Cancer: Radiolabeled Inhibitors of Glutamate Carboxypeptidase II (GCP II)

Publications

Pomper MG, Musachio JL, Zhang J, Zhou Y, Scheffel U, Hilton J, Maini A, Dannals RF, Wong DF, Kozikowski AP. ¹¹C-MCG: Synthesis, uptake selectivity and primate PET of a probe for glutamate carboxypeptidase II (NAALADase.) *Mol Imaging* 2002; 1:96-101.

Foss CA, Mease RC, Fan H, Wang Y, Ravert HT, Dannals RF, Olszewski RT, Heston WD, Kozikowski AP, Pomper MG. Radiolabeled small molecule ligands for prostate-specific membrane antigen: *In vivo* imaging in experimental models of prostate cancer. Clin Cancer Res 2005; 11:4022-4028. [featured on the cover of this issue]

Abstracts

Pomper MG, Ravert HT, Zhang J, Scheffel U, Musachio JL, Dannals RF, Kozikowski AP. New imaging agents for prostate cancer: radiolabeled inhibitors of glutamate carboxypeptidase II (GCP II). Academy of Molecular Imaging 2003 Conference, Madrid, Spain, September, 2003.

Mathews WB, Foss CA, Stoermer D, Ravert HT, Rauseo PA, Dannals RF, Henke BR, Bhujwala ZM, Pomper MG. Synthesis and biodistribution of [¹¹C]GW7845, a positron-emitting agonist for PPAR- α . 52nd Annual Meeting of the Society of Nuclear Medicine, Philadelphia, PA, June, 2004.

Foss CA, Mease RC, Fan H, Ravert HT, Dannals RF, Kozikowski AP, Pomper MG. Imaging PSMA expression in prostate cancer xenografts by PET and gamma scintigraphy. 3rd Annual Meeting of the Society for Molecular Imaging, St. Louis, MO, September, 2004.

Foss CA, Maitra A, Iacobuzio-Donahue C, Kern SE, Hruban R, Pomper MG. [¹²⁵I]Anti-claudin 4 and [¹²⁵I]anti-PSCA monoclonal antibodies as novel imaging agents for human pancreatic cancer in xenograft-bearing mice. 3rd Annual Meeting of the Society for Molecular Imaging, St. Louis, MO, September, 2004.

Song H, Shahverdi K, Fox J, Cho YI, Wang Y, Gimi B, Pomper M, Tsui B, Bhujwala Z, Reilly RT, Sgouros G. A mouse model of breast cancer metastases for targeted alpha-particle radioimmunotherapy in the presence of cross-reactive normal organs. 96th Annual Meeting of the American Association for Cancer Research, Anaheim, CA, April, 2005.

Foss CA, Dusich C, Mease RC, Maitra A, Pomper MG. Synthesis and validation of a novel small-molecule fluorescent probe for PSMA expression in human tumor neovasculature. Molecular Imaging 2005; 4:S321.

Funding resulting from this support

R21CA111982 – PSMA-based PET Ligands for Prostate Cancer Imaging (JHU, 04/07/06-03/31/08)

R21CA114111 – PSMA-based SPECT Tracers for Prostate Cancer Imaging (JHU, 05/01/06-04/30/08)

R21EB005324 – PSMA-based Gene Reporter-Probe System (RMI) (JHU, 09/15/05-08/31/09)

DoDPC050825 – PSMA-based PET Ligands for Prostate Cancer Imaging (JHU, 12/01/05-11/30/07)

THEODORE DEWEESE, M.D.

Pilot Project #4 (2003 – 2005) Non-Invasive Monitoring of Therapeutic Effect of siRNA-Mediated Radiation Sensitization in Human Prostate Cancer Xenografts

None

ZSOLT SZABO, M.D., PH.D.

Pilot Project #5 (2003 – 2006) Imaging of the Endothelin Receptor in Cancer

Abstracts

Animal Model for *In vivo* Investigation of the Endothelin Subtype A Receptor with PET in Prostate Carcinoma J. Xia, Y. Xiang, E. Seckin, W. Mathews, Z. Szabo; Academy of Molecular Imaging Annual Conference Orlando FL March 2006

Animal model for *In vivo* investigation of the endothelin subtype B receptor with PET in Lung Carcinoma Jinsong Xia, Yan Xiang, Esen Seckin, William B. Mathews, Zsolt Szabo. World Congress of Nuclear Medicine and Biology Seoul Korea October 2006

Funding resulting from this support

1R21CA115532-01A1, ENDOTHELIN RECEPTOR IMAGING WITH PET
07/07/2006-06/30/2008

BARJOR GIMI, PH.D.

DAVID GRACIAS, PH.D.

Pilot Project #6 (2005 – 2007) Molecular Imaging with Magnetic Resonance Microsystems

Awards

- The Negendank Cancer Imaging Prize, 2006
- Negendank Award, *outstanding young investigator in the field of cancer MR*, 2004

Publications

Jens Vogel-Claussen*, Barjor Gimi*, Dmitri Artemov and Zaver M. Bhujwala, "Early tumor response to antivasular therapy detected by vascular volume and diffusion-weighted MRI," (in review), 2006

Barjor Gimi, Dmitri Artemov, Timothy Leong, David H. Gracias, Wesley Gilson, Matthias Stuber, and Zaver M. Bhujwala, "Cell viability and non-invasive *In vivo* MRI tracking of 3D cell encapsulating self-assembled microcontainers," *Cell Transplantation: The Regenerative Medicine Journal*, in press, 2006

Barjor Gimi, Noriko Mori, Ellen Ackerstaff, Emma E. Frost, Jeff W.M. Bulte, Zaver M. Bhujwala, "Noninvasive MR imaging of endothelial cell response to human breast cancer cells," *Neoplasia* Volume 8, Issue 3, pp 207-213, 2006

Timothy Leong, Hongke Ye, Emma Call, Barjor Gimi, Zaver Bhujwala and D. H. Gracias, "Microfabrication and Self-Assembly of 3D Microboxes for Biomedical Applications," Paper in Proceedings of the 18th IEEE International Conference on Microelectromechanical Systems (MEMS), Istanbul, January 2006

Barjor Gimi, Timothy Leong, Zhiyong Gu, Michael Yang, Dmitri Artemov, Zaver M. Bhujwala, David H. Gracias, "Self-assembled micropatterned and radio frequency (RF) shielded biocontainers," *Biomedical Microdevices*, Volume 7, Issue 4, pp 341-345, 2005

Abstracts

Barjor Gimi, Dmitri Artemov, Timothy Leong, David H. Gracias, Zhiyong Gu, and Zaver M. Bhujwala, "Implantable Microcapsules for Cell Based Therapy," Poster presentation at the Fifth Annual Meeting of the Society for Molecular Imaging, August-September 2006

Barjor Gimi, Jens Vogel-Claussen, Dmitri Artemov, and Zaver M. Bhujwalla, "Early treatment response assessment to the antivascular agent ZD6126 detected with macromolecular CE-MRI," Poster presentation at the Fifth Annual Meeting of the Society for Molecular Imaging, August-September 2006

Barjor Gimi, Dmitri Artemov, David Gracias, Timothy Leong, Zaver Bhujwalla, "MRI of implantable microcapsules for cell based therapy," Talk at the Gordon Research Conference on *In vivo* Magnetic Resonance, July 2006

Barjor Gimi, Noriko Mori, Maria Mikhaylova, Jeff W.M. Bulte, and Zaver M. Bhujwalla, "MRI assay to study endothelial invasion and motility in a tumor microenvironment," Oral presentation at the International Society of Magnetic Resonance in Medicine, Fourteenth Scientific Meeting, May 2006

Barjor Gimi, Dmitri Artemov, Timothy Leong, Zaver M. Bhujwalla, and David H. Gracias, "Cellular Encapsulation and MRI tracking with self-assembled RF shielded devices," Plenary talk at the International Society of Magnetic Resonance in Medicine, Fourteenth Scientific Meeting, May 2006

Barjor Gimi, Noriko Mori, and Zaver M. Bhujwalla, "Hypoxia increases endothelial cell invasion and migration," Poster presentation at the International Society of Magnetic Resonance in Medicine, Fourteenth Scientific Meeting, May 2006

Barjor Gimi, Noriko Mori, Zaver M. Bhujwalla, "Dynamic noninvasive tracking of response of endothelial cells to hypoxia and cancer cells using MRI," Poster presentation at the Ninety-seventh Annual Meeting of the American Association for Cancer Research, April 2006

Timothy Leong, Hongke Ye, Emma Call, Barjor Gimi, Zaver Bhujwalla and D. H. Gracias, "Microfabrication and Self-Assembly of 3D Microboxes for Biomedical Applications," The 18th IEEE International Conference on Microelectromechanical Systems (MEMS), Istanbul, January 2006

Timothy Leong, Barjor Gimi, Zhiyong Gu, Zaver Bhujwalla and David H. Gracias, Self-assembled, radio frequency (RF) shielded non-invasively trackable micro containers," American Electrophoresis Society annual meeting, 2005

Barjor Gimi, Noriko Mori, Ellen Ackerstaff, Emma E. Frost, Jeff W.M. Bulte, Zaver M. Bhujwalla, "Optimized iron oxide labeling and MR parameters for endothelial cell tracking in a non-invasive angiogenesis assay," Poster presentation at the International Society of Magnetic Resonance in Medicine, Thirteenth Scientific Meeting, May 2005

Jens Vogel-Claussen, Barjor Gimi, Zaver M. Bhujwalla, "Diffusion-weighted MRI detects early treatment response after antivascular therapy of prostate tumors," Poster presentation at the International Society of Magnetic Resonance in Medicine, Thirteenth Scientific Meeting, May 2005

Barjor Gimi, Noriko Mori, Ellen Ackerstaff, Emma E. Frost, Jeff W. M. Bulte, Zaver M. Bhujwalla, "Imaging endothelial cell invasion and network formation in response to human breast cancer cells," Poster presentation at the Ninety-sixth Annual Meeting of the American Association for Cancer Research, April 2005

Ellen Ackerstaff, Barjor Gimi, Dmitri Artemov, Zaver M. Bhujwalla, "Anti-inflammatory Treatment Reduced Breast Cancer Cell Invasion and Caused Metabolic Changes Characteristic of a Less Malignant Phenotype," Poster presentation at the XXI International Conference for Magnetic Resonance in Biological Systems, 2005

Barjor Gimi, Noriko Mori, Ellen Ackerstaff, Emma E. Frost, Jeff W. M. Bulte, Zaver M. Bhujwalla, "An assay to study endothelial cell and network response to paracrine factors secreted by MDA-MB-231 breast cancer cells, using a superparamagnetic T₂ contrast agent," Poster presentation at the International Society of Magnetic Resonance in Medicine Workshop on Advances in Experimental and Clinical MR in Cancer Research, October 2004

Barjor Gimi, Noriko Mori, Ellen Ackerstaff, Emma E. Frost, Jeff W.M. Bulte, Zaver M. Bhujwalla, "MR Imaging Of Superparamagnetically Labeled Endothelial Cells Revealed Directed Migration In Response To Factors Secreted By Human Breast Cancer Cells." Poster presentation at the Third Annual Meeting of the Society for Molecular Imaging, September 2004

Ellen Ackerstaff, Barjor Gimi, Dmitri Artemov, Zaver M. Bhujwalla, "Anti-inflammatory Agent Indomethacin Reduces Invasion and Causes Metabolic Changes in a Human Breast Cancer Cell Line," Poster presentation at the International Society of Magnetic Resonance in Medicine, Twelfth Scientific Meeting, May 2004

Barjor Gimi, Noriko Mori, Ellen Ackerstaff, Emma E. Frost, Jeff W. Bulte, Zaver M. Bhujwalla, "Tracking of Endothelial Cell Response to Angiogenic Factors Using a T₂-weighted Intracellular Contrast Agent," Poster presentation at the International Society of Magnetic Resonance in Medicine, Twelfth Scientific Meeting, May 2004

Funding resulting from this support

Imaging islets in implantable microcapsules (Gimi, B., PI) 09/22/06 – 08/31/09

NIH/NIDDK; NIBIB 1R01 EB007456-01

Role: Principal Investigator

Implantable 3D microdevices for diabetes therapy (Gimi, B., PI; Zaver Bhujwalla, David Gracias, co-PIs) 05/01/06 – 04/30/07

Charles E. Culpeper Biomedical Pilot Initiative

Goldman Philanthropic Partnerships and Partnerships for Cures

Role: Principal Investigator

Molecular imaging with MR microsystems (Gimi, B.) 08/01/05 – 07/31/07

Molecular Imaging in Cancer: Developmental Project

NIH/NCI P50 (The Johns Hopkins University ICMIC Program)

Role: Principal Investigator

Provisional Patent

Barjor Gimi, Zaver M. Bhujwalla and David H. Gracias, "Self-assembled, micropatterned, and radio frequency (RF) shielded biocontainers" (2005)

ALEKSANDER POPEL, PH.D.

Pilot Project #7 (2005 – 2007) Endogenous Angiogenesis Inhibitors

Publications

E.D. Karagiannis and A.S. Popel. Identification of novel short peptides derived from the 4, 5 and 6 fibrils of type IV collagen with anti-angiogenic properties, *Biochem. Biophys. Res. Commun.*, submitted.

E.D. Karagiannis and A.S. Popel. Novel anti-angiogenic peptides derived from ELR containing CXC chemokines, *FEBS Letters*, submitted.

E.D. Karagiannis and A.S. Popel. Anti-angiogenic peptides derived from type I thrombospondin repeat-containing proteins, J. Biol. Chem., submitted.

KATARZYNA MACURA, M.D., PH.D.

MICHAEL JACOBS, PH.D.

Pilot Project #8 (2005 – 2007) Imaging and MR Spectroscopy in Detection and Localization of Prostate Cancer: A Prospective Trial in patients undergoing cystoprostatectomy and Radical Prostatectomy

Macura KJ, Wang WP, Lane Z., Su L-M, Bluemke DA, Bhujwala ZM, Jacobs MA. Multiparametric and Ex-vivo MR Imaging in Diagnosis of Prostate Cancer: Preliminary results from the prospective trial in patients undergoing prostatectomy, ISMRM 2007 (submitted)

CAREER DEVELOPMENT AWARDS

KRISTINE GLUNDE, PH.D.

Career Development Component #1 (2003-2005) "Lysosomal trafficking in breast cancer"

Publications

Glunde, K., Guggino, S. E., Solaiyappan M., Pathak, A. P., Ichikawa, Y., and Bhujwala, Z. M. (2003) Extracellular acidification alters lysosomal trafficking in human breast cancer cells. Neoplasia 5, 533-545.

Glunde, K., Foss, C. A., Takagi, T., Wildes, F., and Bhujwala, Z. M. (2005) Synthesis of 6'-O-lissamine-rhodamine B-glucosamine as a novel probe for fluorescence imaging of lysosomes in breast tumors. Bioconjug. Chem. 16, 843-851.

Li, C., Greenwood, T. R., Bhujwala, Z. M., and Glunde, K. (2006) Synthesis and characterization of glucosamine-bound near-infrared probes for optical imaging. Org. Lett. 8, 3623-3626.

Abstracts

Artemov, D., Okollie, B., Glunde, K., and Bhujwala, Z. M. (2003) Towards MR imaging of cell surface receptors. The Second Annual Meeting of the Society for Molecular Imaging, San Francisco, CA, USA.

Glunde, K., Lempka, S., Guggino, S. E., Solaiyappan, M., Pathak, A. P., and Bhujwala, Z. M. (2003) Acidic extracellular environments cause lysosomal displacement to the cell periphery and filopodia extension in human breast cancer cells. Mol Biol Cell (Suppl) 14, 110a; 43rd Annual Meeting of the American Society for Cell Biology, San Francisco, CA, USA.

Glunde, K., Solaiyappan, M., Pathak, A. P., and Bhujwala, Z. M. (2004) Extracellular acidification increases total lysosomal volume in invasive breast cancer cells. The Third Annual Meeting of the Society for Molecular Imaging, St. Louis, MO, USA.

Glunde, K., Foss, C. A., Tiffany Greenwood, T. R., and Bhujwala, Z. M. (2006) Increased lysosomal burden correlates with the metastatic potential of human breast cancer xenografts. 97th annual meeting of the American Association for Cancer Research (AACR), Washington, DC, USA.

Li, C., Greenwood, T. R., Bhujwala, Z. M., Glunde, K. (2006) Novel glucosamine-bound near-infrared probes for optical imaging of breast tumors. Fifth Scientific Annual Meeting of the Society for Molecular Imaging, Waikoloa Village, Hawaii, USA.

Glunde, K., Foss, C. A., Greenwood, T. R., Bhujwala, Z. M. (2006) Increased lysosomal burden in a metastatic human breast cancer model. Fifth Scientific Annual Meeting of the Society for Molecular Imaging, Waikoloa Village, Hawaii, USA.

Funding resulting from this support

1 R21 CA112216-01 Kristine Glunde (PI) 06/01/05-05/31/07 NIH/NCI

Imaging lysosomes to predict metastasis in breast cancer

The aim of this R21 is to develop novel imaging techniques to optically image lysosomes, and to assess the role of lysosomal trafficking in breast cancer invasion and metastasis.

Role: Principal Investigator

1 R01 Kristine Glunde (PI) 07/01/07-06/30/12 (Pending, under review)

NIH/NCI

Lysosomal trafficking shapes the extracellular matrix in breast tumors

The aim of this R01 is to study the role of lysosomal trafficking in extracellular matrix remodeling and its role in tumor cell dissemination.

Role: Principal Investigator

MICHAEL JACOBS, PH.D.

Career Development Award #2 (2003-2004) "Multi-parametric imaging of breast cancer"

Publications

Ouwerkerk, R, Jacobs MA, Mezban S, Macura K, Wolff A, Stearns V, Bluemke DA, Bottomley PA. 3D Sodium MRI Measurement of Tissue Sodium Concentrations in Malignant Breast Tumors; Breast Cancer Research and Treatment 2007; in press

Kim HS, Tsai J, Jacobs, MA, Kamel IR Percutaneous Image-Guided Radiofrequency Thermal Ablation for Large Symptomatic Uterine Leiomyomata after Uterine Artery Embolization: A Feasibility and Safety Study J Vasc Interv Radiol 2007; in press

Macura KJ, Ouwerkerk R, Jacobs MA, Bluemke DA. Patterns of enhancement on breast MR images: interpretation and imaging pitfalls. Radiographics. 2006 Nov-Dec;26(6):1719-34

Fayad LM, Bluemke DA, McCarthy EF, Weber KL, Barker PB, Jacobs MA. Musculoskeletal tumors: Use of proton MR spectroscopic imaging for characterization. J Magn Reson Imaging. 2005 Nov 28;23(1):23-28

Jacobs MA, Barker PB, Argani P, Ouwerkerk R, Bhujwala, ZM, Bluemke DA. Combined Spectroscopic and Dynamic Breast MR Imaging; a preliminary study. J. Magn. Reson. Imag. 2005; Jan 21(1):23-28

Jacobs, MA. Magnetic Resonance Spectroscopy of Human Breast Cancer: Methodological Aspects, Applied Radiology (www.appliedradiology.com), May 2005:10-16

Bonekamp D, Horska A, Jacobs MA, Arslanoglu A, Barker PB. Fast method for brain image segmentation: Application to proton magnetic resonance spectroscopic imaging. *Magn Reson Med.* 2005 Nov;54(5):1268-72.

Jacobs MA, Herskovits EH, Kim H.S., Diffusion weighted imaging of high intensity focused ultrasound treatment for uterine fibroids. *Radiology.* 2005 Jul;236(1):196-203.

Jacobs MA, Ouwerkerk R, Wolff AE, Stearns V, Bottomley P, Barker, PB, Davidson NE, Bhujwala ZM, Bluemke DA. Multiparametric and Multinuclear Magnetic Resonance Imaging of Human Breast Cancer: Current Applications. *Technol Cancer Res Treat.* 2004 Dec;3(6):543-50

Abstracts

Jacobs MA, Pan L, Macura K, Wolff A, Stearns V, , Okollie B, Lorentz C, Bluemke DA, Whole Body Diffusion Weighted Imaging and ADC Mapping for Detecting Metastatic Cancer, ISMRM 2007 (submitted).

Jacobs MA, Ouwerkerk R, Combination of Multinuclear and Multiparametric Breast MRI with ISODATA Analysis, ISMRM 2007 (submitted).

Jacobs MA, Stearns V, Wolff A, Ouwerkerk, R, Bluemke DA, Wahl, R. Multimodality (MR/PET/CT) Monitoring Preoperative Systemic Therapy in Operable Breast Cancer, ISMRM 2006

Jacobs MA, Sodium MRI Measurement of Tissue Sodium Concentrations after chemotherapy in Malignant Breast Tumors; *European radiology* 2006

Jacobs MA, Smith M, Khouri N, Bluemke DA, Barker PB, .Three-dimensional Proton MR Spectroscopic Imaging of Human Breast Lesions, ISMRM 2006

Ouwerkerk, R, Jacobs MA, Mezban S, Macura K, Wolff A, Stearns V, Bluemke DA, Bottomley PA. 3D Sodium MRI Measurement of Tissue Sodium Concentrations in Malignant Breast Tumors; *RSNA* 2005

Jacobs MA, Smith M, Khouri N, Bluemke DA, Barker PB, .Three-dimensional Proton MR Spectroscopic Imaging of Human Breast Lesions

Ouwerkerk, R, Jacobs MA, Mezban S, Macura K, Wolff A, Stearns V, Bluemke DA, Bottomley PA. 3D Sodium MRI Measurement of Tissue Sodium Concentrations in Malignant Breast Tumors; *RSNA* 2005

Jacobs MA, Herskovits E, Barker, PB, Bluemke D. Statistical Modeling for Differentiation of Clinical Breast Tumors using Multiparametric MRI. *Proc. Intl. Soc. Mag. Reson. Med.* 13 (2005) 94

Fayad L M, Bluemke D A; McCarthy E F; Weber K L; Barker P B; Jacobs MA Characterization of musculoskeletal tumors by proton MR spectroscopic imaging (MRSI) *Radiology*, Vol. 233 (P) 2004: 405

Book Chapter

MA Jacobs, K Glunde, B Gimi, AP. Pathak, E Ackerstaff, D Artemov, ZM. Bhujwala molecular and functional imaging of cancer Chap. 9, Molecular and Cellular MR Imaging by CRC Press (in-press)

Funding resulting from this support

NIH (Jacobs, M. A., P.I.) 06/01/04-05/30/09

1 R01 CA 100184 'Multiparametric MRI in Breast Cancer' This is an application to characterize the vascularization and metabolism of breast cancer using multi-parametric MRI.'

ARVIND PATHAK, PH.D.

Career Development Award #3 (2005-2007) – High Resolution Molecular MR Imaging of Brain Tumor Angiogenesis

Abstract

Pathak, A. P., Kato, Y., Zhang, J., Jones, M. A novel lectin-targeted contrast agent for molecular MR imaging of blood vessels. The Fifth Annual Meeting of the Society for Molecular Imaging, Hawaii, 2006.

MINORITY TRAINING COMPONENT OF CAREER DEVELOPMENT PROGRAM

DOD (Wang, P. P.I.)

07/01/05-06/30/09

'A Partnership Training Program in Breast Cancer Research Using Molecular Imaging.' Historically Black Colleges and Universities/Minority Institutions Partnership Training Award from the DOD Breast Cancer Research Program, in a partnership application between Paul Wang, Dept. of Radiology from Howard University and Z. M. Bhujwala, Dept. of Radiology, JHU.

MOLECULAR BIOLOGY, IMAGING, SYNTHESIS AND TRANSLATIONAL RESOURCES

Publications

Li C., Winnard, P.T. Jr., Takagi, T., Artemov, D., and Bhujwala, Z. M. Multimodal image-guided enzyme/prodrug cancer therapy. *J Am Chem Soc.*, 29;128(47):15072-3, 2006.

Abstracts

Li Çong, Winnard Paul, Stoddard Barry, Takagi Tomoyo, Artemov Dmitri and Bhujwala Z. M. Multimodality Image Guided Enzyme based prodrug cancer therapy. The Fifth Annual Meeting of the Society for Molecular Imaging, Hawaii, 2006.

Funding resulting from this support

R21 CA128957 (Bhujwala, Z. M. PI) (3.2 percentile)

07/01/2007-06/30/2009

Image-Guided Prodrug/Enzyme Therapy