UPENDRA K. KAR, Ph.D.

Curriculum Vitae

Present Position:

Research Scientist, Intestinal Stem Cell Consortium, David Geffen School of Medicine at UCLA

Education:

B.Sc. 1995 (Biology) Utkal University, Orissa.
M.Sc. 1998 (Biotechnology) Jawaharlal Nehru University, New Delhi.
Ph.D. 2004(Molecular Microbiology) All India Institute of Medical Sciences

Fellowships and Honors:

Postdoctoral Fellow, 2007-2010; University of California, Los Angeles, USA.
Postdoctoral Fellow, 2005-2007; Johns Hopkins Medical Institute, Baltimore, USA.
Senior Research Fellow (2003-04) -Indian Council of Medical Research (ICMR), Govt. of India.
Senior Research Fellow/ Junior Research Fellow (1999-03) -Dept. of Science and Technology, Govt. of India. Biotech Industrial Biotech Industrial Training Fellowship (six months, 1999) Dept of Biotechnology, Govt. of India.
National Scholarship (1996-98) -Department of Biotechnology, Govt. of India.
National Scholarship (1996-98) -Department of Biotechnology, Govt. of India.
National Scholarship (1990-95), Department of social welfare, Govt. of India.

Professional Organizations:

International Society for Stem Cell Research (ISSCR)
American Society for Mass Spectrometry (ASMS)
World Society Interdisciplinary Anti-Aging Medicine (WOSIAM)
National Postdoctoral Association
Society of Postdoctoral Scholars (SoPS)
Society of Young Scientists, India.

Professional responsibilities:

Reviewer of Ophthalmic Research, Journal of Virological methods, JAMA Ophthalmology, British journal of Ophthalmology and Pharmacology and Pharmacy.

Communicating Address:

945 Gayley Avenue, Apt No: 304, Los Angeles, CA
Ph: 410-522-8599
Email: upendrakkar@gmail.com
upendrakkar@ucla.edu

BIBLIOGRAPHY Research Papers (Abstracts not included):

- **Kar UK**, Brinkley G, , Lei N, Wang J, Lewis M, Meriwether D, Stelzner M, Dunn CJ, Martín MG. Soluble Factors Secreted by Human Intestinal Subepithelial Myofibroblasts Mediates Spheroid Growth of Human Intestinal Epithelial Stem Cells. (Manuscript is getting communicated to Cell Stem Cell).
- Khalil HA, Lei N, Brinkley G, Scott A, Wang J, **Kar UK**, Jabaji ZB, Lewis M, Martín MG, Dunn CJ, Stelzner G M. Adaptation of the Murine and Human Culture Systems to Adult Porcine Intestinal Crypts. (Under Review PLoS ONE).
- Sarafian TA, Ryan CM, Souda P, **Kar UK**, Faull KF, Whitelegge JP, Watson JB. Impairment of Mitochondria in Adult Mouse Brain Overexpressing Predominantly Full-Length, N-Terminally Acetylated Human a-Synuclein. PLoS One. 2013 May 7;8(5):e63557. doi: 10.1371.
- Yang H, Yung M, Li L, Hoch JA, Ryan CM, **Kar UK**, Souda P, Whitelegge JP, Miller JH. Evidence that YycJ is a novel 5'-3' double-stranded DNA exonuclease acting in Bacillus anthracis mismatch repair. DNA Repair (Amst). 2013 Mar 8. doi:pii: S1568-7864(13)00042-6.
- **Kar UK**, Jiang J, Champion CI, Salehi S, Srivastava M, Sharma S, Rabizadeh S, Niazi K, Kickhoefer V, Rome LH, Kelly KA. Vault Nanocapsules as Adjuvants Favor Cell-Mediated over Antibody-Mediated Immune Responses following Immunization of Mice. PLoS ONE 2012 7(7): e38553.
- Srivastava MK, Zhu L, Harris-White M, **Kar UK**, Huang M, Hong L, Fishbein M, Sharma J, Lee M, Elashoff D, Strieter R, Dubinett S, Sharma S. Myeloid Suppressor Cell Depletion Augments Antitumor Activity in Lung Cancer. PLoS ONE 2012 7(7): e40677.
- Kar UK. Srivastava MK, Andersson A, Baratelli F, Huang M, Kickhoefer VA, Dubinett SM, Rome LH, Sharma S. LH. Intratumoral Vault CCL21 Nanocapsule Generates Potent Antitumor Responses In Vivo. PLoS ONE 2011 6(5): e18758.
- Kumar A, Panda SK, Durgapal H, Acharya SK, Rehman S and **Kar UK** Inhibition of Hepatitis E Virus replication using short hairpin RNA (shRNA) Antiviral Res. 2010 Mar. 541–550.
- Andersson A, Yang SC, Huang M, Zhu L, **Kar UK**, Batra RK, Elashoff D, Strieter RM, Dubinett SM, Sharma S. IL-7 promotes CXCR3 ligand-dependent T cell antitumor reactivity in lung cancer. J Immunol. 2009 Jun 1;182(11):6951.
- Satpathy G, Bhan A, Sharma A, **Kar UK**. Detection of Chlamydophila pneumoniae (Chlamydia pneumoniae) in endarteroctomy specimens of coronary heart diseases patients. Indian J Med Res. 2008 Nov;128(5):658-62.
- **Kar UK**, Satpathy G, Das BK, Panda SK. Characterization of Streptococcus pneumoniae ophthalmic, systemic & commensal isolates by pulsed-field gel electrophoresis & ribotyping. Indian J Med Res. 2008 Feb;127(2):171-7.
- **Kar UK**, Satpathy G, Nayak N, Das BK, Panda SK. Serotype distribution of Streptococcus pneumoniae isolates from ophthalmic and systemic infections and of commensal origin. Indian J Med Res. 2006 Jul;124(1):99-104.
- **Kar UK**, Satapathy G, Panda SK, Das BK. Utility of random amplification of polymorphic DNA assay and BOX-A PCR in molecular characterization of Streptococcus pneumoniae isolates recovered from various ophthalmic infections. Ophthalmic Res. 2006;38(1):36-43. Epub 2005 Oct 13.

Review articles and reports

- **Kar UK**. Vaccination. Encyclopedia of Global Issues 2012, 963-967.
- Gaur AK and **Kar UK** Efficacy of Clarithromycin in the treatment of respiratory tract infections. Indian journal of Clinical Practice Sep. 2003; 14(4): 43-44.
- Aggarwal KK, jayakumar RV and **Kar UK**. Glimepride and metformin combination therapy in the management of Type 2 Diabetes Mellitus. The Asian journal of Diabetology Aug 2003; 5(8): 25-31
- Mahajan DM and **Kar UK**. Psoriasis: Advantage Tazarotene. Derma Grace Sep 2003; 3(1): 2.
- Mahajan DM and **Kar UK**. Skin and Soft Tissue Infections: Role of Clarithromycin. Derma Grace Sep 2003; 3(1): 4.

Conferences and Presentations

- Hassan Khalil, Wenxian Nie, Garrette Brinkley, **Upendra K Kar**, James Yoo. Martín G. Martín, James C. Y. Dunn. Pocrine Conditioned Medium Supports The Long-term Growth of Pocrine Colon and Intestinal stem cells. Digestive Disease Week, Chicago, Illionis, USA May 2014.
- Joseph R. Capri, **Upendra K. Kar**, Garrett Brinkley, Hassan A. Khalil, Matthias Stelzner, James C.Y. Dunn, Julian P. Whitelegge, Martín G. Martín. Identity of Secreted Autocrine Protein Factors of Intestinal Myofibroblasts Necessary for Stem Cell Homeostasis. 10th Annual Conference Frontiers in Proteomics: Advancing Biology through Technology and Computation. Seattle, April 2014 .
- Garrett Brinkley, **Upendra K. Kar**, Nan Ye Lei, Hassan A. Khalil, Ziyad Jabaji, Jiafang Wang, Michael Lewis, David Meriwether, Srinu Reddy, Matthias Stelzner, James C.Y. Dunn, Martín G. Martín. Soluble Factors Secreted by Human Intestinal Subepithelial Myofibroblasts Mediates Spheroid Growth of Human Intestinal Epithelial Stem Cells. Annual CURE research meeting, Los Angeles, Mar 2014.
- **Upendra K Kar**, Hassan Khalil, Wenxian Nie, Garrette Brinkley, Martín G. Martín, James C. Y. Dunn1 and James Yoo. Colonic Myofibroblasts Support the Expansion of Ex-Vivo Organoid Cultures of Primary Mouse and Human Colonic Stem Cells. Academic Surgical Congress, San Diego Feb 2014.
- Garrett Brinkley, **Upendra K. Kar**, Nan Ye Lei, Hassan A. Khalil, Ziyad Jabaji, Jiafang Wang, Michael Lewis, David Meriwether, Srinu Reddy, Matthias Stelzner, James C.Y. Dunn, Martín G. Martín. Soluble Factors Secreted by Human Intestinal Subepithelial Myofibroblasts Mediates Spheroid Growth of Human Intestinal Epithelial Stem Cells. 10th Annual Stem Cell Symposium "Cancer, Stem Cells & the Immune Response", Los Angeles, Jan 2014.
- **Upendra K. Kar**; Alexander Yoon; Chris Ryan; Kym F. Faull; Julian Whitelegge. Top-down Proteomics and High-resolution Mass Spectrometry of Mouse Mitochondrial Membrane Proteins. ASMS 2013.
- Joseph Capri; Puneet Souda; **Upendra K Kar**; Chris Ryan; William McBride; Andrew Norris; Julian Whitelegge. Global Quantitative Proteomics of Irradiated Nrf2 Knockout Mus for Biomarker Discovery. ASMS 2013.
- **Upendra K. Kar**; Christopher M. Ryan; Puneet Souda; Don Puppione; Faull Kym; Julian Whitelegge Immunocapture top-down proteomics and high-resolution mass spectrometry empower the human proteome project. ASMS 2012.
- Minu K Srivastava, Li Zhu, Min Huang, Asa Andersson, Marni Harris-White, **Upendra K. Kar**, Longsheng Hong, Michael Fishbein, Steven Dubinett and Sherven Sharma Tumor Snail Knockdown Reduces Tumor Burden and Metastases by Inducing Antitumor Immune Responses in Lung Cancer. AAC 2011.
- Cheryl I. Champion, **Upendra K. Kar**, Sahar Salehi, Guangchao Liu, Janina Jiang, Shahrooz Rabizadeh, Kayvan. Niazi, Nicole Forrester, David M. Ojcius, Hong Yu, Karuna Karunakaran, Robert C. Brunham, Valerie Kickhoefer, Leonard H. Rome, and Kathleen A. Kelly Vaccination using vault nanoparticles favors cellular immunity. 5th Biennial Meeting of the Chlamydia Basic Research Society Friday, March 18-21, Rodendo Beach, CA, 2011.
- K. Kelly, C. Champion, S. Salehi, **U. K. Kar**, G. Liu, L. Rome, V. Kickhoefer, A. Sater, K. Karunakaran, R. Brunham, S. Rabizadeh, K. Niazi, A. Sater, D. Ojcius, Luigi Franchi, Gabriel Nunez and J. Jiang. Vaccination using vault nanoparticles favors cellular immunity and induces inflammasome formation. Immunological Mechanisms of Vaccination. October 27 -November 1, Seattle, Washington, 2010
- **Kar UK**, Andersson A, Sreevastava M, Baratelli F,, Shaposhnik Z, Kickhoefer VA, Dubinett SM, Sharma S, and Rome LH. CCL21 Vault Nanocapsule Generates Potent Antitumor Responses. NIH Biotechnology Annual Symposium – UCLA June 11, 2010.
- **Kar UK**, Panda SK, Durgapal H, Acharya SK, Rehman S, Kumar A, Inhibition of Hepatitis E virus replication by short hairpin RNA (shRNA) in HepG2 cells. Novel Delivery of siRNA miRNA Symposium - California NanoSystems Institute at UCLA June 10th, 2010
- **Kar UK**, Andersson A, Sreevastava M, Baratelli F,, Shaposhnik Z, Kickhoefer VA, Dubinett SM, Sharma S, and Rome LH. Intratumoral Vault CCL21 Nanocapsule Generates Potent Antitumor Responses In Vivo. Department of Biological Chemistry retreat, UCLA, 2010

- **Kar UK**, S. Rehman, A. Kumar, D. Thakral, Gita S. Panda, S. K. Panda. Development of small interfering RNAs (siRNAs / shRNAs) for Inhibition of Hepatitis E virus (HEV) Replication and Transcription. International Symposium on Viral Hepatitis and Liver Disease, Paris, France, 2006.
- **Kar UK**, Satpathy G.,Panda SK and Das BK. Typing of Streptococcus pneumoniae. In PCA04Phylogenetic Combinatorics and its Applications 5th-9th July 2004, Uppsala University, Sweden.
- **Kar UK**, Panda SK, Das BK, and Satpathy G. Genotyping of Streptococcus pneumoniae strains by pulse field gel electrophoresis. In Proceedings of XXVI National Congress of Indian Association of Medical Microbiologists. 2002: p82.
- Satpathy G, **Kar UK**, Panda SK, Das BK. Molecular analysis of Streptococcus pneumoniae ophthalmic isolates using RAPD, traditional ribotyping and PCR ribotyping. In Proceedings of XXVI National Congress of Indian Association of Medical Microbiologists. 2002: p83.
- **Kar UK**, Satpathy G, Panda SK, Das BK. PCR ribotyping and RAPD analysis o Streptococcus pneumoniae isolates from ocular infections. In: Proceedings of Silver Jubilee Congress of Indian Association of Medical Microbiologists. 2001: p154
- Satpathy G, Bhan A, **Kar UK**, Reddy KS, and Panda SK. Detection of C pneumoniae in coronary artery disease patients by PCR assay and antigen detection. In: Proceedings of Silver Jubilee Congress of Indian Association of Medical Microbiologists. 2001: p 84.
- **Kar UK**, Satpathy G, Panda SK, Das BK. RAPD: A powerful method to differentiate the Streptococcus pneumoniae strains isolated from ocular infections. In Proceedings of XXIV National Congress of Indian Association of Medical Microbiologists. Nov. 2000, p 55-56, Belgaum, Karnataka, India.

Invited scientific presentations

- "Gut Stem Cells and its potential therapeutic applications": NISER Bhubaneswar, India, 24th, October 2014.
- "Recent advances in Gut Stem Cell Research and future directions": JNU, New Delhi, India, 20th, October 2014.
- "Gutsy approached to study Gut Stem Cells": AIIMS, New Delhi, India, 14th, October 2014.
- "Deliver cargos with confidence: Using vault natural nanocapsules": Arizona state university, May 2013.
- "Vaults: Hold Promise to Develop Effective Nanocarriers for Cancer Therapy": Young investigators meeting on Integrating Education with Research, Jodhpur, India. 2012.
- "Developing innovative cancer vaccine utilizing vault delivery system": Charles R. Drew University of Medicine and Science, 2011.
- "Modulating immune response against cancer using cancer antigens": Centre for Biotechnology and Environment (CBE), C V Raman College of Engineering. 2010.
- "Genetic Analysis of Microorganisms Isolated from Various Infections: Experience with S. pneumoniae": Center for Biotechnology, JNU, New Delhi 2004.
- "Apoptotic and non-apoptotic Cell Death in Cancer Development": Lecture Series of Society of Young Scientists, AIIMS, New Delhi, India. September 2002.

Patents: Vault Nanoparticles for Cancer Immunotherapy (U.S. Prov. App Ser No. 61/257,358)
Vault Complexes for Cytokine Delivery (U.S. Patent App Pub. No.: US 2012/0213809 A1)

Work Experience

June-2013- present: David Geffen School of Medicine, University of California, Los Angeles, USA

Research Scientist (Dr J C Dunn)

My research program investigates the dynamic interplay between gut stem cells and their niche. Intestinal stem cells are responsible for the maintenance and regeneration of the epithelium in both health and diseases. Located at the crypt base, these stem cells are surrounded, nurtured, and protected by their neighboring cells that form the

stem cell microenvironment, or Niche. The general approach of my research is to apply sophisticated human and mouse ex vivo crypt manipulations (organoid culture) coupled with high, or super-resolution microscopy and advanced molecular techniques to address many fundamental unanswered questions. I investigated the requisite signaling network in human Intestinal stem cell and showed Wnt signaling is indispensable for the growth of the spheroid cells as culture condition without Wnt agonist (Rspondin-1) and with Wnt antagonist (IWP-2) significantly influence the biology of the spheroid cells. Leveraging multiple approaches (RNAi against adenomatosis polyposis coli, TCF/LEF reporter system and from FAP clinical specimen) I demonstrated that canonical wnt signaling is not absolutely required for long term survival of hISCs. Among the Complex non canonical signaling pathways PKA and JNK plays a vital role on spheroid cells. I also demonstrated the role of PGE2 and showed Ras/Raf/MEK/ERK axis is imperative for spheroid growth than PI3K/PTEN/Akt/mTOR Axis. I have developed methods to induce differentiation of spheroids into enteroid structures that recapitulate all the cell types of intestinal epithelium (absorptive; enterocytes and secretory; Paneth cells, goblet cells and enteroendocrine cells (Manuscript under preparation).

2007 – May 2013; University of California, Los Angeles, USA

Post-Doctoral Fellow (Supervisor: Dr L.H.Rome)

My research was to design, construct, and test novel cancer vaccine using Vaults (a natural ribonucleoprotein). I packaged different immunomodulatory molecules i.e. CCL-21, IL-4, IL-6, IFN-gamma, P53, Ovalbumin etc in Vaults utilizing genetic engineering tools. I demonstrated that co-formulations of vaults with Chemokine Ligand 21 (CCL-21) can (i) retain CCL-21 in the tumor microenvironment; (ii) eradicate tumors and (iii) generate durable protection. Vaults packaged with Chemokine Ligand 21 (CCL21-vaults) inhibited lung cancer growth more than 60% in mice (PLoS One. 2011 May 3;6(5):e18758). I also compared the delivery efficiency of vault nanoparticles with commercial liposomes using a novel antigen Ovalbumin (PLoS One 2012 2012;7(7):e38553). My research highlighted the potential of vault nanocapsule-based vaccines against antigens for human pathogens and cancer. The technology is been patented (pct/us2010/055146 WO 2011/053991A2) and gained phase I and II SBIR grant. In a collaborative study with Dr Sherven Shrama, we showed the mechanistic role of MDSC depletion on antigen presenting cell (APC), NK, T cell activities and therapeutic vaccination responses in murine models of lung cancer (PLoS One 10.1371/journal.pone.0040677 published 16 Jul 2012).

2005 – 2007; Johns Hopkins Medical Institute, Baltimore, USA.

Post-Doctoral Fellow (Supervisor: Dr P. ACampochiaro)

The molecular events that contribute to retinal degeneration are highly complex, reflecting in part the interdependence of different retinal cell types and the intimate functional and structural contacts between photoreceptors and the adjacent retinal pigment epithelium. Although loss of rods has substantial functional consequences such as night blindness and some constriction of visual fields, rod death by itself does not cause severe vision loss. My research was to understand the complexity of gene expression in both rod and Cones particularly the chaperones. I evaluated differential chaperone expressions by Cone and rod cells in response to paraquat induced Oxidative stress. I purified rods and cones from the retina of rod-GFP mouse using flow cytometry followed by paraquat injection. The differential expression of Alpha-A Crystallin, Alpha B crystalline, HSP27, HSP60, HSP70, HSP90, glucose regulated protein (GRP)78, and GRP94 of mRNA was evaluated by real time PCR. I also evaluated the protective role of Heat Shock Factor -1 (HSF-1) in an attempt to develop therapeutic agents against Age-related macular degeneration (AMD) and Retinitis pigmentosa (RP) induced by oxidative stress. I showed alleviation of endogenous HSF-1 (in both mRNA and protein level) in stressed induced cells compared to control cells. Also by localization study I further confirmed the induction of HSF-1 in the nucleus. I also evaluated the physiological role of different domains of HSF-1 (dominant positive, dominant negative and wild type). My research showed transient expression of HSF-1 (but not the dominant negative of HSF-1) rescues the A RPE-19 cells from paraquat induced cell death.

1999-2005; All India Institute of Medical Sciences (AIIMS), New Delhi, India

Graduate Student (Supervisors: Dr G Satpathy, Dr S.K. Panda and Dr Bimal Das)

My graduate thesis research was to answer whether any particular pneumococcal serotypes/ genotype, have predilection for ophthalmic infections, in comparison to the strains associated with invasive systemic infections and nasopharyngeal colonizers. Using different molecular typing methods I showed the genetic similarities between *S. Pneumonie* involved in various ophthalmic infections i.e. Corneal ulcer, Keratitis, Dachryocystitis etc from carriers and systemic infections. (Ophthalmic Res. 2006; 38(1): 36-43., Indian J Med Res. 2006 Jul; 124(1):

99-104. and Indian J Med Res. 2008 Feb; 127(2): 171-7. I also investigated the genetic similarities between *C.pneumoniae* isolated from coronary artery diseases (Indian J Med Res. 2008 Nov;128(5):658-62.). I designed and developed RNAi against different region of Hepatitis E virus, which is one of the leading causes of viral hepatitis and showed that combination of RNAi against Helicase and RNA-dependent RNA polymerase could inhibit the viral replication significantly (antiviral research 2010).

LEADERSHIP AND MANAGEMENT EXPERIENCE:

- **Vice President, Entrepreneurship Committee Co-Chair and External Affairs Officer** for Society of Postdoctoral Scholars at UCLA (2007-2010). Collaborated with Business Science Center at UCLA (UCLA BSC) and eagerly pursued key initiatives for connecting the graduate student and postdoctoral fellows and increase their awareness to the University's entrepreneurial ecosystem. Organized cultural events and exchange meetings between postdoctoral organizations at Caltech and USC.
- **Chairman** of the Post-Doctoral Journal club at Wilmer Eye Institute, Johns Hopkins Medical Institute, Baltimore, USA. Initiated and moderated numerous seminars. Organized a workshop on how to write grant applications and establish collaborations for transition from postdoctoral fellow to principal investigator.
- **Executive Member of Library Committee:** Represented for the graduate students body and engaged with the faculty/administrative group members to recommend the inclusion of scientific text books and journals in the library. Advocated for implementation of special facilities for students with disabilities.
- **Secretary and Socio-Cultural secretary** of Society of Young Scientists (SYS) (2002-04), a scientific organization at All India Institutes of Medical Sciences (AIIMS), New Delhi, India. Organized national symposium "Trends in Molecular Medicine" and national science day.
- Created digital footprints for "Life Sciences/Biotechnology Product and Business Development" and "Academia-BioPharma Industry Partnership".
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