

RANAJAY MULLICK

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Scientist

International AIDS Vaccine Initiative (IAVI), India
HVTR Lab, Translational Health Science & Technology Institute

CAREER OVERVIEW

May 2004 - May 2011 worked at Division of Virology, National Institute of Cholera and Enteric Diseases, Kolkata, as Junior Research Fellow and Senior Research Fellow.

June 2011-May 2012 worked at Department of Microbiology and Cell Biology, University of Chicago, Illinois USA as Postdoctoral Scholar.

June 2012 - March 2017 worked as a Senior Research Associate at the Department of Microbiology and Cell Biology, Indian Institute of Science, Bangalore, India

Visiting fellow at University of Adelaide, Adelaide, South Australia, Feb-March 2013

April 2017 onwards working at International AIDS Vaccine Initiative (IAVI), New Delhi, India (currently working as IAVI Scientist at IAVI-THSTI HVTR Lab India)

Adjunct Faculty at Translational Health Science and Technology Institute, Faridabad, India

RESEARCH SKILLS

Proficient with the following techniques :

- Virus characterisation.
- Virus production, Titration, Propagation and Transduction.
- Sequencing, blast search and phylogenetic analysis.
- Cloning.
- Site directed mutagenesis.
- *in vitro* transcription and translation studies.
- Experience in mammalian cell culture experiments :
 - Transfection and cotransfection studies.
 - Gene expression study through western blot or reporter gene based assay.
 - Lentiviral production, transduction and shRNA mediated knockdown experiments studies.
 - Immunofluorescence and confocal studies.
- Development of vaccine (VLP and DNA based), immunization and performing related assays (T cell proliferation assay, Flow Cytometry).
- Studies on different antivirals (small RNA, peptides, herbals) targeting viral entry and replication.
- Studies on envelope based monoclonal Abs against targeting viral entry process.
- Studies on immune biomarkers from patient plasma samples and their effect on the disease progression.
- Nanocapsule mediated targeted delivery studies in *ex vivo* system.

PROJECTS EXECUTED

- Studied Molecular Characterisation of *tat* Regulatory Gene of Human Immunodeficiency Virus Type-1 of India.
- Studied the effect of host cellular receptor (nectin) knockdown on HSV infection process.
- Studied effect of various herbal compounds and modified small RNA molecules in blocking HCV replication and further propagation in *ex vivo* and *in vivo* condition.
- Worked on Indo-Australian project for the designing of a suitable candidate VLP and DNA vaccine for HCV in India and further immunization studies in mice and pigs.
- Studies on immune biomarkers (chemokines) from stage specific patient plasma samples (HCV) and their effect on disease progression.

- Currently working on assessing some of the lead HIV-1 broadly neutralizing antibodies which are already in clinical trials to check their suitability in neutralizing currently circulating Indian stage specific viruses.

WORK DONE DURING PHD TENURE AND BEYOND

During my Phd tenure at NICED, Kolkata I have worked on HIV-1 positive patient samples from eastern and north eastern regions of India (Manipur). I did majorly subtyping of the patient samples based on HIV-1 structural genes [*gag* and *env*] by Heteroduplex Mobility Assay, Multiregion Hybridization Assay and sequencing for identification of new recombinant strains of HIV-1 circulating in this part of India. I have identified some of the BC recombinant strains from Manipur which showed identical recombination breakpoints in the *tat* regulatory gene. Further I did functional characterisation of those recombinant regulatory genes compared to the wild type subtype C variant which showed enhanced regulatory gene activity compared to the wildtype. Along with these I also did genetic characterisation of the Long Terminal Repeat region or LTRs (as *tat* transactivation is mediated by LTRs of HIV-1). Unlike the *tat* gene, LTR region was conserved and showed indications of no recombination even in the recombinant samples.

During my postdoc tenure at the University of Chicago, USA I worked on different viral and host protein interaction at the cellular level controlling viral entry and replication. I studied the effect of the knockdown of the cellular Cbl protein (a multifunctional oncoprotein that also functions as an E3 ubiquitin ligase) by lentiviruses on cellular surface nectin protein mediated entry of Herpes Simplex Virus (HSV). I also studied the role of cytoplasmic viral regulatory protein ICP0 in blocking IRF3 mediated dimerization and nuclear relocalization and subsequent inhibition of ISGs (Interferon Stimulatory Genes) thus promoting viral propagation.

During my post-doctoral tenure at IISc I have been majorly working on a DBT Indo-Australian Vaccine Project on developing a prophylactic and therapeutic candidate vaccine against the prevalent Gt3a Hepatitis C virus in India by inducing humoral and cell mediated immune response in mice. During my short visit to University of Adelaide, South Australia, in Prof. Eric Gowans lab, I worked on developing the HCV Gt3a based DNA vaccine construct which showed promising cellular immune response (CMI) in mice. At IISc we have developed a VLP based vaccine as well for generating humoral immune response against the virus. At IISc I have also parallelly worked with different antivirals (small RNA, peptides, herbals) that blocks the virus entry as well as replication. Towards this objective, we have explored highly potent and selective small molecule inhibitors, the ellagitannins, from the crude extract of Pomegranate (*Punica granatum*) fruit peel and juice extract. The pure compounds punicalagin, punicalin, and ellagic acid isolated from the extract specifically blocked the HCV NS3/4A protease activity in vitro. Further, punicalagin and punicalin significantly reduced HCV replication as well as entry in HCV subgenomic replicon as well as infectious cell culture system. Our study has provided a proof-of-concept approach for the potential use of antiviral and non-toxic principle ellagitannins from pomegranate in prevention and control of HCV induced complications. Further we similar kind of studies was also done with the purified bioactive components (Corilagin) from the plant *Phyllanthus amarus*. Other than these we have also designed small RNA molecules targeting the SLIII region of HCV IRES termed as SLRef which binds to the S5 region of the 40S ribosomal subunit of the translation initiation complex and blocks HCV IRES translation and as a consequence blocks the replication. Further we have modified the SLRef base with 2'-O-methyl phosphorothioate modification to increase the stability of the antiviral RNA and checking the effect in HCV translation and replication. I have also extensively worked on the chemokine induced pathogenesis on HCV infection from Gt3a stage specific patient plasma samples.

Presently I am working as a Scientist at THSTI (Translational health Science and Technology Institute) at THSTI-IAVI HVTR Lab (HIV-1 Vaccine Translational Research Lab) on HIV-1. My work here as mentioned above is focussed on the characterization of the currently circulating HIV-1 strains in India, preparing pseudovirus panel and studying the neutralization sensitivity of the panel towards known and unknown monoclonal Abs.

AWARDS WON

- **Junior Research Fellowship & Lectureship** on 26th Jun'03, under **UGC Fellowship Scheme** by qualifying for **National Eligibility Test (NET)** jointly conducted by Council of Scientific & Industrial Research (CSIR), Govt. of India and University Grants Commission (UGC).
- **Junior Research Fellowship & Lectureship** on 1st Nov'03, under **CSIR Fellowship Scheme** by qualifying for the **National Eligibility Test (NET)** jointly conducted by the Council of Scientific & Industrial Research (CSIR), Govt. of India and University Grants Commission (UGC).
- **Conference Scholarship** for Poster Presentation at AIDS Vaccine Conference 2010 during 28th Sep - 1st Oct'10 held at Atlanta, Georgia, USA.

- **Won the best poster presentation award** at the 17th Indo-US Cytometry workshop on “Application of laser Flow Cytometry in Biomedical Research” jointly conducted by Indian Institute of Science, Bangalore and National Centre for Biological Sciences, Bangalore 14-16th March 2016.
- Won MVP award from International AIDS Vaccine Initiative for performance September 2019.

SCHOLASTICS

- **Ph.D.** from Division of Virology, National Institute of Cholera & Enteric Diseases (ICMR, Govt. of India), Jadavpur University, Kolkata in 2011.
 - Thesis submitted on ‘Molecular Characterisation of Tat Regulatory Gene of Human Immunodeficiency Virus Type-1 of India’ under the guidance of Dr. Sekhar Chakrabarti, NICED, Kolkata.
- **M.Sc. (Zoology)** with specialisation in Mammalian Reproductive Physiology from Banaras Hindu University with First Class marks in 2002.
- **B.Sc. (Hons.) Zoology** from Calcutta University with First Class marks in 2000.

WORKSHOPS AND SEMINARS ATTENDED

- Poster Presentation at AIDS Vaccine Conference 2010 held at Atlanta, Georgia, USA from 28th Sep - 1st Oct’10.
- Workshop on “Sequence Analysis and Protein Modeling” by Biomedical Informatics Centre of NICED, Kolkata during 18th - 19th Jun’10.
- Indo-US Workshop on “Laboratory Diagnosis of Enteric Parasites” organised by Centre for Disease Control (CDC), Atlanta, USA and National Institute of Cholera and Enteric Diseases, Kolkata from 18th - 20th Feb’08 at Kolkata, India.
- Poster Presentation at 74th Annual Meeting of Society of Biological Chemists (India) during 7th - 10th Nov’05 held at CDRI, Lucknow.
- Workshop on “Molecular Genetics of Vibrio Cholerae” by the American Society for Microbiology (ASM) and Indian Council of Medical Research (ICMR) at National Institute of Cholera and Enteric Diseases, Kolkata on 12th Nov’04.
- **Oral presentation on “Prophylactic and therapeutic approaches to develop candidate vaccines against Hepatitis C virus.”** at the 4th Molecular Virology Meeting, Rajiv Gandhi Centre for Biotechnology, Thiruvanthapuram, 16-17th April, 2015.
- **Participated in 17th Indo-US Cytometry workshop on “Application of laser Flow Cytometry in Biomedical Research”** jointly conducted by Indian Institute of Science, Bangalore and National Centre for Biological Sciences, Bangalore 14-16th March 2016.
- **Actively participated in the UGC workshop for teachers training refreshers course on Molecular Biology & Genetics** organized jointly by Indian Academy of Science and Indian Institute of Science, Bangalore from 16th Jan - 29th Jan 2017. Conducted practical sessions for the teachers.

PUBLICATIONS

Papers

First author :

1. **Mullick R**, Sengupta S, Sarkar K, Saha MK, Chakrabarti S. 2006. Phylogenetic Analysis of Env, Gag and Tat Genes of HIV Type 1 detected among Injecting Drug Users in West Bengal, India. **AIDS Res Hum Retroviruses.**, 22 (12): 1293-99. Impact Factor : 2.7 Cited :14
2. **Mullick R**, Sengupta S, Sarkar K, Chakrabarti S. 2010. Molecular Characterisation of Tat Gene and Long Terminal Repeat Region of Human Immunodeficiency Virus Type-1 Detected among Injecting Drug Users (IDUs) of Manipur, India: Identification of BC Recombinants. **Virus Res.** 147, 195-201. Impact Factor : 2.58 Cited :12
3. **Mullick R**, Sengupta S, Sarkar R, Singh N N, Singh N B, Singh Y M, Sarkar K, Chakrabarti S 2012. Genotypic Distribution of Different Variants of Oncogenic Human Papilloma Virus (HPV) among the

Coauthor :

1. Sarkar R, Sengupta S, **Mullick R**, Singh NB, Sarkar K, Chakrabarti S. 2009. Implementation of a Multiregion Hybridization Assay to Characterise HIV-1 Strains Detected among Injecting Drug Users in Manipur, India. **Intervirology**. 11; 52(4): 175-178. Impact Factor : 1.7 Cited :14
2. Sarkar M, Agrawal A, Dey R S, Chattopadhyay S, **Mullick R**, De P, Chakrabarti S, Sarkar M C.2011. Molecular Characterisation and Comparative Analysis of Pandemic H1N1/2009 Strains 1 with Co-circulating Seasonal H1N1/2009 Strains from Eastern India. **Arch Virol**. 156(2): 207-17. Impact Factor : 2.11
3. Sarkar R, Pal R, Bal B, **Mullick R**, Sengupta S, Sarkar K, Chakrabarti S. 2011. Genetic Characterisation of HIV-1 Strains among the Injecting Drug Users in Nagaland, India. **Open Virol J**.; 5:96-102. Impact Factor : NA Cited : 5
4. Kumar A, Manna A K, Ray U, **Mullick R**, Basu G, Das S and Roy S. 2014. Specific Sequence of a Beta-turn in Human La Protein May Contribute to Species Specificity of Hepatitis C Virus. **J Virol**. 88(8): 4319-27. Impact Factor : 4.6 Cited : 4
5. Reddy B U, **Mullick R**, Kumar A, Sudha G, Srinivasan N and Das S 2014. Small molecule inhibitors of HCV replication from Pomegranate. **Scientific Reports (nature publishing group)**. 4:5411. Impact Factor : 4.25 Cited : 15
6. Grubor-Bauk B, **Mullick R**, Das S, Gowans E, Yu W. 2014. Immunocompetent mouse models to evaluate intrahepatic T cell responses to HCV vaccines. **Hum Vaccin Immunother**.10(12) :3576-8. Impact Factor : 3.6 Cited : 1
7. Gummow J, Li Y, Yu W, Garrod T, Wijesundara D, Brennan A J, **Mullick R**, Voskoboinik I, Grubor-Bauk B, and Gowans E. 2015. A multi-antigenic DNA vaccine that induces broad HCV-specific T-cell responses in mice. **J Virol**. 89(15):7991-8002. Impact Factor : 4.6 Cited : 7
8. Shwetha S, Kumar A, **Mullick R**, Vasudevan D, Mukherjee N, Das S. 2015. HuR displaces PTB to facilitate La binding to the 3'UTR and enhances HCV replication. **J Virol**. 89(22):11356-71. Impact Factor : 4.6
9. Kumar A, Das S, **Mullick R**, Lahiri P, Tatineni R, Goswami D, Bhat P, Karande AA, Das S. 2015. Immune responses against hepatitis C virus genotype 3a virus-like particles in mice: A novel VLP prime-adenovirus boost strategy. **Vaccine**. 34(8):1115-25. Impact Factor : 3.6 Cited : 4
10. Pandita E, Rajan S, Rahman S, **Mullick R**, Das S, Sau AK. 2016. Tetrameric Assembly Of hGBP1 Is Crucial For Both Stimulated GMP Formation And Antiviral Activity. **Biochem J**. Jun 15;473(12):1745-57. Impact Factor : 4.39
11. Bose M, **Mullick R**, Das S, Das S, Karande AA. 2016. Combination of neutralizing monoclonal antibodies against Hepatitis C virus E2 protein effectively blocks virus infection. **Virus Res**. 15;224:46-57. Impact Factor : 2.58
12. Das S, **Mullick R**, Kumar A, Tandon H, Bose M, Gouthamchandra K, Chandra M, Ravishankar B, Khaja MN, Srinivasan N, Das S, Melkote Subbarao S, Karande AA. 2017. Identification of a novel epitope in the C-terminus of HCV-E2 protein that induces potent and cross-reactive neutralizing antibodies. **J Gen Virol**. Impact Factor : 3.36 Cited : 1
13. Bose M, Kamra M, **Mullick R**, Bhattacharya S, Das S, Karande AA. 2017. A plant-derived dehydrorotenoid: a new inhibitor of hepatitis C virus entry. **FEBS Lett**. 591(9):1305-1317. Impact Factor : 3.51
14. Deschamps T, Dogrammatzis C, **Mullick R**, Kalamvoki M. 2017. The Cbl E3 ligase mediates The removal
15. of Nectin-1 from the surface of the herpes simplex virus type 1 infected cells. **J Virol**. Impact Factor : 4.6
16. Bose M, Kamra M, **Mullick R**, Bhattacharya S, Das S, Karande AA. 2017. Identification of a flavonoid isolated from plum (*Prunus domestica*) as a potent inhibitor of Hepatitis C virus entry. **Scientific Reports**. Jun 21; 7(1): 3965. Impact Factor : 4.25
17. Reddy BU, **Mullick R**, Kumar A, Sharma G, Bag P, Roy CL, Sudha G, Tandon H, Dave P, Shukla A, Srinivasan P, Nandhitha M, Srinivasan N, Das S. A natural small molecule inhibitor corilagin blocks HCV replication and modulates oxidative stress to reduce liver damage. **Antiviral Res**. 2017 Dec 7. [Epub ahead of print] Impact factor : 4.9

1. Emerging Recombinants of HIV-1 in Proceedings of the 15th Round Table Conference Series by Ranbaxy Science Foundation-HIV and Tuberculosis: Co-infection. Sekhar Chakrabarti, P.Bhanja, S.Sengupta & R.Mullick. Jan, 2005; 15: 135-147.
2. MVA-Based Vaccines in Proceedings of the 7th Sir Dorabji Tata Symposium on HIV/AIDS Research Issues, 2007, Vol.7, 257-273. Sekhar Chakrabarti, Ranajoy Mullick, Satarupa Sengupta.
3. Molecular Biology of HIV in India. NARI Bulletin from National AIDS Research Institute (ICMR), India. Ranajoy Mullick, Roni Sarkar & Sekhar Chakrabarti. July 2010, Volume 1, Issue 2, 2-3.

Abstracts

1. Distribution of HIV-1 Subtypes Detected among the Injecting Drug Users (IDUs) of West Bengal, India. Ranajoy Mullick, Sekhar Chakrabarti. 74th Annual Meeting of Society of Biological Chemists (India). 7-10 November 2005, CDRI, Lucknow.
2. Molecular Characterisation of HIV-1 Detected among Injecting Drug Users and Female Sex Workers in India. Sengupta S, Bhanja P, Mullick R, Sarkar K, Chakrabarti S. AIDS Vaccine Conference, 19th - 22nd Oct, 2009. Paris. Meeting Abstracts, AIDS Vaccine 2009. Retrovirology. Vol. 6, Suppl 3, 2009.
3. Molecular Characterisation of Tat Regulatory Gene of Human Immunodeficiency Virus Type-1 of India. R. Mullick, S. Sengupta, R. Sarkar, S. Chakrabarti. AIDS Vaccine Conference, 26th Sep - 1st Oct, 2010. Meeting Abstracts, AIDS Vaccine 2010. AIDS Res Hum Retroviruses, Vol. 26, No.10, 2010.
4. Prophylactic and therapeutic approaches to develop candidate vaccines against Hepatitis C virus. Anuj Kumar, Soma Das, Ranajoy Mullick, Saumitra Das. Meeting Abstracts, 4th Molecular Virology Meeting, Rajiv Gandhi Centre for Biotechnology, Thiruvanthapuram, 16-17th April, 2015.

PATENTS

Patent filed for : DIETARY SUPPLEMENTS AND DRUGS BASED ON *PUNICA GRANATUM* FOR USE AS HEPATITIS C VIRUS INHIBITORS. Application No. 3473/CHE/2015 Date of filing: 07-07-2015 (Post dated to 07 January 2017) Applicant: INDIAN INSTITUTE OF SCIENCE, Bangalore. Inventors: Saumitra Das, *et al.* Ref.: IPA10140006.

Provisional patent filed for : Title: HEPATITIS C EPITOPES AND MONOCLONAL ANTIBODIES Indian Patent Application No. 201741002367 Date of filing: 20-01-2017. Applicant: INDIAN INSTITUTE OF SCIENCE, Bangalore Inventors: Anjali Karande, *et al.*,
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