BIOGRAPHICAL SKETCH

Senior Trainer

NAME: Patankar Manish Suresh

eRA COMMONS USER NAME: patankar

POSITION TITLE: Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Bombay	B.Sc.	1987	Chemistry
University of Bombay	M.Sc.	1990	Organic Chemistry
Old Dominion University, Norfolk, VA	M.S.	1993	Chemistry
Old Dominion University and Eastern Virginia Medical School (Joint Program), Norfolk, VA	Ph.D.	1998	Biomedical Sciences

A. Personal Statement

The primary focus of my research is studying the crosstalk between the immune system and normal and pathologic tissue with special emphasis on preeclampsia and ovarian cancer. The goal of this exploration is to develop understand of the underlying pathology and develop novel therapies and biomarkers for treatment and detection by using modern RNA sequencing technology. My lab is actively recruiting patients and healthy control subjects to isolate and preserve immune cells that will be used for the transcriptome analysis. In addition, these immune cells are also being used by my lab to conduct functional immunologic assays. My laboratory has developed expertise in molecular and cell biological assays. I serve as the Faculty Director of the Flow Cytometry core lab of the University of Wisconsin-Madison Comprehensive Cancer Center. This core facility is extensively used by researchers on campus. My leadership of the Flow Cytometry lab has allowed me to develop understanding of the flow cytometry methods and data analysis that will be important for completion of the experiments proposed in this R01 application. I serve in several leadership positions in the UW-Madison graduate school and in the Department of Obstetrics and Gynecology. I am the Director of a Tissue Bank in the Department of Obstetrics and Gynecology through which we are collecting obstetric and gynecologic samples from patients treated by our physicians. I train graduate students and clinicians and have established several strong collaborations with researchers on the UW-Madison campus and other institutions. I also serve on various study sections of the NIH and the Department of Defense Ovarian Cancer Research program on an ad hoc basis. In 2016 I was appointed as the Associate Director of the Endocrinology and Reproductive Physiology graduate program at the University of Wisconsin-Madison. Through this role I am involved in recruiting, advising and mentoring MS and PhD-level students enrolled in this program. My research is multidisciplinary and involves collaborations with numerous labs on the UW-Madison campus as well as at other institutions. Through this extensive research and administrative responsibilities I continue to strive to be a productive researcher, mentor and faculty member at the University of Wisconsin-Madison.

B. Positions.

1990	Research Assistant, Hoechst Research Center, India
1990-1993	Graduate Teaching Assistant, Old Dominion University, Norfolk, VA
1993-1998	Graduate Research Assistant, Eastern Virginia Medical School, Norfolk, VA
1998-1999	Post-Doctoral Fellow, Eastern Virginia Medical School, Norfolk, VA
1999- 2002	Instructor, Eastern Virginia Medical School, Norfolk, VA
2002-2004	Research Assistant Professor, Eastern Virginia Medical School, Norfolk, VA

2004-2010	Assistant Professor, University of Wisconsin-Madison and member of the University of Wisconsin-Madison Comprehensive Cancer Center
2010-2015	Associate Professor, University of Wisconsin-Madison and member of the University of Wisconsin-Madison Comprehensive Cancer Center
2016-Present	Professor, University of Wisconsin-Madison and member of the University of Wisconsin-Madison Comprehensive Cancer Center
2011-Present	Faculty Director, Flow Cytometry Core, University of Wisconsin-Madison Comprehensive Cancer Center
2016	Associate Director, Endocrinology and Reproductive Physiology graduate program at the University of Wisconsin-Madison

Other Experience and Professional Memberships

2001- Member NIH Minority Biomedical Research Support (MBRS) program study section
2007- Member of AACR
2008- Member of Consortium for Functional Glycomics, an NIH Funded consortium for studying and identifying carbohydrate binding proteins in the immune system
2009- Reviewer for National Institutes of Health RC1 challenge grants
2009- Member of National Institutes of Health study section (Special Emphasis Panel/Scientific Review Group 2009/10 ZRG1 IMM-G (10) B) to review Immunology-focused STTR and SBIR grants.
2009- Reviewer for grants submitted to the Wellcome Trust, UK
2009- Reviewer for Journal of Immunology, Disease Markers, Journal of Ovarian Research, and Biomaterials
2010- Member of National Institutes of Health study section (Special Emphasis Panel/Scientific Review Group) to review Immunology-focused STTR and SBIR grants.
2011- Member of the Department of Defense Cell Biology study section for the Ovarian Cancer Research Program
2012- Member of the Department of Defense Cell and Molecular Biology study section for the Ovarian Cancer Research Program
2013- Member of the Developmental Therapeutics study section of the National Institutes of Health
2013- Member of National Institutes of Health study section (Special Emphasis Panel/Scientific Review Group) to review Immunology-focused STTR and SBIR grants.
2014- Member of the Department of Defense Cell and Molecular Biology study section for the Ovarian Cancer Research Program
2015- Member of training grants and P01 study section of the National Institutes of Health
2016- Member of P01 and SPORE grants study section of the National Institutes of Health

C. Contribution to Science

***1. Developing biomarkers for early detection of Preeclampsia and ovarian cancer*.** Currently, there are no biomarkers available for early detection of ovarian cancer. The only biomarker for this disease is CA125, a repeating peptide epitope present in a large (3-5 million Da) mucin, MUC16. The exact structure of the CA125 epitope that is recognized in a clinically used serum assay for this antigen is not well defined. I therefore undertook a project to define the complex structure of MUC16 with hopes to not only identify the CA125 epitope but also detect other facets of this mucinous molecule that can be exploited to develop a novel bioassay that can be used for early detection of ovarian cancer. With this intent I collaborated with Drs. Anne Dell and Howard Morris, the world's experts on mass spectrometry of oligosaccharides to characterize the N- and O-

linked glycans attached to MUC16. This data is now being used in an collaboration with Dr. Ola Blixt (University of Copenhagen) to develop a lectin-based assay for detection of ovarian cancer. My studies also allowed us to determine that the α2,3-sialic acid residues present in MUC16 are recognized by the immune cell receptor Siglec-9 and this interaction leads to binding of the mucin to specific immune cells. Since MUC16 is also expressed during pregnancy, we also explored if binding of this mucin to immune cells in preeclamptic patients also follows a different pattern than that observed in normal pregnancy. This hypothesis was proven to be correct by our work published. These results led us to further hypothesize that monitoring the proteome and transcriptome of circulating immune cells can lead to a novel method for identification of ovarian cancer and preeclampsia biomarkers. We have recently conducted RNASeq analysis of immune cells from preeclamptic women and women with healthy pregnancies as well as ovarian cancer patients and healthy women and have found major differences in their transcriptomes. This data is being mined using bioinformatics tools in collaboration with Dr. Jesus Gonzalez-Bosquet and further analysis of additional samples from human subject and mouse models for preeclampsia ovarian cancer is currently underway to prove our hypothesis that circulating immune cells can serve as an important source for biomarker discovery. Although our studies are focused on preeclampsia and ovarian cancer, if proven, this concept can also be applied to other cancers and pathological conditions. Provided below is a list of published manuscripts that describe my work with MUC16 and proteomics of Natural Killer cells are pasted below along with details of patents awarded on related topics.

a. Felder M, Kapur A, Gonzalez-Bosquet J, Horibata S, Heintz J, Albrecht R, Fass L, Kaur J, Hu K, Shojaei H, Whelan RJ, Patankar MS. MUC16 (CA125): tumor biomarker to cancer therapy, a work in progress. Molecular cancer. 2014;13:129. doi: 10.1186/1476-4598-13-129. PubMed PMID: 24886523; PubMed Central PMCID: PMC4046138. Highly Accessed.
b. Ma D, Cao W, Kapur A, Felder M, Scarlett CO, Patankar MS, Li L. Differential expression of proteins in naive and IL-2 stimulated primary human NK cells identified by global proteomic analysis. Journal of proteomics. 2013;91:151-63. doi: 10.1016/j.jprot.2013.06.024. PubMed PMID: 23806757.
c. Belisle JA, Horibata S, Jennifer GA, Petrie S, Kapur A, Andre S, Gabius HJ, Rancourt C, Connor J, Paulson JC, Patankar MS. Identification of Siglec-9 as the receptor for MUC16 on human NK cells, B cells, and monocytes. Molecular cancer. 2010;9:118. doi: 10.1186/1476-4598-9-118. PubMed PMID: 20497550; PubMed Central PMCID: PMC2890604.
d. Kui Wong N, Easton RL, Panico M, Sutton-Smith M, Morrison JC, Lattanzio FA, Morris HR, Clark GF, Dell A, Patankar MS. Characterization of the oligosaccharides associated with the human ovarian tumor marker CA125. The Journal of biological chemistry. 2003;278(31):28619-34. doi: 10.1074/jbc.M302741200. PubMed PMID: 12734200.

***Patents*.**

Methods and kits to detect and monitor ovarian cancer and preeclampsia US 8492104 B2

***2. Developing natural product-based therapies for cancer*.** Over the past three years, I have undertaken a major research initiative to identify natural products found in botanicals and dairy products that inhibit proliferation of ovarian and other tumors. These efforts have led to identification of cis10:trans12 conjugated linoleic acid as a potent inhibitor of tumor cell proliferation through the induction of endoplasmic reticulum stress and autophagy (Shahzad et al, manuscript submitted). In addition to this project, my lab has now also identified that specific monoterpenes present in the rhizomes of the commonly used spice, ginger, are very effective in reducing tumor progression. This project is most relevant to the proposal being submitted. Research conducted by my lab shows that the monoterpenes that contain an α,β-unsaturated carbonyl compound are potent mediators of cancer cell death. These compounds induce an oxidative response which causes DNA damage and subsequent activation of apoptotic and autophagic signaling cascades in the cancer cells. In collaboration with Dr. May Xiong's group (College of Pharmacy, we have now developed a nanoparticle-based delivery system that

allows us to deliver these monoterpene agents to tumors and reduce the progression of breast tumors in mice. Our initial results on this project are published in the two papers listed below. A third paper explaining the mechanism of action of the monoterpenes is under review.

a. Zeng S., Kapur A., Patankar M.S., Xiong M. Formulation, Characterization, and Antitumor Properties of Trans- and Cis-Citral in the 4T1 Breast Cancer Xenograft Mouse Model, 2015 (In press).
b. Liu Y, Whelan RJ, Pattnaik BR, Ludwig K, Subudhi E, Rowland H, Claussen N, Zucker N, Uppal S, Kushner DM, Felder M, Patankar MS, Kapur A. Terpenoids from Zingiber officinale (Ginger) induce apoptosis in endometrial cancer cells through the activation of p53. PloS one. 2012;7(12):e53178. doi: 10.1371/journal.pone.0053178. PubMed PMID: 23300887; PubMed Central PMCID: PMC3534047.

***3. Understanding the importance of MUC16 in ovarian tumor progression*.** Ovarian tumors overexpress MUC16. A major focus of my research effort is to understand biology of MUC16 and its importance in ovarian cancer progression. To this end we have demonstrated that MUC16 facilitates peritoneal metastasis of ovarian tumors by serving as a binding partner for mesothelin, a GPI-linked glycoprotein expressed on the peritoneal mesothelial cells. Additionally we have also shown that because of MUC16 expression, ovarian tumors exhibit a higher degree of growth as shown in the accompanying mouse survival plot. This increase in tumor growth is associated with the ability of MUC16 to inhibit the cytolytic function of natural killer cells. Representative manuscripts published on this topic are listed below.

a. Gubbels JA, Felder M, Horibata S, Belisle JA, Kapur A, Holden H, Petrie S, Migneault M, Rancourt C, Connor JP, Patankar MS. MUC16 provides immune protection by inhibiting synapse formation between NK and ovarian tumor cells. Molecular cancer. 2010;9:11. doi: 10.1186/1476-4598-9-11. PubMed PMID: 20089172; PubMed Central PMCID: PMC2818693.
c. Gubbels JA, Belisle J, Onda M, Rancourt C, Migneault M, Ho M, Bera TK, Connor J, Sathyanarayana BK, Lee B, Pastan I, Patankar MS. Mesothelin-MUC16 binding is a high affinity, N-glycan dependent interaction that facilitates peritoneal metastasis of ovarian tumors. Molecular cancer. 2006;5(1):50. doi: 10.1186/1476-4598-5-50. PubMed PMID: 17067392; PubMed Central PMCID: PMC1635730.
d. Patankar MS, Jing Y, Morrison JC, Belisle JA, Lattanzio FA, Deng Y, Wong NK, Morris HR, Dell A, Clark GF. Potent suppression of natural killer cell response mediated by the ovarian tumor marker CA125. Gynecologic oncology. 2005;99(3):704-13. doi: 10.1016/j.ygyno.2005.07.030. PubMed PMID: 16126266.

***4. Developing immunocytokines to treat ovarian cancer*.** Immunocytokines are antibody-cytokine chimeras that can bind to cancer cells and recruit innate and adaptive immune responses against the tumors. In collaboration with Dr. Paul Sondel (UW-Madison) and Dr. Steve Gillies (Provenance Pharmaceuticals) we are exploring the use of 215-IL2 an immunocytokine that binds to ovarian cancer cells and recruits immune response via its IL-2 chains. We are developing data in preclinical models to demonstrate efficacy of this immunocytokine. This data will be used to develop future clinical trials with the 215-IL2 immunocytokine. Our work has led to the novel observation that the immunocytokines recruit immune cells to the tumor by mediating an immunologic synapse that is formed by clustering of IL-2 Receptor on the immune cells at the junction between tumor target and Natural Killer cells. We are now exploiting this observation to develop methods by which the immune cells can be further attracted to the tumor by developing more efficient and selective ways of displaying IL-2 on the surface of the tumor cells. Representative publications on this topic are listed below.

a. Buhtoiarov IN, Neal ZC, Gan J, Buhtoiarova TN, Patankar MS, Gubbels JA, Hank JA, Yamane B, Rakhmilevich AL, Reisfeld RA, Gillies SD, Sondel PM. Differential internalization of hu14.18-IL2 immunocytokine by NK and tumor cell: impact on conjugation, cytotoxicity, and targeting. Journal of leukocyte biology. 2011;89(4):625-38. doi: 10.1189/jlb.0710422. PubMed PMID: 21248148; PubMed Central PMCID: PMC3058817.

b. Gubbels JA, Gadbaw B, Buhtoiarov IN, Horibata S, Kapur AK, Patel D, Hank JA, Gillies SD, Sondel PM, Patankar MS, Connor J. Ab-IL2 fusion proteins mediate NK cell immune synapse formation by polarizing CD25 to the target cell-effector cell interface. Cancer immunology, immunotherapy : CII. 2011;60(12):1789-800. doi: 10.1007/s00262-011-1072-9. PubMed PMID: 21792658.

***URL to access the complete list of my publications*:**
http://www.ncbi.nlm.nih.gov/sites/myncbi/manish.patankar.1/bibliography/47617168/public/?sort=date&direction=ascending.

D. Research Support

Current funded grants

1R01CA206561-01 National Institutes of Health
Quantitative assessment of the role of collagen alterations in ovarian cancer
Role: Multiple PI with Drs. Paul Campagnola and Kevin Elicieri
Goal: Develop understanding and imaging tools to study the changes in collagen occurring in the ovarian tumor microenvironment
Overlap: None

National Science Foundation 05/01/2014-04/30/2017
Second Harmonic Generation imaging and optical scattering probes of ovarian cancer
Role: co-PI (PI: Campagnola)
Goal: Using Second Harmonic Generation Imaging we demonstrated that collagen in the ovarian tumor microenvironment has a distinct structural appearance. In this project we are investigating if this imaging modality can be used as a screening modality for detection of ovarian tumors.
Overlap: None

Morphotek LLC 07/01/2015-06/30/2016
Demonstrating immunosuppressive role of MUC16
Role: PI
Goal: We have previously shown that the mucin MUC16 inhibits immune responses. In this project we will test if high level of MUC16 in patients impedes immunotherapy against ovarian cancer.
Overlap: None

Wisconsin Ovarian Cancer Alliance 07/01/2015-06/30/2016
Developing a novel assay for accurate quantitation of ovarian cancer biomarkers
Role: PI
Goal: A novel cell-based assay is under development to detect and quantify CA125, mesothelin, HE4 and other markers in blood of ovarian cancer patients. Our goal is to develop a assay that is more specific and selective than the existing tests used for clinical diagnosis of ovarian cancer.
Overlap: None

University of Wisconsin Paul P. Carbone Comprehensive Cancer Center
Combined activation of macrophages, NK cells and T cells in ovarian tumor microenvironment
Role: Co-I (PI: Rakhmilevich)
Goal: This project will explore a triple combination immunotherapeutic regimen for the treatment of ovarian cancer. This regimen will include agents that activate natural killer cells, T cells and macrophages.
Overlap: None

Colleen's Dream Foundation 9/1/2015-8/31/2016
Developing novel assay platform for cancer biomarker discovery
Role: PI

Goal: A novel cell-based assay is under development to detect and quantify CA125, mesothelin, HE4 and other markers in blood of ovarian cancer patients. Our goal is to develop a assay that is more specific and selective than the existing tests used for clinical diagnosis of ovarian cancer.
Overlap: None

University of Wisconsin Paul P. Carbone Comprehensive Cancer Center
Investigating transcript-level heterogeneity of the ovarian tumor mucin, MUC16
Role: PI
Goal: This project will explore the heterogeneity of the ovarian cancer biomarker MUC16 (CA125) in the tumor microenvironment and its impact on the sensitivity and specificity of the CA125 assay.
Overlap: None

Completed Research Support in past three years

Department of Defense Ovarian Cancer Research Program Pilot grant 7/01/2011-6/30/2012
Mining the Immune Cell Proteome to Identify Ovarian Cancer-Specific Biomarkers
Role: PI
Goal: The project led to development of proteomic analysis methods that can be used once biomarkers are identified through transcriptomic profiling.
Overlap: None

1R21CA143616-01 National Institutes of Health 08/04/2010-08/03/2012
Ovarian cancer diagnosis by monitoring immune cell bound MUC16 (CA125)
Role: PI
Goal: This project examined the diagnostic potential of MUC16 binding to immune cells for detection of ovarian cancer. The results from this study have led to development of current R21 proposal.
Overlap: None