# Rajagopal Ramesh, Ph.D.

Professor Department of Pathology Jim and Christy Everest Endowed Chair in Cancer Developmental Therapeutics Oklahoma TSET Cancer Research Scholar Stanton L. Young Biomedical Research Center College of Medicine The University of Oklahoma Health Sciences Center

# **Contact Information:**

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## **Education:**

1985: B.S., Biology, Osmania University, India 1987: M.S., Microbiology, Osmania University, India 1994: Ph.D., Molecular Biology, All India Institute of Medical Sciences, India 1996: Pathology, Postdoctoral Fellow Tulane University School of Medicine, LA 1992: Diploma in Business Admin (DBA) Annamalai University, India 1998-2001: Research Associate, Department of Thoracic and Cardiovascular Surgery, The University of Texas M. D. Anderson Cancer Center, TX 1997-1998: Research Instructor, Department of Surgery, Louisiana State University Medical 1996-1997: Research Associate, Mentor: Dr. Scott M. Freeman, M.D., Department of Pathology, SL79, Tulane University School of Medicine, LA 1993-1996 Postdoctoral Fellow, Mentor: Scott M. Freeman, M.D., Department of Pathology, SL79, Tulane University School of Medicine, LA 1991-1993: Senior Research Fellow, Advisor: S.K. Panda, M.D., Department of Pathology, All India Institute of Medical Sciences, India 1988-1991 Junior Research Fellow, Advisor: S.K. Panda, M.D., Department of Pathology, All India Institute of Medical Sciences, India

## Academic Appointments:

1996-1997: Research Associate, Department of Pathology, Tulane University School of Medicine, LA 1997-1998: Instructor, Department of Surgery, Louisiana State University Medical Center, LA

1997-1998: Instructor, Department of Surgery, Louisiana State University Medical Center, LA

1998-2001: Research Associate, Department of Thoracic and Cardiovascular Surgery, The University of Texas M. D. Anderson Cancer Center, TX

2001-2005: Assistant Professor, Department of Thoracic and Cardiovascular Surgery, The University of Texas M. D. Anderson Cancer Center, TX

2005-2010: Associate Professor, Department of Thoracic and Cardiovascular Surgery, The University of Texas M. D. Anderson Cancer Center, TX

2010-present: Professor (Tenured), Department of Pathology, The University of Oklahoma Health Sciences Center, OK

2017-present: Research Health Science Specialist, Veterans Affairs (VA) Health Care System, OK

2010-present: Adjunct Professor, Department of Pharmaceutical Science, College of Pharmacy, The University of Oklahoma Health

2018-present: Co-Program Leader, Cancer Biology Program, Stephenson Cancer Center, OK
2015-present: Co-Director, Nanomedicine Program, Stephenson Cancer Center, OK
2016-present: Co-Program Leader, Preclinical Translational Cancer Research, Stephenson Cancer Center, OK
2010-2015: Program Leader, Experimental Therapeutics Program, Stephenson Cancer Center, OK
2010-present: Director, Small Animal Bioluminescence Imaging Core Facility, Stephenson Cancer Center, OK

#### Awards and Honors:

1991: Best Paper in Basic Sciences Research, Annual Conference of the Indian Association for Study of Liver 1992: Searle Award, Best Oral Paper, Annual Conference of Indian Society of Gastroenterology

1993: Young Investigator Award in Medical Sciences, Indian National Science Academy (INSA) New Delhi 2005: Ben and Jay Lori Fellowship for Translational Research in Lung Cancer- Awarded to Dr. Began Gopalan, Post-Doctoral Fellow

2009: Manish Shankar, Merck-AACR-in Training Scholars Award- Awarded to Dr. Manish Shanker, Post- Doctoral Fellow

#### **Other Professional Experiences and Memberships:**

1994-present: Member, American Association for Cancer Research (AACR)
1995-present: Member, American Society of Cell and Gene Therapy (ASCGT)
2007-present: Member, American Society of Clinical Oncology (ASCO)
2006-present: NCI Career Development study section member
2008: Co-Chair, Suicide gene therapy and apoptosis section, American Society of Cell and Gene Therapy (ASCGT)
2009: NIH/NCI GDD Study section member (ad hoc)
2010-present: Member, American Association of Pharmaceutical Sciences (AAPS)
2010-present: Member, Graduate Program in Biological Sciences, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma

## **Research Support:**

Current:

- 01/01/19-12/31/23: NIH/NCI Grant # 1R01CA233201-01, "An improved IL-24 gene-based therapeutic for cancer", Role: Principal Investigator, Awarded: \$224,529
- 05/01/18-04/30/23: NIH/NCI Grant # P30 CA225520-01, Cancer Center Support Grant (CCSG), Role: Program Co-Leade
- 04/01/17-03/31/21: VA Merit Grant # 101BX003420A1, "Molecular impact of platinum drugs on the proteasome and SQSTM1/P62 complexes: A paradigm shift in resistance", Role: Principal Investigator, Awarded: \$262,325
- 09/05/18-08/31/23: NIH/NIGMS Grant # 2P20GM103639-01, COBRE: Mentoring Translational Cancer Research in Oklahoma, Role: Mentor for Dr. Katherine Morris (Project # 2), Awarded: 150,000
- 09/05/18-08/31/23: NIH/NIGMS Grant # 2P20GM103639-01, COBRE: Mentoring Translational Cancer Research in Oklahoma, Role: Director of Small Animal Bioluminescence Imaging Core Facility (Core # 3), Awarded: \$70,000
- 07/08/2019-10/31/21: NIH/NIGMS Grant# 2P20 GM10347-19, INBRE: Oklahoma IDEA Network for Biomedical Excellence, Role: Mentor for Horrick Sharma (Project title: Development of Small Molecules Targeting Cancer Metabolism)
- 09/15/19-09/14/20: DOD-Lung Cancer Research Program Concept Grant # XXX, Role: PI, Awarded: \$100,000
- 07/01/18-06/30/20: Presbyterian Health Foundation (PHF) Symposium Grant, "END2CANCER: Emerging Nanotechnology and Drug Delivery Applications for Cancer", Role: Principal Investigator, Awarded: \$25,000
- 07/01/18-06/30/20: Stephenson Cancer Center Symposium Matching Grant, "END2CANCER: Emerging Nanotechnology and Drug Delivery Applications for Cancer", Role: Principal Investigator, Awarded: \$25,000
- 09/01/18-08/31/21: Oklahoma Center for Advanced Science and Technology (OCAST) Grant # HR18-088, "Noninvasive liquid approach as a surrogate for determining immunotherapy response in lung cancer patients", Role: Principal Investigator, Awarded: \$45,000

- 07/01/19-06/30/20: Presbyterian Health Foundation (PHF) Equipment Grant # C5121201, 'KrosFlo 2i TFF system for producing high-yield exosome and microvesicle', Role: PI, Awarded: \$42,000
- 07/01/19-06/30/20: Presbyterian Health Foundation (PHF) Symposium Grant Grant # C5122701, "END2CANCER: Emerging Nanotechnology and Drug Delivery Applications for Cancer", Role: Principal Investigator, Awarded: \$50,000
- 07/01/19-06/30/20: Stephenson Cancer Center Symposium Matching Grant, "END2CANCER: Emerging Nanotechnology and Drug Delivery Applications for Cancer", Role: Principal Investigator, Awarded: \$25,000
- 05/01/19-04/30/20: Stephenson Cancer Center (SCC), Trainee Research Award, Role: Mentor, Awarded: \$7,500 Past:
- 2008-2012: NCI/NIH, "Systemic non-viral gene therapy for cancer", Role: Principal Investigator
- 2009-2011: NCI/NIH, "Preclinical Development and Testing of Multifunctional Tumor-Targeted Nanoparticles for Lung Cancer", Role: Principal Investigator
- 2009-2011: Joan's Legacy Foundation," Targeted IMAT multifunctional nanoparticles for bronchioalveolar lung cancer", Role: Principal Investigator
- 07/01/16-09/30/18: Presbyterian Health Foundation (PHF) Bridge Grant, "BRG1 targeted therapy for non-small cell lung carcinoma", Role: Collaborator, Awarded: \$35,000
- 07/01/16-06/30/18: Presbyterian Health Foundation (PHF) Bridge Grant, "Nanodelivery of biomolecules targeting the Proteasome/SQSTM1 Complexes in Cancer", Role: Principal Investigator, Awarded: \$75,000
- 10/01/18-09/30/19: Presbyterian Health Foundation (PHF) Bridge Grant, "Fexosomes as a theranostic for lung cancer", Role: Principal Investigator, Awarded: \$75,000
- 09/15/18-09/14/19: DOD-Lung Cancer Research Program Concept Grant # W81XWH-18-1-0637, "Development of exosome-based theranostic for lung cancer", Role: Mentor, Awarded: \$100,000
- 09/01/18-08/31/19: National Science Foundation (NSF) Grant # 1828234, "MRI Acquisition of an inductively coupled mass spectrometer to study interactions of engineered materials with biological systems", Role: Collaborator, Awarded: \$500,000
- 07/01/18-06/30/19: Presbyterian Health Foundation (PHF) Seed Grant, "Mitigating therapy resistance by targeting ARID1A in breast cancer", Role: Collaborator, Awarded: \$50,000
- 07/01/18-06/30/19: IBEST-OUHSC Funding for Interdisciplinary Research, "3D In vitro models to study the role of exosomes in tumor progression", Role: Collaborator, Awarded: 10,000

# **Selected Publications:**

- 1. Srivastava, A., Amreddy, N., Razaq, M., Towner, R., Zhao, Y.D., Ahmed, R.A., Munshi, A., **Ramesh, R.**<sup>\*#</sup> Exosomes as theranostics for lung cancer. Adv. Cancer Res. 139: 1-33, 2018. PMCID: PMC6548197; PMID: 29941101.
- Srivastava, A., Moxley, K., Ruskin, R., Dhanasekaran, D.N., Zhao, Y.D., Ramesh, R.<sup>\*#</sup> Non-invasive liquid biopsy screening of urine-derived exosomes for miRNAs as biomarkers in endometrial cancer patients. AAPS J. 20:82, 2018. doi: 10.1208/s12248- 018-0220-y. PMID: 29987691.
- Amreddy, N., Babu, A., Muralidharan, R., Panneerselvam, J., Srivastava, A., Ahmed, R., Mehta, M., Munshi, A., Ramesh, R.<sup>\*#</sup> Recent advances in nanoparticle-based cancer drug and gene delivery. Adv. Cancer Res. 137: 115-170, 2018. PMCID: PMC6550462; PMID: 29405974.
- Amreddy, N., Babu, A., Panneerselvam, J., Srivastava, A., Muralidharan, R., Chen, A., Zhao, Y.D., Munshi, A., **Ramesh, R**.<sup>\*#</sup> Chemo-biologic combinatorial drug delivery using folate receptor-targeted dendrimer nanoparticles for lung cancer treatment. Nanomedicine. 14:373-384, 2017. PMID: 29155362.
- Andrade, D., Mehta, M., Griffith, J., Panneerselvam, J., Srivastava, A., Kim, T-D., Janknecht, R., Herman, T., Ramesh, R., Munshi, A. YAP1 inhibition radiosensitizes triple-negative breast cancer cells by targeting the DNA damage response and cell survival pathways. Oncotarget 8:98495-98508, 2017. PMCID:PMC5716745; PMID: 29228705.
- Babu, A., Amreddy, N., Muralidharan, R., Pathuri, G., Gali, H., Chen, A., Zhao, Y.D., Munshi, A., Ramesh, R.<sup>\*#</sup> Chemodrug delivery using integrin-targeted PLGA- Chitosan hybrid nanoparticle for lung cancer therapy. Sci. Rep. 7, 14674; doi:10.1038/s41598- 017-15012-5, 2017. PMID: 29116098.
- Muralidharan, R., Mehta, M., Ahmed, R., Roy, S., Xu, L., Aube, J., Chen, A., Zhao, Y.D., Herman, T., Ramesh, R,<sup>\*#</sup> Munshi, A.<sup>\*#</sup> HuR-targeted small molecule inhibitor exhibits cytotoxicity towards human lung cancer cells. Sci. Rep. 7, 9694; doi: 10.1038/s41598-017-07787-4, 2017. PMID: 28855578.
- Muralidharan, R., Babu, A., Amreddy, N., Srivastava, A., Kompella, U.B., Chen, A., Zhao, Y.D., Munshi, A., Ramesh, R.\*# Tumor-targeted nanoparticle delivery of HuR siRNA inhibits lung tumor growth *in vitro* and *in vivo* by disrupting the oncogenic activity of the RNA-binding protein HuR. Mol Cancer Ther. 8:1470-1486, 2017. PMCID: PMC5544587; PMID: 28572169.

- 9. Babu, A., Munshi, A., **Ramesh, R**.<sup>\*#</sup> Combinatorial therapeutics approaches with RNAi and anticancer drugs using nanodrug delivery systems. Drug Dev Ind Pharm. 43: 1391- 1401, 2017.PMID: 28523942.
- 10. Babu, A., **Ramesh, R**.<sup>\*#</sup> Multifaceted applications of chitosan in cancer drug delivery and therapy. Marine Drugs, 2017 Mar; 15(4) pii: E96. doi: 10.3390/md15040096. PMID: 28346381.
- 11. Amreddy, N., Babu, A., Muralidharan, R., Munshi, A., **Ramesh, R**.<sup>\*#</sup> Polymeric nanoparticle-mediated gene delivery for lung cancer treatment. Topics Curr Chem. 2017 Apr; 375(2):35. doi: 10.1007/s41061-017-0128-5. PMID: 28290155.
- Griffith, J., Andrade, D., Mehta, M., Berry, W., Benbrook, D.M., Aravindan, N., Herman, T.S., Ramesh, R., Munshi, A. Silencing BMI1 radiosensitizes human breast cancer cells by inducing DNA damage and autophagy. Oncol Rep. 37:2382-2390, 2017 PMID:28260023.
- 13. Babu, A., Muralidharan, R., Amreddy, N., Munshi, A., **Ramesh, R**.\*# Tumor-targeted HuRsiRNA nanotherapy for lung cancer. IEEE Tran Nanobioscience. 15: 849-863, 2016. PMID: 28092499.
- Srivastava, A., Amreddy, N., Babu, A., Panneerselvam, J., Mehta, M., Muralidharan, R., Chen, A., Zhao, Y.D., Razaq, M., Riedinger, N., Kim, H., Liu, S., Wu, S., Abdel- Mageed, A.B., Munshi, A., **Ramesh, R**.<sup>\*#</sup> Nanosomes carrying doxorubicin exhibit potent anticancer activity against human lung cancer cells. Sci. Rep. 6, 38541; doi: 10.1038/srep38541, 2016. PMCID: PMC5150529; PMID:27941871.
- Mehta, M., Basalingappa, K., Griffith, J., Andrade. D., Babu, A., Amreddy, N., Muralidharan, R., Gorospe, M., Herman, T., Ding, W-Q., **Ramesh, R**., Munshi, A. HuR silencing elicits oxidative stress and DNA damage and sensitizes human triple negative breast cancer cells to radiotherapy. Oncotarget. 7: 64820-64835, 2016. PMID: 27588488.
- Panneerselvam, J., Srivastava, A., Muralidharan, R., Wang, Q., Zheng, W., Zhao, L., Chen, A., Zhao, Y.D., Munshi, A., **Ramesh, R.**<sup>#</sup> IL-24 modulates the high mobility group (HMG) A1/miR222/AKT signaling in lung cancer cells. Oncotarget 7:70247- 70263, 2016.PMID: 27602961.
- Muralidharan, R., Babu, A., Amreddy, N., Basalingappa, K., Mehta, M., Chen, A., Zhao, Y.D., Kompella, U.B., Munshi, A., **Ramesh, R**.\*# Folate receptor-targeted nanoparticle delivery of HuR-RNAi suppresses lung cancer cell proliferation and cell migration. J Nanobiotechnology 14: 47, 2016. DOI: 10:1186/s12951-016-0201-1. PMID: 27328938.
- Klionsky, D.J., Abdelmoshen, K., Abe, A., Abdedin M.G., Hagai, A., Arozena, A.A., Adachi, H., Adams, C.M., Adams, P.D. et al. Guidelines for the use and interpretation of assays for monitoring autophagy. Autophagy 12:1-222, 2016. PMID:26799652
- Muralidharan, R., Pannerselvam, J., Chen, A., Zhao, Y.D., Munshi, A., Ramesh, R.\*# HuR-targeted nanotherapy in combination with AMD3100 suppresses CXCR4 expression, cell growth, migration and invasion in lung cancer. Cancer Gene Ther. 22: 581-590, 2015. PMCID: PMC4679684; PMID:26494555.
- Amreddy, N., Muralidharan, R., Babu, A., Mehta, M., Johnson, E.V., Zhao, Y.D., Munshi, A., Ramesh, R.<sup>\*#</sup> Tumortargeted and pH controlled delivery of doxorubicin using gold nanorods for lung cancer therapy. Intl J Nanomed. 10:6773-6788, 2015. PMID: 26604751.
- Ha, J-H., Gomathinayagam, R., Yan, M., Jayaraman, M., Ramesh, R., Dhanasekaran, D.N. Determinant role for the gep oncogenes, Ga12/13, in ovarian cancer cell proliferation and xenograft tumor growth. Genes and Cancer 6: 356-364, 2015. PMCID:PMC4575922; PMID: 26413218.
- Srivastava, A., Babu, A., Filant, J., Moxley, K.M., Ruskin, R., Dhanasekaran, D., Sood, A., McMeekin, S., Ramesh, R.\*# Exploitation of exosomes as nanocarriers for gene-, drug-, and immune-therapy of cancer. J Biomed Nanotechnol. 12: 1174-1182, 2016.
- Al Mubarak, Z.H., Ramesh, R., Liu, L., Krishnan, S. Surface plasmon resonance imaging of low levels of small organic compounds by direct adsorption onto gold microarray spots. J Colloid Interface Sci.460: 209-213, 2015. PMCID: PMC4592839; PMID: 26321574.
- Panneerselvam, J., Shanker, M., Jin, J., Branch, C.D., Muralidharan, R., Zhao, D.Y., Chada, S., Munshi, A., Ramesh, R.\*# Phosphorylation of interleukin (IL)-24 is required for its anticancer activity. Oncotarget 18: 16271-16286; 2015. PMID: 26009991.
- Panneerselvam, J., Jin, J., Shanker, M., Lauderdale, J., Bates, J., Wang, Q., Zhao, D.Y., Archibald, S.J., Hubin, T.J., **Ramesh, R**.<sup>\*#</sup> IL-24 inhibits lung cancer cell migration and invasion by disruption the SDF/CXCR-4 signaling axis. PLoS One 10:e0122439; 2015. PMCID:PMC4361489; PMID:25775124.
- 26. Babu, A., Amreddy, N., **Ramesh, R**.<sup>\*#</sup> Nanoparticle based cisplatin therapy for cancer. How far has it advanced in cancer therapy? Ther Deliv. 6: 115-119; 2015. PMID: 25690081.
- Srivastava, A., Filant, J., Moxley, K.M., Sood, A., McMeekin, S., Ramesh, R.<sup>\*#</sup> Exosomes: A role for naturally occurring nanovesicles in cancer growth, diagnosis and treatment. Curr Gene Ther. 15: 182-192; 2015. PMID:25537774.
- Kuroda, S., Tam, J., Roth, J.A., Sokolov, K., Ramesh, R.<sup>\*#</sup> EGFR-targeted plasmonic magnetic nanoparticles induce DNA damage and inhibit G2/M checkpoint in non-small cell lung cancer cells. Int J Nanomedicine 9: 3825-3839, 2014; PMCID:PMC4134185; PMID:25143731.

- 29. Babu, A., Wang, Q., Muralidharan, R., Shanker, M., Munshi, A., **Ramesh, R**.<sup>\*#</sup> Chitosan coated poly(lactic acid) polymeric nanoparticle-mediated combinatorial delivery of cisplatin and siRNA/plasmid DNA chemosensitizes cisplatin-resistant human ovarian cancer cells. Mol Pharm. 11: 2720-2733, 2014; PMID: 24922589.
- Babu, A., Templeton, A. K., Munshi, A., Ramesh, R.<sup>\*#</sup> Nanodrug delivery systems: A promising technology for detection, diagnosis, and treatment of cancer. AAPS PharmSciTech 15: 709-721, 2014. PMCID: PMC4037475; PMID: 24550101.
- 31. Templeton, A.K., Miyamoto, S., Babu, A., Munshi, A., **Ramesh, R**.<sup>\*#</sup> Lung cancer stem cells: growing evidence and unresolved Issues. Stem Cell Invest. 2014, 1:9. doi: 10.3978/j.issn.2306-9759.2014.03.06. PMID: 27358855
- 32. Panneerselvam, J., Munshi, A., **Ramesh, R**.<sup>\*#</sup> Molecular signaling events modulated by interleukin (IL)-24 in exerting its anticancer activity in cancer cells. J Mol Signal. 8:15. DOI: 10.1186/1750-2187-8-15, 2013. PMID: 24377906.
- 33. Munshi, A., **Ramesh, R**. Mitogen-activated protein kinases and their role in radiation response. Genes Cancer. 4: 401-408, 2013. PMID: 24349638.
- 34. Babu, A., Templeton, A.K., Munshi, A., **Ramesh, R**.<sup>\*#</sup> Nanoparticle-based Drug Delivery for Therapy of Lung Cancer: Progress and Challenges. J Nanomat. 2013: 863951; 2013. dx.doi.org/10.1155/2013/863951
- 35. Neves, L.F.F., Krais, J.J., Van Rite, B.D., **Ramesh, R**., Resasco, D.E., Harrison, R.G. Targeting single-walled carbon nanotubes for the treatment of breast cancer using photothermal therapy. Nanotechnology. 24:375104; 2013. PMID: 23975064.
- Lu, C., Stewart, D., Lee, J.J., Ji, L., Ramesh, R., Jayachandran, G., Nunez, M., Wistuba, I.I., Erasmus, J.J., Hicks, M.E., Grimm, E.A., Reuben, J., Baladandayuthapani, V., Templeton, N.S., McMannis, J.D., Roth, J.A. Phase I clinical trial of systemically administered TUSC2 (FUS1)- nanoparticles mediating functional gene transfer in humans. PLoS ONE. 7: e34833; 2012. PMID:22558101.
- 37. Yokoyama, T., Tam, J., Kuroda, S., Scott, A.W., Aaron, J., Larson, T., Correa, A.M., Shanker, M., Kondo, S., Roth, J.A., Sokolov, K., Ramesh, R.\*\* EGFR-targeted hybrid plasmonic magnetic nanoparticles synergistically induce autophagy and apoptosis in non-small cell lung cancer cells. PLoS ONE. 6: e25507; 2011. PMID:22087216
- Ma LL, Tam JO, Willsey BW, Rigdon D, Ramesh R, Sokolov K, Johnston KP. Selective Targeting of Antibody Conjugated Multifunctional Nanoclusters (Nanoroses) to Epidermal Growth Factor Receptors in Cancer Cells. Langmuir. 27:7681-7690, 2011. PMID: 21591638.
- Mandal, P., Gao, F., Lu, Z., Ramesh, R., Sanderson Birtwistle, J., Ren, Z., Chen, X., Kaluarachichi, K.K., Ekmekcioglu, S., Bast, R.C., Liao, W.S., McMurray, J.S. Potent and selective phosphopeptide mimetic prodrugs targeted to the Src homology 2 (SH2) domain of signal transducer and activator of transcription 3. J Med Chem. 54:3549-3563 2011. PMID: 21486047
- 40. Yokoyama, T., Miyamoto, S., **Ramesh, R**.<sup>\*#</sup> Interleukin (IL)-24: A regulator of autophagy and apoptosis-mediated programmed cell death. Trends in Cell and Mol Biol. 5; 61-67, 2010. PMID:
- 41. Shanker, M., Jin, J., Branch, C.D., Miyamoto, S., Grimm, E.A., Roth, J.A., Ramesh, R.\*\* Tumor suppressor genebased nanotherapy: from test tube to the clinic. J Drug Deliv. 1-10; 2011 doi:10.1155/2011/465845. PMID: 21490751
- 42. Li, Y., Efferson, C.L., **Ramesh, R**., Peoples, G.E., Hwu, P., Ioannides, C. G. A peptidogylcan, (PGN) monomer with a glutamine to serine change and charged peptides bind to close positions on TLR-2. Implications for design of novel synthetic vaccines. Cancer Immunol Immunother; 60:515-524, 2011; PMID: 21188584
- 43. Shanker, M., Willcuts, D., Roth, J.A., **Ramesh, R.**<sup>\*#</sup> Drug resistance in lung cancer. Lung Cancer: Targets and Therapy. 1: 1-14, 2010.