CV-Kulbhushan Sharma

Born: Marital status:	Sep 15, 1980, India. Married.	
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Professional profile

Molecular biologist with 16 years of experience including latest hands-on expertise in Stem cells (iPSC and ESCs), Autophagy and Genome editing (CRISPR-Cas9) at the University of Oslo and Oslo University Hospital, Norway. Group leader experienced in managing own independent research group with 4 PhDs (one awarded) and one postdoctoral fellow in DRDO, one of the topmost organizations in India. Mentoring many M.Sc. students as well. Result driven, motivated & forward thinking scientist with hybrid profile of academic and research training.

Aug 2018-Presesnt

Scientist D, INMAS, DRDO

After completing four years of experience as Marie Curie researcher in stem cells, autophagy and genome editing at the University of Oslo, Norway, I have joined as an independent group leader in DRDO, New Delhi, India. I have one postdoctoral fellow (ICMR funding) and two PhDs in the group. One PhD, Dr Shashank Misra has got his doctoral degree recently and now working for a flow cytometry company. The main focus of the lab is cancer biology, Inflammation (COX2 and PPAR signaling) and autophagy. The group has published various papers in peer-reviewed journals (10 papers from the group till now and many in the pipeline). The students have got several poster as well as oral presentation awards at national and international conferences along with various travel grants. We are a part of the stem cell centre of DRDO. We are in the process of introducing new technologies in the group including 3D-printing, single cell picking, improved genome editing and organoid cultures.

Aug 2015-Aug 2018

Marie Curie Scientia fellow at Center for Excellence, University of Oslo.

Awarded with prestigious Marie Curie fellowship from EU. Worked on the role of **Autophagy and Mitophagy** in DNA damage repair and differentiation of **Human iPSCs and ESCs** in collaboration with Dr Gareth Sullivan, Stem cell Centre, University of Oslo. We differentiated these cells to hepatocytes, neurons and beating cardiomyocytes. We made genetic modifications in these cells using **CRISPR-Cas9** method. In addition, a number of **fluorescent reporter iPSC lines** were made using piggyBac system and were characterized (QC). During this tenure, I also made fluorescent reporter lines using **clinical iPSCs** from Parkinson patients and Alpers-Huttenlocher syndrome (AHS) in Norway. Various novel findings are in the process of communication to peer-reviewed journal. I extended my expertise in genome editing and used CRISPR Cas9 to make knock-ins and knockouts for inducing changes in genes of iPSCs coding for Factor VII, Autophagy proteins, DNA repair machinery proteins etc. During this tenure, I was fortunate to get a brief exposure to protocols for making liver organoids and the 3D printing facility of the stem cell center.

July 2014-Aug 2015

Scientist D, DRDO, Delhi, India

Promoted to Scientist D position. My lab had one postdoctoral fellow (ICMR funding) and two PhDs in the group. One PhD student completed his degree. The focus of the lab is ESC and iPSC differentiation, Cancer biology, Inflammation (COX2 and PPAR signaling) and Autophagy. We are a part of the stem cell center of DRDO. We are in the process of introducing new technologies in the group using human iPSCs and ESCs including high quality line generation, 3D-printing, single cell picking and improved genome editing. Worked on the molecular mechanism of autophagy and role of prostaglandin signaling in cancer initiation and progression. Major area of interests included (i) Autophagy: Studying the effect of radiation induced stress on autophagic and mitophagic pathways (ii) NSAID and other COX-2 signaling inhibitors: Exploring novel targets for COX-2 signaling pathway inhibition like EP receptors and PTGS2 for a better anti-cancer therapy and off target free pain killers. (iii)

Kulbhushan Sharma

Chronic Inflammation Exploring the role of PPAR gamma, RAS blockers and other key molecules involved in chronic inflammation.

Sep 2011-June 2014

Scientist C, DRDO, Delhi, India

Worked on the molecular mechanism of autophagy and role of prostaglandin signaling in cancer initiation and progression. Major areas of interest include (i) **Autophagy**: Studying the effect of radiation induced stress on autophagic and mitophagic pathways (ii) NSAID and other **COX-2 signaling** inhibitors: Exploring novel targets for COX-2 signaling pathway inhibition like EP receptors and PTGS2 for a better anti-cancer therapy.

Sep 2009-Sep2011

Scientist C, DRDE, India

Worked on basic **molecular virology** of H5N1, H1N1 and receptor identification of Chikungunya virus. Also worked on scale up and downstream processing of various important proteins.

Aug 2008-Aug 2009

Postdoctoral fellow, International Centre for Genetic Engg. & Biotechnology, Delhi, India

Worked as **post-doctoral fellow** with Dr. Sunil Lal at Virology group, International Centre for Genetic Engineering and Biotechnology **(ICGEB)**, New Delhi, India. Worked on **host-pathogen interactions** of pathogenic "Bird Flu" H5N1 and "Swine flu" H1N1 viruses.

Education

Doctoral degree (PhD)

Oct 2003-Sep2008

International Centre for Genetic Engg & Biotechnology, Delhi, India

Ph.D. program in molecular virology at ICGEB, New Delhi, India. Worked on cellular and molecular biology of three viruses: SARS-CoV, H5N1 and Hepatitis A virus (HAV). Supervisor: Dr. Sunil K. Lal, Senior Scientist, Virology lab, ICGEB, New Delhi, India. Thesis defended in Aug 2008. Title of Thesis: Protein-protein and RNA-protein interactions of SARS coronavirus.

Masters in Science (MSc), Molecular Biology & Biotechnology

May 2001-Jun 2003

G.B. Pant University of Agri. & Tech, Pantnagar, Uttaranchal, India

Selected through Jawaharlal Nehru university common entrance exam for biotechnology, 2001 batch, G.B. Pant University. Worked on the development of immunological assays including HA, HI, ELISA and other viral diagnostic assays for Canine Parvovirus (CPV). Subjects: Molecular Biology, Cell Biology, Genetics, Immunology, Recombinant gene technology, Biophysics, Microbiology, Biochemistry etc.

Bachelor in Science (BSc)

Apr 1998-May2001

Delhi University, Delhi, India

Studied subjects including Zoology, Botany and Chemistry. In addition, had various practical classes for the subjects mentioned. Additional subjects of English language and Agriculture sciences.

Scientific activity

• **Publications:** Published **more than 20 articles** with 272 citations (journals, invited reviews, books, chapters, edited proceedings). See publication list for details.

• **Invitations and conferences:** Invited speaker at high-profile international research conferences e.g. National Virology Conference, India, 2008; ASM conference, India 2007 etc. Also presented research at various conferences including ISSCR, Boston, 2017; Neuromit conference, Bergen, 2018; Nucleophagy meeting, Prague, 2017; CRISPR Cas9 workshop, Berlin, 2018; Stem Cell conference, University of Oslo.

• **Referee assignments:** Ad hoc-referee for more than 5 international journals/organisations, including Autophagy, Frontiers, Cell Death and Diseases, Protein peptide letters, PloSone etc. Grant evaluator for Israel Science Foundation (ISF), Department of Biotechnology (India), Deptt of Science and Technology (DST) and the Wellcome Trust/DBT India Alliance.

• International networking: Partner in Autophagy Network, India, Nordic Autophagy Society (NAS). Member of Stem Cell Society and American Society of Microbiologists. Collaborations with labs from 7 institutions in 3 countries.

• Organizer of international conferences: Radiation Biology conference (ICRB), New Delhi, India, 2014. Virology conference, New Delhi, India, 2007, Hepatitis conference, New Delhi, India, 2005.

• PhD students trained as main supervisor: Shashank Misra (PhD 2019, Gold medalist), Madhuri Chaurasia (PhD 2019 – PhD defence awaited), Simran Kaur (PhD continued), Suchitra Sharma (PhD started in 2019). Several master students trained.

• **Teaching:** Taught DNA damage and repair course at University of Delhi. Taking virology course at CBRN workshops, DRDO. Teaching stem cells at CEP courses, DRDO, India. Trained many medical and Erasmus students in the lab.

• Funding ID (Participate or leader of the following recent research projects)

INM-311, DRDO project, Young scientist project, DRDO, India, NuArch (UiO in collaboration with Czech republic) Marie Curie Scientia fellowship project (EU), Neuromit (Helse-EU), ICMR funding, India

<u>Key skills</u>

• Human iPSCs and ESCs • Small molecule mediated stem cell differentiation • CRISPR Cas9 • Autophagy • Mitophagy • Cancer • Inflammation • Virology • Radiation biology • Microscopy • Animal handling (mouse model) • GLP and GMP (generating and following SOPs)

Awards and Honors

• Marie Curie Scientia fellowship award (EU) 2015 •Radiation Safety Officer I (RSO I) certification given by Atomic Energy Regulatory Board (AERB) 2012 •Rana Memorial Best Poster Award, 2009, American Society for Microbiologists (ASM) •Best oral presentation award 2008, National academy of Science, India (NASI) •Best Performer Award consecutively in 2005 and 2006, 3rd and 4th Asia-Pasteur Virology course, Pasteur Institute, Hong Kong •Junior Research Fellowship (JRF) from UGC and CSIR, Govt of India, 2003 (to pursue PhD).

Selected Publications

https://orcid.org/0000-0001-5226-4209

- 1. Sharma K, Sullivan GJ, Simonsen A, The role of autophagy and mitophagy in lineage commitment. Manuscript ready to submit in Cell stem cell.
- 2. Siller R, Harrison S, **Sharma K**, Sullivan GJ, The generation of scalable human pluripotent stem cell derived liver organoids. Manuscript being prepared for Cell stem cell.

- Simran Kaur, Alo Nag, GU Gurudutta, Kulbhushan Sharma. Peroxisome Proliferator Activated Receptor Gamma Sensitizes Non-small Cell Lung Carcinoma to Gamma Irradiation Induced Apoptosis. Front. Genet., 13 June 2019, PMID: 31263479
- 4. Madhuri Chaurasia, Swapnil Gupta, Asmita Das, B.S. Dwarakanath, Anne Simonsen, Kulbhushan Sharma* Radiation induces PERK and IRE1 mediated pro-survival autophagy, accepted (In press), Autophagy, 2018
- 5. Kaur S, Nag A, Singh AK, **Sharma K*.** PPARγ-targeting potential for radioprotection. **Curr Drug Targets**. 2018 PubMed PMID: 29384061
- Misra S, Saini M, Ojha H, Sharma D, Sharma K*. Pharmacophore modelling, atom-based 3D-QSAR generation and virtual screening of molecules projected for mPGES-1 inhibitory activity. SAR QSAR Environ Res. 2017 PubMed PMID: 28094550.
- Himanshu Ojha, Kulbhushan Sharma, Simhachalam Kallepalli, Sheetal Raina and Paban Kumar Agrawala. In vitro evaluation of rutin and rutin hydrate as potential radiation countermeasure agents. Int J Radiat Res 2016, 14(1): 9-16.
- 8. Chaurasia M and **Sharma K*.** Radiation induced autophagy and mitophagy, beneficial or detrimental? Free Radic Res. 2016;50(3):273-90. PubMed PMID: 26764568.
- Shashank Misra, Himanshu Ojha and Kulbhushan Sharma*, Quantitative Structure Activity Relationship Study of MF-63 (Phenanthrene Imidazole Series) Derivatives for mPGES-1 Inhibitory Activity. Int. J. Curr. Res. Med. Sci. 2016 2(6): 32-42
- Pal I, Dey KK, Chaurasia M, Parida S, Das S, Rajesh Y, Sharma K, Chowdhury T, Mandal M. Cooperative effect of BI-69A11 and celecoxib enhances radiosensitization by modulating DNA damage repair in colon carcinoma. Tumor Biol. 2016 PubMed PMID: 26631035.
- 11. Bhardwaj V and **Sharma K**. Parallel DNA polymerase chain reaction: Synthesis of two different PCR products from a DNA template **F1000Research** 2014, 3:320
- 12. Misra S, Sharma K*. COX-2 Signaling and Cancer: New Players in Old Arena. Curr Drug Targets. 2014 Mar;15 (3):347-59.
- S Tripathi; J Batra; W Cao; K Sharma; JR Patel; P Ranjan; JM Katz; NJ Cox; RB Lal; S Sambhara and SK Lal. Influenza A virus Nucleoprotein induces cell death in human lung epithelial cells by targeting Clusterin. Cell Death and Disease, 2013, Mar 28; (4): e562.
- K Sharma, M Surjit, N Satija, B Liu, VTK Chow, SK Lal. The 3a accessory protein of SARS coronavirus specifically interacts with the 5'UTR of its genomic RNA, Using a unique 75 amino acid interaction domain. Biochemistry 2007-05-09 | journal-article PMID: 17488094
- 15. **K Sharma**, S Åkerström, AK Sharma, VTK Chow, S Teow, B Abrenica, SK Lal. SARS-CoV 9b protein diffuses into nucleus, undergoes active Crm1 mediated nucleocytoplasmic export and triggers apoptosis when retained in the nucleus, **PLoS One** 6 (5), e19436
- 16. K Sharma, S Tripathi, P Ranjan, P Kumar, R Garten, V Deyde, JM Katz, SK Lal. Influenza A virus nucleoprotein exploits Hsp40 to inhibit PKR activation. **PloS one** 6 (6), e20215

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<u>References</u>

- Dr Anne Simonsen, Professor, iCAM Autophagy, CANCELL Centre of Excellence, University of Oslo. <u>anne.simonsen@medisin.uio.no</u>Sognsvannsveien 9 Domus Medica 0372 OSLO Ph: +47-22851110.
- Dr Gareth Sullivan, Vice director, HYBRID TECH HUB, Centre of Excellence, Oslo University Hospital, Forsker, Stem cell centre, University of Oslo. gareth.sullivan@medisin.uio.no Sognsvannsveien 9 Domus Medica 0372 OSLO Ph: +47-22851415