Profiles of the Faculties at NIAB

Dr. Nagendra R. Hegde

Dr. Hegde's laboratory is interested in virology, virus-host interactions and viral pathogenesis. Dr. Hegde has in the past worked on viruses and bacteria of importance to animals and humans, covering topics such as epidemiology, genomics, host-pathogen interactions, vaccines and diagnostics. His current and future interests include livestock and zoonotic viruses, their biology and interaction with host cells, potential mechanisms of pathogenesis, and vaccines and diagnostics. The group also works on understanding, and mitigating bovine mastitis caused by major bacteria. Research techniques will include isolation and identification of organisms, genome analysis and genetic manipulation, cloning and mutagenesis, protein expression and purification, protein-protein interactions, recombinant viral vector generation, immune responses, and omics approaches. The laboratory closely works with other researchers at state, national and international levels on other extramurally funded projects addressing various aspects of animal health, zoonosis and one health.

Dr. Sandeep Goel

Deciphering therapeutic potential of mesenchymal stem cell

Mesenchymal stem cells (MSCs) have become widely studied over the past ~30 years for their exciting cell biology, broad-ranging clinical potential, and central building block in the rapidly growing field of tissue engineering. MSCs grow readily in the culture dish, have intrinsic differentiation potentials and immunomodulatory properties not found previously in other cells, and produce an abundance of useful growth factors and cytokines. The isolation of MSCs from various tissues and their re-implantation at other sites raises questions about the natural in vivo MSCs and their ability to repair endogenous tissues. Mesenchymal cell replacement in the large numbers needed to treat significant tissue injury requires engraftment, structural organisation and cellular differentiation—a complex process that has made much progress but remains unperfected.

Our lab focuses on developing mesenchymal stem cell-based therapeutics to treat livestock diseases. We have standardised the isolation and culture of MSCs from the adipose tissues and amniotic membrane. These MSCs have been characterised to express mesenchymal-specific cell surface markers such as CD73, CD90 and CD105. The ADSCs have also been characterised for the expression of anti-apoptotic and anti-inflammatory proteins. The MSCs are multipotent cells that can differentiate into the various lineages of mesodermal origin such as adipogenic, chondrogenic and osteogenic

lineages, and we are looking for the differentiation potential of MSCs in vitro. We have also standardised the cryopreservation protocols for the long-term storage of MSCs. Currently, we are working towards deciphering the epigenetic changes in the long-term cultured and cryopreserved MSCs. We propose to dissect the therapeutic potential of MSCs using the *in vitro* and *in vivo* models, especially in inflammation and wound healing.

Dr Sanjay Singh

Nanomaterials for Animal Health, Nutrition and Reproduction

About the Investigator: Dr Sanjay Singh completed Ph.D. from CSIR-National Chemical Laboratory, Pune, India and postdoc research from University of Central Florida, Orlando, USA and Pennsylvania State University, Hershey, USA. He also worked at Ahmedabad University as an Associate Professor prior to joining NIAB. Dr Singh has been a visiting professor at RMIT University, Melbourne, Australia, University of Pennsylvania, Philadelphia, USA, and University of Twente, Netherlands.

Research Interest: Dr Singh's research focuses on the development of novel and multifunctional nanomaterials for various biological applications including cell imaging, drug delivery, antimicrobial, and mitigation of oxidative stress. A current major area is the development of nanoparticles of essential trace elements to satiate the nutritional requirement of economically important animals. The nanoparticles can be further surface modified with variety of additional functional groups to facilitate better absorption and biocompatibility. Another area of interest is the development of free radical scavenging nanozymes that can mitigate the oxidative/nitrosative stress and maintain the redox homeostasis in mammalian cells under disease conditions. Additionally, these nanozymes may also be investigated to protect animal parts and products from free radical mediated damages. Related area of interest is development of pro-oxidant nanozymes as novel antibacterial materials to control the growth of pathogenic species causing diseases in animals, such as mastitis and foot rot. These approaches are expected to realize the full potential of nanotechnology in improving the health, nutrition and reproductive abilities of animals. Research publications on above topics may be found at - https://scholar.google.co.in/citations?user=sQr5shUAAAAJ&hl=en

Dr Madhuri Subbiah

Dr. Madhuri Subbiah's laboratory focuses on studying viruses such as Newcastle disease virus, Porcine circovirus and Porcine Reproductive and Respiratory Syndrome virus with three pronged approach, namely, (i) Viral assay biology (ii) Molecular viral epidemiology and (iii) Viral biologicals. Apart from basic molecular biology techniques involving DNA, RNA and protein, advanced tools such as reverse genetics and CRISPR/Cas are employed for these studies. The molecular biology work undertaken in this laboratory is aimed at enhancing the current understanding of viruses and the host-virus interactions. The ultimate emphasis is on translational research – for developing rapid on farm diagnostics, pan-antivirals and recombinant next generation vaccines against economically important animal viruses.

Dr Sonu Gandhi

Our lab is working mainly in two key areas.

1- To find out novel biomarkers for therapeutic treatment of disease-

Here, we are identifying new targets and making chimeric antagonists to block the certain pathways that help in the progression of the disease. The designed nanocarriers further boost the targeted delivery and subsequent therapy. The process involves cloning, expression, in-vitro and in-vivo analysis of developed antagonists. Preference will be given to the candidate with hands-on experience of molecular biology and nanotechnology techniques.

2- Biosensor development-

In this area, we are developing diagnostic assays using peptides/aptamers/antibodies, and biosensors for rapid detection of molecules of interest. The area involves in-silico analysis, chemical functionalization, and its analysis by various biophysical techniques such as TEM, SEM, Uv-Vis, DLS, FT-IR, XRD, AFM, XPS to name a few. The proposed area requires expertise and understanding in the area of sensor development based on lateral flow, electrochemical, optical, microfluidic, CRISPR to name a few.

Our lab is looking for highly motivated candidates who show interest in the interface of chemistry, biology, nanotechnology, and physics. Preference will be given to the candidate with hands-on experience of assay development.

Dr Shailesh Sharma

Dr. Sharma's research experience spans bioinformatics and structural biology, including application of data mining, application of bioinformatics tools, computational biology, and structure-activity relationships. His earlier work has included investigations into structural, functional and dynamic properties of metalloproteins. His research at NIAB will involve genome annotation, protein structure, target identification, and molecular dynamics simulations.

Long non-coding RNAs: Long non-coding RNAs are the RNA molecules which do not code for any proteins and have length more than 200 bases. They are transcribed by RNA Polymerase II, same as messenger RNA. Similar to mRNA, many lncRNA contain a 5' cap and some lncRNA can also have a 3' poly-A tail. Some long non-coding RNAs contain introns and undergo splicing similar to mRNA. Although they donot encode any proteins, they are involved in various cellular activities. They are relatively very unstable and are poorly conserved, while a few are known to be conserved. Long non-coding RNAs are involved in guiding the chromatin modifying complexes to specific genomic loci, providing molecular scaffolds, and regulating miRNA activity and gene expression. An increasing number of research publications are providing evidence that long non-coding RNAs mediate disease pathogenesis, thereby challenging the concept that protein-coding genes are the sole contributors to the development of diseases. Thus long non-coding RNAs have emerged as a major category of regulatory eukaryotic transcripts.

Presently we are focusing on following two topics:

1. Transcriptomic analysis to infer key molecular players involved during host response to NDV challenge in Leghorn and Fayoumi breeds of Gallus gallus

2. Analysis of RNA-Seq data for identification of lncRNA involved in sex determination of Bos Taurus

Dr. Nirmalya Ganguli

Gene and Protein Engineering Laboratory:

The theme of research of my laboratory is the generation of transgenic animals or animals with somatic genomic modification for using them as a bioreactor for the generation of biotherapeutics and nutraceuticals as well as a model system for the study of functional genomics of farm animals. We are also working on Germ cell/ Stem cell transplantation studies to explore avenues for the production of sperm with elite characteristics.

We have established methods for the generation of transgenic mice and working on extrapolating the same to establish new easier techniques for making transgenic farm animals. We are also working on developing new methods, based on various nanoparticles, for direct transfection of the mammary gland to alter the somatic genome of the mammary epithelial cells by CRISPR-Cas9 mediated genome engineering technique. We have established an Extensible Mammalian Modular Assembly (EMMA) cloning system for the generation of multicistronic mammalian expression vector based on synthetic biology approach for ubiquitous and cell/tissue-specific expression of the desired gene. We have developed an easy method of evacuation of testis from spermatogonial stem cells (SSC) in mice followed by transplantation and repopulation of isolated and cultured SSC in it. Parallelly we have established CRISPR-Cas9 based Knock-Out as well as Site Specific Knock-In in the genome of farm animals, specifically in goat.

We are using these technologies for generating transgenic animal bioreactor expressing biotherapeutics for human or animal, in the milk for an easy extraction process, increasing its affordability. We are also adopting these technologies for developing a platform enabling easy germline genomic modification through multiplex CRISPR-Cas9 mediated genome engineering for the production of sperm with the elite trait (transgenic sperm).

We are planning to undertake Next Generation Sequencing (NGS) of the whole transcriptome from Mammary Gland of Indian Goat for detecting differentially expressed mRNA/Micro RNA (miRNA)/Long noncoding RNA (lncRNA) in different lactational time followed by Functional Genomics Study of such transcripts in transgenic mice models.

We are also working on generation of transgenic mice model to addresses various problems related to production and reproduction in farm animals as well as to study functional genomics of farm animals.

Dr Sandeep Kushwaha

About Lab

Broad research focus of Dr Kushwaha's lab: a) to develop biological and computational resources to support livestock research in India (b) to develop methods and approaches for disease diagnosis and treatment by using advanced molecular and computational tools and techniques to support livestock production in India.

Current Research Area:

Dairy industry is the second largest economic activity in India and shares approximately 16.2% of the world milk production. But, bovine infertility is severely affecting milk production and profit worldwide. Various research studies were performed and identified a range of factors associated with bovine infertility, such as reproductive disturbance or disorder (ovarian aplasia and atrophy), physiological and hormonal imbalance, uterine infection, and nutritional deficiency, which may work separately or in combination. Late maturity age, reducing first service conception rate, low anestrus and conception rate in heifers, increasing calving interval and repeat breeding are the significant field observations in Indian dairy cattle. A large number of indigenous cattle (10.7%:6.05 million), crossbred cattle (7.8%: 1.26 million,) and buffalo (7.7%: 4.18 million) do not have single calving during their lifetime. The causes of infertility are not known because these animals look normal clinically. Since, the average annual maintenance cost of a non-reproductive dairy animal is approximately Rs 24,000/- in India. Therefore, 11.49 million non-reproductive animals cost around Rs 275,760,000,000 /- annually, a substantial non-recoverable economic loss of Indian dairy owners and farmers. Nowadays, bovine infertility is a major setback of the dairy industry which needs a strategic scientific research approach to understand the different causes of infertility.

Recent host-associated microbiome studies in humans showed significant influences of the host-microbiome on host health, physiology, development, digestion, and reproductive performance. Various microbiome studies in bovine were performed to explore the functional significance of microorganisms on cattle performance. However, studies to explore the potential of the microbiome causing infertility are minimal. Therefore, a functional understanding of the pervasive and non-pervasive microbial communities and pathogens associated with host organelles and its interplay between digestive and reproductive systems can help us to understand bovine infertility cases.

In this project, a strategic research plan will be conducted to explore microbial aspects of bovine infertility cases in India. This study will investigate infertility cases in the farm and clinical settings. Non-reproductive animals will be identified and used to collect biological samples such as vaginal fluid, rumen, faeces and blood samples for (Meta)-genomic and transcriptomics sequencings. To understand bovine infertility, hormones and biochemical profiling of animals will also be performed to correlate microbial communities association with animal's physiological and reproductive status.

Dr. Anand Srivastava

Dr. Srivastava laboratory is interested in Tick and Tick borne diseases and immunology of the ruminants. Currently he is working in the board areas such as host-pathogen interactions, vaccines, diagnostics and drug discovery.

PhD students are required in following research areas: Identification and characterization of CDK-cyclin pair in Theileria annulata and identification of small molecule inhibitor perturbing CDK-cyclin interactions

Summary: T. annulata and T. parva are only eukaryotes which can transform another eukaryotic cell i.e. host lymphocytes. Thus, the infected bovine lymphocytes have hallmarks of cancer. Further, this parasite has developed an ability to synchronize its cell division with the host cell by an unknown mechanism. In order to induce transformation in host cell and to synchronize it cell division along the host, parasite must regulate its cell division. However, there is a gap in the knowledge about how this parasite regulate its cell division in the infected host cells. In this project we will attempt to fill these gaps.

Dr. Srivastava laboratory regularly uses techniques such as, cloning and mutagenesis, protein expression and purification, genetic manipulation, bioinformatics, protein-protein interactions, Yeast two hybrid techniques, Proteomics and transcriptomics. The incumbent will be allowed to choose topic of their research in the broad area as mentioned above.

Dr HBD Prasada Rao

Mammalian oocytes can be very long-lived cells. Consequently, throughout their lifespan, they are highly likely to experience DNA damage. Failure to detect and repair this DNA damage or trigger cell death to remove damaged oocytes could cause severe problems that result in embryonic death or congenital disorders. Given the fact that each human cell undergoes ~ 70000 lesions per day. Most lesions (75%) are single-strand DNA (ssDNA) breaks, which can arise from oxidative damage during metabolism or base hydrolysis. ssDNA breaks can also be converted to DNA double-strand breaks (DSBs), which although much less frequent, are more dangerous. Despite the importance of DNA damage for reproductive capacity, the molecular mechanisms in oocytes remain poorly characterized. Dr. Prasad's laboratory is interested in studying the molecular mechanisms of DNA damage and repair pathways which may further pave the way for developing diagnostics and therapeutics for reproductive problems.

Dr. Pankaj Suman

The Pankaj lab brings together interdisciplinary experimental approaches to engineer aptamer and antibodies to tackle major challenges in animal health and production through development of advanced microfluidic devices, sensors and diagnostics. A dynamic collaborative research team is handling projects aiming to develop technologies in a variety of contexts through development of rapid apatmer selection strategies, generation of monoclonal antibodies, understanding the role and diversity of phages (viruses) in ruminant digestion, point-of-care testing of venom, antibiotic, mastitis; microneedle-assisted transdermal delivery of hormones, drugs and antibodies. In past, his basic research efforts have led to development of a versatile method for aptamer selection and characterization without need of high end equipments and facilities. Using this technology, several field applicable and farmer centric products have been developed that include an aptamer based lateral flow device for detection of antibiotic (oxytetracycline) in milk and meat, diagnostic kit for early detection of subclinical mastitis and microbial quality of milk, point-of-care diagnostics for differential detection of snake venom using antibodies and aptamers.