REVISED PROPOSAL

DBT-University of Hyderabad

School of Life Sciences for Advanced Research and Education

Under Up-Gradation/Re-engineering/Re-modeling/ Creation of Boost to University Interdisciplinary Life Sciences Department for Education and Research program (DBT-BUILDER)

Submitted

by

School of Life Sciences

University of Hyderabad

Principal Investigator:

Dean, School of Life Sciences

University of Hyderabad

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Overview

School of Life Sciences includes the Departments of Biochemistry, Plant Sciences, Animal Biology, Biotechnology & Bioinformatics and Computational and Systems Biology. The School offers several Masters' programs, Integrated Masters' and PhD programs and M. Tech in Bioinformatics. Research has been an active component of the academics in the School, with a total of 240 Ph.D. scholars and 25 Post -Doctoral fellows. Considerable advances in teaching and research were made with support from the DBT-CREBB program in 2007. There is a need to replace several of the obsolete equipments, establish essential facilities including Animal House, Green House, pathogen facilities and purchase sophisticated hardware and software for bioinformatics. In addition, basic infrastructure, equipments for teaching are needed for the newly-formed Department of Systems Biology and Computational Biology. Hence, the present proposal is being submitted to DBT for funding under the Builder Program.

The School of Life Sciences comprises of 56 faculty members and they can be categorised broadly into five thematic groups owing to their overlapping expertise, as given below:

1. **Bioresources and innovations**: focus is to explore the biological resources for production of compounds and products useful for agriculture, environment and human health.
2. **Intra- and inter-cellular communications**: an integrative and fundamental approach to understand how signals generated either within or received from outside are communicated between various organelles to mount a coordinated cellular response.
3. **Post-translational modifications: role in pathogen biology and pathogenesis**: focus is to study PTMs in both the pathogens and the host to identify and characterize post-translationally modified proteins, PTM-modified protein interaction networks and associated post-translational modification of host signaling interactive pathways.
4. **Molecular cancer therapeutics**: a molecular therapeutic approach involving synthetics, biologicals, stem cells and natural products to design drugs against specific pathways and targets involved in promoting tumor microenvironment to overcome drug resistance and metstasis.
5. **Structural, Computational and Systems Biology:** The converging aim of this group is to explore spatio-temporal organisation of different biomolecular components, their regulation and interactions that give rise to different emergent properties (disease and health) of living systems in different milieu and niche.

a) Name of the University with address: **University of Hyderabad, Gachibowli, Hyderabad 500046, Telangana**

b) Status of the University: **Central University**

c) Title of the proposed centre: **DBT-University of Hyderabad School of Life Sciences for Advanced Research and Education**

d) Details of existing departments related to Life Sciences:

i. Name of existing departments

a) Department of Biochemistry

b) Department of Plant Sciences

c) Department of Animal Biology

d) Department of Biotechnology and Bioinformatics

e) Department of Computational and Systems Biology

ii. Existing facilities/infrastructure/equipment (Enclosure-1)

- Genomics Facility, Proteomics facility, Metabolomics Facility, Green House, Large scale protein purification facility are established under DBT-CREBB in 2007
- BSL-3 facility was established utilizing funds from DBT-CREBB, DBT-UoH CoE (MTb) and University funds. The facility is catering to the needs of SLS, UoH and NIAB.
- Bioinformatics Infrastructure Facility established under DBT Bioinformatics Program in 2006
- Microscopic / Radioactivity / Animal cell culture / Plant Cell Culture facilities was established from funds made available from UGC-UoH
- A dedicated skill development centre is established by UoH to train fresh graduates and postgraduates in Biology and Biotechnology to aquire skills required for obstining employment in Industry and Biotechnology start-up establishment.

- A state –of- the- art Animal House is constructed with funds sanctioned from the University resources.

iii. Number and Level of faculty and students

a) **Faculty**

S.No	Designation	Total number
1.	Professors	28
2.	Associate Professors	4
3.	Assistant Professors	27
4.	UGC-FRP faculty	4

b) **Students**

S.No	Course	Discipline	Annual-Intake	On roles
1	M.Sc	Biochemistry	26 + 2	28
2	M.Sc	Plant Biology & Biotechnology	22	22
3	M.Sc	Animal Biology & Biotechnology	18 + 2	16
4	M.Sc	Biotechnology	25	10
5	M.Sc	Molecular Microbiology	15	12
6	M.Tech	Bioinformatics	24	13
7	PhD	Biochemistry/ Plant Sciences/ Animal Biology/ Biotechnology/ Computa-tional and Systems Biology	54	272
8	Integrated M.Sc/PhD	Biotechnology/ Biochemistry and Molecular Biology	12	12
9	Integrated B.Sc / M.Sc	MSc Systems Biology (5 years)	16	40
11	PDF	Respective areas of study	--	27

iv. Areas of research being pursued with details of the projects (Ongoing Project operated by faculty in Enclosure-2)

Name of faculty member	Research area	Projects For the past 5 years		Publications	
		Completed	Ongoing	Total	Past five years
Akash Gulyani	Cellular Dynamics and Imaging, Biosensors	2	1	18	13
Akif, Md	Structural Biology & Molecular Recognition, Molecular Basis of infectious disease & host-pathogen interaction, Structural Vaccinology	2	1	17	4
Anil Kumar, P	Diabetic Complications	2	3	37	21
Arun Kumar, K	Plasmodium berghei	3	1	19	7
Arunasree, MK	Epigenetics: Basic & translational research	6	1	47	23
Banerjee, Sharmistha	Mycobacteria and HIV	5	4	37	20
Bhattacharyya, Mrinal K	Biology of malaria parasites	5	2	27	12
Bhattachayya, Sunanda	DNA damage-induced singaling pathways and epigenetic regulation of gene expression	5	1	20	10
Dayananda, S	Membrane Transport / biodegradation / bioremediation	3	5	55	15
Ghazi, IA	Rice Functional Genomics, Anticancer properties of Medicinal Plants	2	1	25	11
Gopinath, K	Melon necrotic spot virus and Papaya ringspot virus	2	0	29	2
Jagota, Anita	Aging, Neurodegeneration and Clock Dysfunction	13	1	44	15
Khan, Nooruddin	Dengue, Influenza	7	2	19	13
Kiran, Manjari	Computational Systems Biology	0	0	13	9
Kondapi, AK	Drug and Biologic development and delivery against communicable and non-communicable diseases	5	1	85	34
Sreenivasulu, K	Chromatin dynamics and modelling	6	2	17	6
Madhu Babu, GB	Neurodegeneration and Behavioral Neuroscience	1	1	2	1
Madhuprakash, J	Microbial Biotechnology (Enzyme Discovery and Engineering)	1	1	13	13

Makandar, Ragiba	Signaling mechanisms of plants	3	0	24	7
Manavathi, Brahmanandam	Cancer Biology	4	2	44	11
Mishra, Krishnaveni	Epigenetics and nuclear architecture	3	1	16	5
Mishra, Seema	Computational Systems Biology and Structural Bioinformatics	0	1	25	8
Mishra, Parul	Regulation of protein homeostasis in cancers and neurodegenerative disorders	0	2	11	6
Maurya, Radheshyam	Leishmaniasis	3	1	30	18
Moumita Saharay	Bioinformatics	0	0	20	6
Nadimpalli, Siva Kumar	Glycobiology, nanotechnology	6	2	86	25
Nagarajaram, HA	Computational and systems biology	2	1	75	22
Padhi, Santosh K	Biocatalysis & protein engineering	2	2	19	6
Padmaja, G	Plant Genetics and Biotechnology	2	0	28	10
Padmasree, KPS	Plant Biochemistry & Biotechnology	5	0	53	15
Podile, Appa Rao	Molecular plant microbe interactions; Microbial biotechnology in agriculture	4	2	92	37
Pongubala, Jaganmohan Rao	Systems Immunology	2	1	26	1
Prabhu, NP	Protein folding and dynamics	3	2	28	18
Prakash Babu, P	Glioma and stem cell therapy in CNS and PNS	2	5	76	30
Prakash, JSS	Functional genomics of cyanobacteria	6	3	29	5
Pramod Rajaram S	Bioinformatics	0	0	11	10
Qureshi, IA	X-ray structural elucidation of proteins of immunological significance from human pathogens	2	2	37	21
Raghavendra, AS	Redox signaling in plant cells	5	4	224	22
Rahul Kumar	Plant functional genomics & Biotechnology	2	1	21	13
Rajagopal, S	Structural Biology & Biophysics	6	4	84	34

Ramaiah, KVA	Molecular Biology, Translational regulation, Cellular Signaling, Protein and Cellular Homeostasis	2	1	35	5
Gutti, Ravikumar	Stem Cell Biology,Developmental Biology, Signal transduction, Epigenetics, Molecular and translational medicine.	7	3	42	27
Muthamilarasan M	Molecular genetics and genomics of underutilized crops	0	2	63	29
Reddanna, P	Eicosanoids, Inflammation and Cancer	5	1	195	27
Reddy, Aramati BM	Cell signaling and gene regulation Mechanism involved in glaucoma and metabolic complications, viz. diabetes	3	1	32	6
Roy, Rajaramohan	Epithelial Biology	0	1	28	5
Shashi Kiran	Protein ubiquitination and deubiquitination in cellular processes and disease	0	0	11	6
Santhosh, RK	Epigenetics and cell signaling, lectin biology	3	1	25	14
Senthilkumaran, B	Molecular Endocrinology and Reproductive Biology	2	4	125	26
Sepuri, Naresh BV	Mitochondrial redox biology, retrograde signaling	4	4	30	12
Sivahari Prasad, Gorantla	Leukemia models and novel therapeutic approaches	1	1	8	4
Sharma, RP	Tomato functional genomics	3	4	99	21
Singh, Pankaj	Biological data modelling &mining	0	1	6	4
Sreenivasulu Y	Plant Reproductive Biology	0	9	28	15
Srilakshmi, Y	Tomato functional genomics	4	2	36	21
Sritharan, Manjula	Tuberculosis and Leptospirosis	5	2	48	12
Suresh, Y	Reproductive Biology	2	5	46	13
Tammineni, Prasad	Membrane Trafficking and Organelle Quality Control	1	1	15	12
Tetali, Sarada Devi	Molecular Phytomedicine	5	0	34	11
Thakur, Vivek	Computational Systems Biology	0	1	12	5
Venkata Ramana, Ch	Bacterial diversity & innovations	1	2	212	96
Venkataramana, M	Dengue	3	2	12	3

Vijay Morampudi	Host-Commensal-Pathogenic Interactions, Intestinal Inflammation	0	0	15	7
Vindal, Vaibhav	Computational &Functional genomics	3	0	12	5

e) Proposed Research groups in emerging areas of Life Sciences

i) Title of the proposed research groups

a. Bio-resources and Innovations

b. Intra- and Inter-Cellular Communications

c. Post-Translational Modifications: Role in Pathogen Biology and Pathogenesis

d. Molecular Cancer Therapeutics

e. Structural, Computational and Systems Biology

ii) Research Group Leaders along with their biodata

- **Principal Investigator: Prof. S. Dayananda, Dean, School of Life Sciences, University of Hyderabad**

- **Co-Investigator:**
  - **Prof. N. Siva Kumar, Dept Biochemistry, School of Life Sciences**
  - **Prof. Naresh Babu V Sepuri, Department of Biochemsitry, School of Life Sciences (Coordinator)**

- **Research Teams and Team Leaders**

a. Bio-resources and Innovations: Prof. Ch. Venkata Ramana

b. Intra- and Inter-Cellular Communications: Prof. Naresh V. Sepuri

c. Post-Translational Modifications: Role in Pathogen Biology and Pathogenesis: Prof. Manjula Sritharan

d. Molecular Cancer Therapeutics: Prof. Anand K. Kondapi

e. Structural, Computational and Systems Biology: Prof. H.A. Nagarajaram

iii) Name of Participating Departments for each Team

a. Bio-resources and Innovations (Depts of Plant Sciences, Animal Biology & Biotechnology and Bioinformatics)

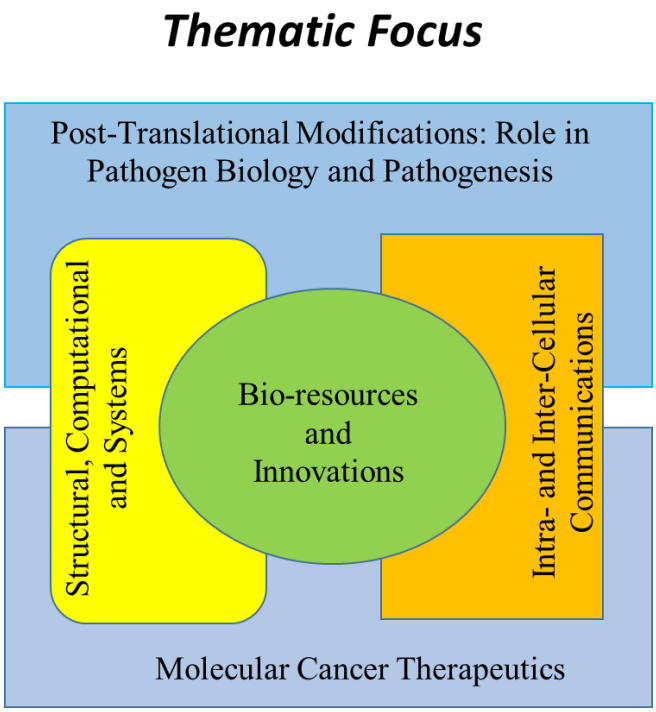
b. Intra- and Inter-Cellular Communications (Depts of Biochemistry, Plant Sciences, Animal Biology & Biotechnology and Bioinformatics)

c. Post-Translational Modifications: Role in Pathogen Biology and Pathogenesis (Depts of Biochemistry, Plant Sciences, Animal Biology & Biotechnology and Bioinformatics)

d. Molecular Cancer Therapeutics (Depts of Biochemistry, Animal Biology & Biotechnology and Bioinformatics)

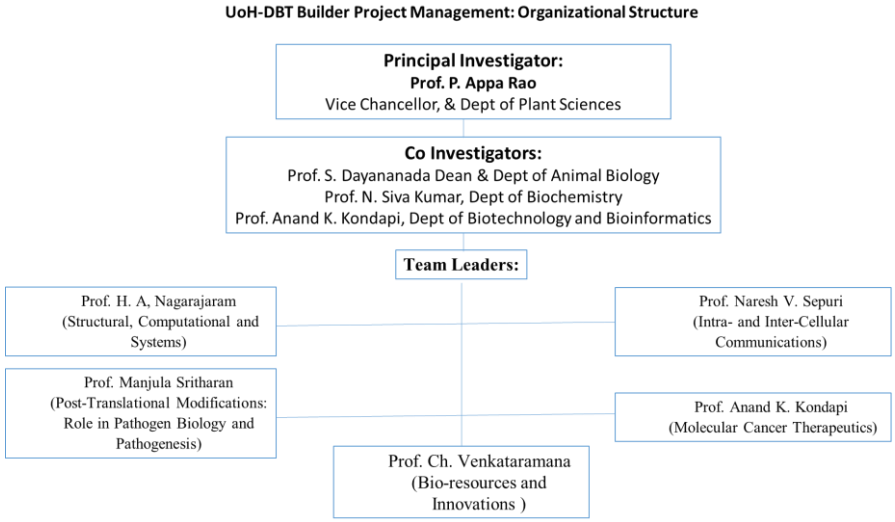
e. Structural, Computational and Systems Biology (Depts of Biochemistry, Plant Sciences, Animal Biology, Biotechnology and Bioinformatics & Department of Computational and Systems Biology)

iv) **Details of the faculty involved in each thematic area**
(Group leaders are show in bold)



The proposed project focuses on identification of novel targets, potential agents and their scale-up and industrial applications by integrating five research teams. Each team while working on the proposed research component collaborates with other teams to achieve a viable outcome. The results obtained through collaborations will be translated by Technology Enabling Centre to develop into commercially viable product. The manpower trained will be encouraged to start entrepreneurial activity through a Innovation club at Traslation Core Facility developed by the School of Life Sciences.

***Project Management**: PI will be involved in overall project management, while Coinvestigators will be associated in the infrastructure development, manpower training and coordination of research components under thematic focus area, which will be implemented by Team Leaders through respective groups. Following organization structure is proposed:*



1. Bio-resources and Innovations

1.1 Investigators: SD, Prof. S. Dayananda; ARP, Prof. Appa Rao Podile; **CHVR, Prof. Ch. Venkata Ramana**; GP, Prof. G. Padmaja; SDT, Prof. Sarada Devi T.; KPS, Prof. K. Padmasree; JSSP, Prof. J.S.S. Prakash;SRK, Dr. Santosh R. Kanade; IAG, Dr. Irfan Ahmad Ghazi;RK, Dr. Rahul Kumar; JM, Dr. J. Madhuprakash

1.2 Overview: Plants and microbes not only serve as resources for human survival but also inspire innovations, serve as model systems for understanding biology thereby developing biomimetics / technology needed for advancing in the sectors of agriculture, medicine and environmental management. They are natural factories of wide range of chemical compounds, with many of these compounds synthesized for their defense and adaptation to abiotic/biotic stress conditions. These compounds offer tremendous value owing to their nutritional and pharmacological activities in treating various health ailments. Diversity of microorganisms is greater by several orders of magnitude than plant species. Microbial derived compounds also play a significant role in drug discovery and other high value compounds. Based on this background, the study aims at discovering novel microbial species and screening of diverse plant/microbial species for novel proteins/metabolites, and development of platforms for large scale production of useful proteins and products for exploitation in the areas of agriculture, medicine and biomass conversion.

The School of Life Sciences has microbial repository with a rich collection of bacterial diversity from all over the country (ARP, CHVR). The collection consists of several new/novel bacteria which have been well characterized taxonomically and the genomes of almost 50 bacteria have been sequenced. The uniqueness of this repository is having a large collection of anaerobic bacteria and members of phyla which were previously unexplored (CHVR) will be explored in this study. The microbial resources with genome sequence databases available globally and existing novel or yet to discover bacterial strains will be optimally used to discover commercially useful enzymes and products. These microbial resources will be the major source for the team to work

on identification and engineering of novel enzymes which have implications in biofuel production (SD, JM), valorization-of-chitin, particularly the transglycosylation based approaches for the production of long-chain chitooligosaccharides for improving plant health (ARP, JM). In addition, the group members will also aim at developing biofertilizers and nano-fertilizers for betterment of agriculture with a focus on nitrogen fixation (ARP) and phosphate solubilization (JM, RK). In addition to the exploitation of bacterial diversity, the team with expertise in heterologous expression and downstream processing will use novel expression systems such as *Sphingophyxis wildii* (SD) and cyanobacteria (JSSP) for coding enzymes involved in scarification (SD, JM), chitinases (JM) for the production of these commercially important enzymes. The research also aims at achieving sustainable yield increases by deploying rhizobial strains with high nitrogen fixing capacity and phosphate solubilizing bacteria and development of alternate fertilizers to improve the nutrient use efficiency in crop plants. Research is also directed towards development of formulations for the management of lepidopteran insects using recombinant Bowman-Birk inhibitors expressed in *Synechocystis* / bacteria / *Pichia pastoris* (KPS, JSSP, SDT).

The team (GP, SDT, IAG, SK) working on medicinal plants would be also a part of this theme, who have identified specific secondary metabolites with therapeutic value. Exploitation of these medicinal plants as a source of secondary metabolites endangers their existence. Therefore, the team would like to exploit *in vitro* plant cell culture strategies for enhancing the production of valuable secondary metabolites and identify the biosynthetic pathways associated with their synthesis. The alternate expression systems for scaling up the production of secondary metabolites in a cyanobacterium, *Synechocystis* (JSSP) would also be explored particularly when biosynthetic pathway already exists in the bacterium as expression of minimal genes from medicinal plants should be able to reorient the existing metabolic pathways to produce bioactive molecules in *Synechocystis*.

1.3 Objectives

1) Discovery and development of products for sustainable agriculture.
2) Identification and discovery of pharmacologically active biomolecules from plants and microbes and development of strategies for their enhanced production.

1.4 Technical approach

1.41 Sustainable Agriculture solutions: India is an agriculture-based country and better productivity can be achieved through efficient utilization of resources and reduction in crop losses due to pests and pathogens. The crop production is largely limited by low phytoavailability of essential mineral elements. Post green-revolution, agriculture has become hugely dependent on application of mineral fertilizers for optimum yield of crops. The over-use of nitrogen and phosphorous fertilizers has serious ecological implication. Thus, alternative sources/solutions are needed to reduce the fertilizer use and improve the nutrient availability for achieving higher crop yields. The exploitation

of rhizobial strains (free living and nodule associated) of leguminous plants with high nitrogen fixation efficiency (ARP) and phosphorous solubilizing bacteria (JM) and development of phosphate nano-fertilizers (RK) offer promise in improving crop yields. The exploitation of induced resistance through efficient and large-scale production of chito-oligosaccharides using recombinant bacterial chitinases as an alternative for crop protection would be investigated (ARP, JM). The use of plant-based Bowman-Birk inhibitors as biopesticides through development of formulations for protection of crops against lepidopteran insects (KPS) would also be explored.

1.411 Microbial biotechnology in agriculture: Investigations on selection of superior rhizobial strains associated with pigeonpea, phosphate solubilizing bacteria and nano fertilizers, and domain shuffling/swapping of recombinant bacterial chitinases, bioprocess development for production of chitooligosaccharides by enzymatic methods would be carried out with specific objectives of (1) selection of optimal pigeon pea-rhizobia combinations for improved nodulation, nitrogen fixation and grain yield (ARP), (2) characterization of identified phosphate-solubilizing bacteria for their growth promoting effects in plants growing under low Pi availability and development of phosphate-nanofertilizers formulations for enhanced nutrient use efficiency (NUE) in plants (RK, JM), (3) production of long chain chitooligosaccharides (CHOS) using recombinant bacterial chitinases for inducing plant immunity (ARP, JM).

1.412 Development of formulations using Bowman-Birk inhibitors to manage lepidopteran insects: Bowman-Birk inhibitors (BBI) purified from black gram seeds were found to inhibit the growth and development of polyphagous pests, *Helicoverpa armigera* and *Spodoptera litura* (unpublished data, KPS). Investigations on production of recombinant BBI-isoforms will be carried out towards development of formulations for controlling insect pests. The research team (KPS, JSSP, SDT) would work together for achieving this research goal. The genetic tools developed in the laboratory (JSSP) with *Synechocystis* will be utilized for enhanced production of plant protease inhibitor for use in formulations to control insect pests in black gram. The specific objectives are: (1) isolation and characterization of full-length gene sequence of various BBI-isoforms from immature seeds of black gram (2) cloning and scaling up of BBI-isoforms using suitable expression systems (3) purification of recombinant BBI-isoforms and testing their insecticidal efficacy individually or in combination on different lepidopteran pests using *in vitro* and *in vivo* bioassays.

1.42 Medicinal and other high value compounds from plants and microbes: Plants and microbes synthesize structurally diverse chemical compounds that function in their defense and interactions with environment. The secondary metabolites produced by plants and microbes are of great interest to human beings as they support good health by preventing and/or curing of various diseases. These compounds have capacity to interact with human physiology by modulating their biochemical pathways, gene expression and also epigenetics. Thus, several plant and microbial species are bioresources for neutraceuticals, drugs and several other high value compounds. Most of

the high value compounds are produced for their defense against biotic and abiotic stresses and often their abundance is low. Biosynthetic pathways as well as environmental cues that trigger the production of several of these compounds remain unexplored. A combined approach using genetic, biochemical and molecular tools in understanding their synthesis and use of different platforms such as plant cell cultures and *Synechosystis* for their enhanced production would be explored (GP, SDT, JSSP, SRK, IAG).

1.421 Bacterial diversity and innovations: The rich repository of bacterial diversity of India with a unique collection of anaerobic bacteria and unexplored wealth of members from rare phyla's (Planctobacteria, Acidiobacteria, Spirochaeta) and yet to discover bacterial diversity using culture dependent (pure and culturomics) and independent (metagenomics) would be the major source for high value compounds in the sectors of environmental and human health. Major focus is on cultivating some of the unique taxa of rare phyla and explore their potentials in environmental and human health. Work will be carried out with specific objectives to (1) discover, index, catalogue, biogeography and exploit the bacterial wealth of India for environmental and human health (CHVR).

1.422 Bioactive potential of secondary metabolites: The medicinal plants that are widely used in traditional medicine are selected for the study with the goal to isolate the bioactive compounds that have the potential to be used for treating cardiovascular and inflammatory diseases, cancer and as epigenetic inhibitor/modulator targeted for epigenetic therapy. The major focus is on medicinally important plant species such as *Terminalia arjuna, Givotia moluccana, Pterocarpus santalinus, Piper nigrum, Butea monospera, Rauwolfia serpentina* and *Artemisia* species, which are traditionally used for treating several diseases including inflammatory and cardiovascular diseases. The rice bran of pigmented rice would also be used as it is reported to improve human health because of anti-allergic, anti-mutagenic and anti-carcinogenic effects. The research labs (GP, SDT, SRK, IAG) are well established for medicinal plant-based studies and have identified important bioactive compounds from few of these species. These findings form the basis for present research that is interdisciplinary in nature and the team with diverse expertise and backgrounds (GP, SDT, JSSP, SRK, IAG) are involved for translating the results into products for the benefit of human beings. The research goals will be achieved by working on specific objectives of (1) isolation and characterization of the bioactive compounds from medicinal plants using bioassay guided fraction method and assessment of their pharmacological activities against cardiovascular and anti-inflammatory diseases, cancerand epigenetic-based therapeutics activities using *in vitro* systems. The pharmacological activities of the compounds against atherosclerosis, a cardiovascular disease would be assessed using cultured human cells (THP-1 monocytic cells and aortic endothelial cells) having role in atherosclerosis development (2) enhancement of selected bioactive compounds from plant cell cultures by elicitation treatments and gene discovery associated with their biosyn-

thesis using transcriptome and metabolomic approaches (GP, SDT, SK, IAG). (3) explore the phytochemicals as a potential epigenetic inhibitor/modulator targeted for epigenetic therapy (SRK), (4) Try to scaling up the production of selected bioactive compounds using *Synechocystis* as a platform (JSSP).

1.423 Photosynthetic cyanobacterium *Synechocystis* as a platform for efficient production of medicinally and agriculturally important plant compounds: Plants produce various secondary metabolites like alkaloid, phenolic and terpenoid compounds to perform diverse range of biological functions. Although some of these compounds have essential functions in primary photosynthetic process, some of them are secondary metabolites having roles in biotic and abiotic stress responses. Majority of these secondary metabolites have medicinal and commercial values. Cyanobacteria are considered to be progenitors of plant- chloroplasts, share common pathway for terpenoid synthesis. However, certain terpenoid skeletal modifying enzymes do not exist in cyanobacteria. But these modifications are evolved in certain higher plant species. Since, cyanobacteria are easily amenable to genetic and metabolic manipulations, the genetic tools developed in the laboratory (JSSP) would be used to express relevant genes that encode terpene-modifying enzymes such as cyclases, hydroxylases isolated from plants for the production of medicially important secondary metabolites, triterpenoids in *Synechocystis* (Fig. 1). These genes will be mobilized and integrated into the neutral site (*slr2030-31)* of the *Synechocystis*-genome. Several important bioactive compounds have been identified in *Terminalia arjuna* (SDT). It is proposed to express the relevant genes known to be involved in the synthesis of modified terpernoids, eg. Arjunolic acid in the *Synechocystis* using the genetic tools developed in the laboratory (JSSP).

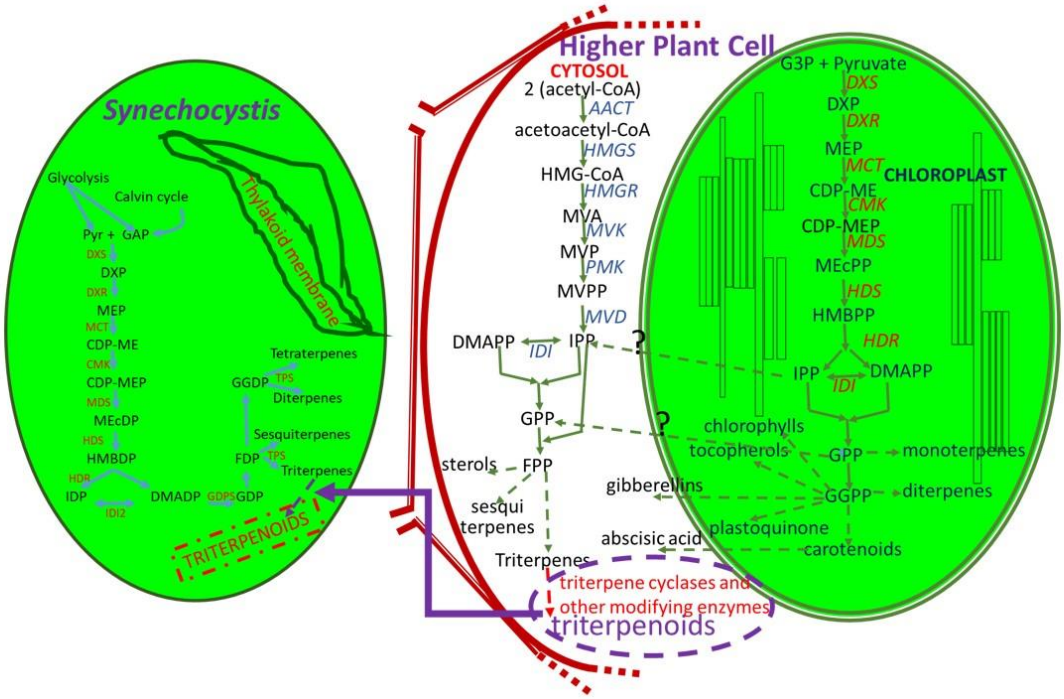


Figure 1. Isoprenoid biosynthetic pathway in *Synechocystis* and higher plants.

A series of plasmid vectors for both expression of gene(s) by integrating them into the *Synechocystis*-genome at a neutral site and also in a stable plasmid based controllable expression were developed (JSSP). The plasmid vectors were designed in such a way that the gene or cluster of genes cloned into *Synechocystis* strain could be expressed under the control of Cobalt, Copper or light inducible promoters. The advantage of using *Synechocystis* for gene cloning and / or pathway engineering, is that it is naturally transformable and genetic manipulations are much easier than other bacterial hosts. The research group of JSSP developed genetic tools for integrating gene(s) or cluster of genes in to the neutral genome sites of *Synechocystis*-genome by sequential cloning. Currently the group of JSSP with the support of DBT, has been attempting to introduce entire pathway of a secondary metabolite, Scytonemin by integrating a large gene cluster (23 Kbp DNA fragment having 18 gene-cluster) from the genome of *Nostoc punctiforme*, which encode for enzymes involved in the biosynthetic pathway, in to the genome of *Synechocystis.* Thus this group has all the expertise to inactivate and / or over express selected gene(s) to alter / divert a selected pathway to enhance the substrate(s) level for production of desired secondary metabolite by genetic and metabolic engineering.

These studies will help in developing innovative technologies and platforms for biomass conversion and biofuel production.

1.431 Enzyme discovery and engineering for efficient use of recalcitrant polymers like cellulose and/or chitin and enhanced production of biomolecules using alternate platform: Novel enzymes will be identified for biomass conversion/degradation/recycling: The enzymatic conversion of lignocellulose requires the concerted action of a battery of enzymes which are exquisitely tailored to tackle the complexity of a co- and heteropolymeric, partly insoluble and even crystalline substrate. The classical model for enzymatic depolymerization of cellulose entails the synergistic action of exo-acting processive glucanases (or cellobiohydrolases) and endo-glucanases. The recent discovery of the Lytic Polysaccharide Monooxygenases (LPMOs) has changed this classical paradigm. These novel enzymes, including members acting on chitin, cellulose, hemicelluloses and starch, are abundantly encoded in microbial genomes and are expected to have a variety of novel functions that remain to be discovered. In view of this, the present project aims at generating novel insights into LPMO functionality by studying the LPMO machineries of one fungus and/or one bacterium. Work will be carried out with specific objectives of (1) screening of different microbial isolates for novel LPMOs for biomass utilization (JM), (2) in-depth characterization of selected LPMOs: Activity; substrate specificity; effects of pH, temperature and the type of electron supply; affinities for copper and substrate; structure-function studies of selected LPMOs (JM), (3) discovery of bacteria for fermentation of pentoses and production of enzymes involved in scarification process for biofuel production

(SD, JM), (4) establishment of novel expression systems such as *Sphingopyxis wildii* and *Synechocystis* for scale-up production of industrially important cellulases/chitinases/LPMOs (SD, JSSP, JM).

1.5 Expected outcome: The studies outlined by the group of 'Bioresources and Innovations' would lead to: (a) selection of best combinations of pigeon pea genotypes and specific rhizobia would aid in boosting pigeon pea production as well as improve its seed protein content, (b) selection of efficient phosphate solubilizing bacteria and development of alternative phosphate fertilizers with enhanced phosphate use efficiency, (c) improved production of long-chain chitooligosaccharides for elicitor activity to boost plant immunity, (d) development of formulations using recombinant Bowman-Birk inhibitors to combat both host (*Helicoverpa armigera*) and non-host (*Spodoptera litura*) insect pests in black gram, (e) discovery of novel bacterial taxa and metabolites useful for human health and environment, (f) identification of pharmacologically important bioactive compounds, (g) their enhanced production using plant cell culture based approaches, (h) production of commercially important enzymes involved in biomass conversion and biofuel generation using novel expression systems such as *Sphingophyxis wildii* and *Synechocystis*.

1.6 Technology development: The following is anticipated from the research work to be undertaken by the group of 'Bioresources and Innovations': (a) contribution of native and inoculated competitive rhizobial strains with respect to yield enhancement will be known, as well as the selection of superior rhizobial strains would help in increasing the yield/productivity of pigeonpea and other related legumes, (b) exploiting the phosphate solubilizing bacteria and development of nano-based phosphate fertilizer would improve the nutrient use efficiency and contribute towards sustainable agriculture, (c) scaling up of chitooligosaccharide production at low cost will allow field application for enhancing the plant immunity to pathogens, (d) scaling up the production of Bowman-Birk inhibitors using alternate expression platforms *i.e.*, *Synechocystis* would aid in developing formulations for controlling insect pest community in blackgram (production of bioactive compounds for industrial applications,

1.7 Selected (recent) publications:

1. Sravani A, Rani TS, Podile AR (2018) Changes in root exudates and root proteins in groundnut–Pseudomonas sp. interaction contribute to root colonization by bacteria and defense response of the host. J. Plant Growth Regul. Doi: 10.1007/s00344-018-9868-x.
2. Sravani A, Rani TS, Podile AR (2018) Partner-triggered proteome changes in the cell wall of Bacillus sonorensis and roots of groundnut benefit each other. Microbiol. Res. 217: 91-100.

3. Vaikuntapu PR, Mallakuntla MK, Das SN, Bhuvanachandra B, Ramakrishna B, Nadendla SR, Podile AR (2018) Applicability of endochitinase of Flavobacterium johnsoniae with transglycosylation activity in generating long-chain chitooligosaccharides. Int. J. Biol. Macromol. 117: 62-71.
4. Ramakrishna B, Vaikuntapu PR, Mallakuntla MK, Bhuvanachandra B, Sivaramakrishna D, Uikey S, Podile AR (2018) Carboxy-terminal glycosyl hydrolase 18 domain of a carbohydrate active protein of Chitinophaga pinensis is a non-processive exochitinase. Int. J. Biol. Macromol. 115: 1225-1232.
5. Madhuprakash J, Dalhus B, Rani TS, Podile AR, Eijsink VGH, Sørlie M (2018) Key residues affecting transglycosylation activity in family 18 chitinases: Insights into donor and acceptor subsites. Biochemistry. 57: 4325-4337.
6. Bhuvanachandra B, Madhuprakash J, Podile AR (2018) Active-site mutations improved transglycosylation by chitinase-A from Stenotrophomonas maltophilia. BBA Proteins and Proteomics. 1866: 407–414.
7. Madhuprakash J, Dalhus B, Vaaje-Kolstad G, Sakuda S, Podile AR, Eijsink VGH, Sørlie M (2019) Structural and thermodynamic signatures of ligand binding to the enigmatic chitinase D of Serratia proteamaculans. J. Phys. Chem. B.123: 2270-2279.
8. Manjeet K, Madhuprakash J, Mormann M, Moerschbacher BM, Podile AR (2019) A carbohydrate binding module-5 is essential for oxidative cleavage of chitin by a multi-modular lytic polysaccharide monooxygenase from Bacillus thuringiensis serovar kurstaki.Int. J. Biol. Macromol. 127: 649-656.
9. Parthasarathy S, Gudla R, Dayananda S (2017) Evolution of phosphotriesterases (PTEs): How bacteria can acquire new degradative functions? Proc. Indian Natn. Sci. Acad. 83: 865-875.
10. Parthasarathy S, Parapatla H, Dayananda S (2017) Topological analysis of the lipoprotein organophosphate hydrolase from Sphingopyxis wildii reveals a periplasmic localization. FEMS Microbiol Lett. 364: 19, 187.
11. Ramurthy Gudla, Guruprasad Varma Konduru, Hampapathalu Adimurty Nagarajaram, and Dayananda Siddavattam* (2019) Organophosphate hydrolase interacts with Ton components and targets membrane only in presence of ExbB/ExbD complex, FEBS Letters, 593, 581-593.
12. Lakshmi Prasuna M, Mujahid M, Sasikala Ch and Venkata Ramana Ch (2019) Pyomelanin production: Insights into the incomplete aerobic L-phenylalanine catabolism of a photosynthetic bacterium, Rubrivivax benzoatilyticus JA2. Int. J. Biol. Macromolecules. (In press; https://doi.org/10.1016/j.ijbiomac.2018.12.142)
13. Tushar L, Indu B, Sasikala Ch and Venkata Ramana Ch (2019) Transcriptome analysis of hopanoid deficient mutant of Rhodopseuodomonas palustris TIE-1. Microbiol. Res. 218: 108-117.
14. Lakshmi VNS, Tushar L, Maaged A, Lalitha G, Sasikala Ch and Venkata Ramana Ch (2018) Insights into the carbonic anhydrases and autotrophic carbon dioxide fixation pathways of high CO2 tolerant Rhodovulum viride JA756. Microbiol. Res. 215: 130-140.
15. Suresh G, Lakshmi KVNS, Tushar L, Sasikala Ch and Venkata Ramana Ch (2018) Rhodobacter alkalitolerans sp. nov. isolated from an alkaline fresh water pond. Arch. Microbiol. 200: 1487-1492.

16. Ramaprasad EVV, Ganesh M, Sasikala Ch and Venkata Ramana Ch (2018) Rhodococcus electroldiphila sp. nov., a marine electrogenic actinobacterium isolated from coral reef. Int J. Syst. Evol. Microbiol. 68: 2664-2649.
17. Divyasree B, Suresh G, Sasikala Ch and Venkata Ramana Ch (2018) Chryseobacterium salipaludis sp. nov., isolated at a wild ass sanctuary. Int. J. Syst. Evol Microbiol. 68: 542-546.
18. Subhash Y, Radha V, Srinivas S, Ramaprasad EVV, Shivani Y, Ojha R, Tushar L, Sasikala Ch and Venkata Ramana Ch (2018) Planctopirus hydrillae sp. nov., an antibiotic producing Planctomycete isolated from the aquatic plant Hydrilla and its whole genome shotgun sequence analysis. J. Antibiotics. 71: 575-483.
19. Kuruma M, Narasimha Rao B, Suresh G, Venkata Ramana Ch and Tushar J (2018) Organic/inorganic hybrid nanocolloids of water dispersible polyurethanes with antibacterial activity. J. Colloid and Polymer Science. 296: 95-106.
20. Samuel K, Reddanna P, Anil Kumar P, Surya Satyanarayana S and Padmaja G (2017) Benzoylsalicylic acid derivatives as defense activators in tobacco and Arabidopsis. Phytochemistry. 143: 160-169.
21. Mohanraj SS, Tetali SD, Mallikarjuna N, Dutta Gupta A and Padmasree K (2018) Biochemical properties of a bacterially-expressed Bowman-Birk inhibitor from Rhynchosia sublobata (Schumach.) Meikle seeds and its activity against gut proteases of Achaea janata. Phytochemistry. 151: 78-90. doi: 10.1016/j.phytochem.2018.02.009.
22. Srikanth S, Swathi M, Rao MV, Mallikarjuna N, Padmasree KPMSV (2017) Protease inhibitors of Cajanus conferring resistance to pod borer of pigeonpea (Cajanus cajan L. Millsp.). Electronic J. Of Plant Breed. 8: 26-37.
23. Afshan S, Sankarakrishna P, Ramakrishna D, Kofman S, Hess W, Swamy MJ, Lin-Chao S, Prakash JSS (2017) Ssl2245-SII1130 toxin-antitoxin system mediates heat-induced programmed cell death in Synechocystis sp. PCC6803. J. Biol. Chem. 292: 10.
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25. Kumar RK, Heuchel M, Kratz K, Lendlein A, Jankowski J and Tetali SD (2018) Effects of extracts prepared from modified porous poly (ether imide) microparticulate absorbers on cytotoxicity, macrophage differentiation and proinflammatory behavior of human monocytic (THP-1) cells. Clin Hemorheol Microcirc. 69: 175-185.
26. Chatterjee B, Ghosh K, Suresh L, Kanade SR (2018) Curcumin ameliorates PRMT5-MEP50 arginine methyltransferase expression by decreasing the Sp1 and NF-YA transcription factors in the A549 and MCF-7 cells. Mol. Cell. Biochem. 455:73-90.
27. Chatterjee B, Ghosh K, Kanade SR (2019) Curcumin-mediated demethylation of the proximal promoter CpG island enhances the KLF4 recruitment that leads to increased expression of p21Cip1 in vitro. J. Cell. Biochem. 120: 809-820.
28. Ghosh K, Chatterjee B, Kanade SR (2018) Lead induces the up-regulation of the protein arginine methyltransferase 5 possibly by its promoter demethylation. Biochem J. 475: 2653-266.

29. Bhat MY, Gul MZ, Maurya RS, Khan N, Qureshi IA and Ghazi IA (2018) Growth inhibition and apoptosis inducing effects of Artemisia absinthium L. fractions on chronic myeloid leukemia (K562) cells. Journal of Biologically Active Product from Nature. 8: 70-89.
30. Gul MZ, Chandrasekaran S, Manjulatha K, Bhat MY, Maurya RS, Qureshi IA and Ghazi IA (2018) Antiproliferative and apoptosis-inducing potential of Abrusprecatorius against human monocyticleukaemia (THP-1) cell line - a bioassay-guided approach. Indian Journal of Pharmaceutical Sciences. 80: 307-317.
31. Gul MZ, Chandrasekaran S, Manjulatha K, Bhat MY, Maurya R, Qureshi IA, Ghazi IA (2016) Bioassay-guided fractionation and in vitro antiproliferative effects of fractions of Artemisia nilagiricaon THP-1 cell line. Nutrition and Cancer 2016 68: 1210-24.
32. Thula SK, Akash, Naik NK and Kumar R (2018) A ripening-induced SlGH3-2 gene regulates fruit ripening via adjusting auxin-ethylene levels in tomato (Solanum lycopersicum L.)". Plant Mol. Biol. 98: 455-469. (DOI: 10.1007/s11103-018-0790-1).
33. Parida AP, Raghuvanshi U, Pareek A, Singh V, Kumar R and Sharma AK (2018) Genome-wide analysis of genes encoding MBD domain-containing proteins from tomato suggests their role in fruit development and abiotic stress responses. Mol. Biol. Reports. (https://doi.org/10.1007/s11033-018-4435-x).
34. Zhou J, Liu D, Wang P, Ma X, Lin W, Chen S, Mishev J, Lu D, Kumar R, Vanhoutte I, Meng X, He P, Russinova E, Shan L (2018) Regulation of Arabidopsis brassinosteroid receptor BRI1 endocytosis and degradation by plant U-box PUB12/PUB13-mediated ubiquitination. Proc. Natl. Acad. Sci. USA. 20: 115(8): E1906-E1915.
35. Madhuprakash J, Dalhus B, Rani TS, Podile AR, Eijsink VGH and Sørlie M (2018) Key residues affecting transglycosylation activity in family 18 chitinases – Insights into donor and acceptor subsites. Biochemistry 57: 4325–4337.

2. Intra- and Inter-Cellular Communications

2.1 Investigators: NSK: Nadimpalli, SK, KVAR: Ramaiah, KVA, SB: Senthilkumaran, B, JP: Jagan Mohan Rao, Pongubala, **NBV: Naresh Babu V, Sepuri,** AJ: Jagota, Anita, SK: Srinivasulu, K, YS: Srilakshmi, Y, BM: Aramati BM, Reddy, GBM: G. B Madhu Babu, ASR: Raghavendra, AS, RPS: Sharma, RP

2.2 Overview: A dynamic relationship betweenintra cellular organelles and inter cellular communications are essential for optimal function, development, growth and survival of a cell. Unraveling the spatially and temporally organized biological signaling is crucial and fundamental to our understanding of the cell. In addition, retrograde signaling is gaining a lot of attention due to its pivotal role in maintaining organelle integrity, quality control, and in allowing necessary adaptation to stress in a spatial and temporal manner in both plants and animals. In this proposal, we are proposing an integrative and fundamental approach to understand how signals generated either within or received from outside are communicated between various organelles to mount a coordinated cellular response. The combined expertise of the participants will address this question under two specific themes. Both sub-themes are overlapping in nature and members in

the both groups collaborate within and outside of their subgroup to achieve the following objectives:

2.21 Retrograde Signaling: How does retrograde signaling regulateorganellar dynamics, communication and metabolic homeostasisinplants and animals?

To address this question, the membersof this group would like to use state-of-the-art imaging modules combined with biochemical and metabolite profiles; and advanced molecular biology techniques including genome architecture to investigate the mechanism and the underlining framework of retrograde signalling generated within or received from outside; and relayed between organelles in response to an elicitor (chemical, redox or light). The group members would liketo utilize animal cell lines, plant and animal models systems to gain insights into the process of circadian rhythms, protein homeostasis, neurological disorders and plant development.

2.22 Development and Differentiation: What are the regulators that drives the cell fate decision and development in plants and animals?

Members of this group will address fundamental questions of cell development, differentiation and maintenance of identity at systems level. In particular, the members will study the genetic code and functional genomics that affect cell fate and also study the underlying mechanisms that control their differentiation and development. Systems like hematopoietic lineage differentiation, neuronal cell development, sex reversal of fish as well as tomato fruit development and ripening will be studied.

2.3 Technical Approach:

2.3.1 Sub-theme A: **Retrograde Signaling**: How does retrograde signaling regulate organellar dynamics, communication and metabolic homeostasis in plants and animals?

2.3.1.1 We propose to investigate the stress specific responses emanating from translational attenuation mediated by eIF2α phosphorylation and transcriptional induction of ATF4 expression of the Integrated stress response (ISR) pathway on the functioning of **mitochondria and endoplasmic reticulum**, and the communication between them. We will be employing chemical and biological agents that disrupt organellar physiological function to study the possible integration of ISR with other signaling pathways like mTOR (mammalian target of rapamycin) AMPK, and UPR (unfolded protein response) that regulate protein and cellular homeostasis (KVAR and NBVS). The importance of ISR pathway mediated changes in gene expression from stress - specific changes and its cross talk with other signaling pathways such as mTOR (mammalian target of rapamycin), UPR (unfolded Protein Response) and AMPK (Adenosine monophosphate kinase activation) will be evaluated using small molecule inhibitors like ISRIB, rapamycin, etc. We also propose to study organellar dynamics of ER, mitochondria and nucleus using appropriate bio-markers. We will include study of the genome architecture (SK) and metabolic profile (ASR) under the aforementioned conditions to gain a comprehensive understanding.

2.3.1.3 Resource sharing and maintenance of optimal redox state is the basis of interorganelle interactions between chloroplasts, mitochondria and peroxisomes. The interplay

of these three pathways is facilitated by two major phenomena: sharing of energy/metabolite resources and maintenance of optimal levels of ROS.The resource sharing among different compartments of plant cells is based on the production/utilization of reducing equivalents (NADPH, NADH) and ATP as well as on the metabolite exchange. Since the bioenergetic reactions tend to generate ROS, the cells modulate chloroplast and mitochondrial reactions, so as to ensure that the ROS levels do not rise to toxic levels. Thus retrograde signaling araises from these organelles can have ardent effects in the function and development of plant cell. We propose to use algae or plant protoplast cultures to understand the relevance of communication between the organelles during light and stress. We would like to analyze organellar dynamics, metabolite profile and genome architecture to have a comprehensive picture as described above (ASR. SR, SK, NBVS, JP, NSK).

2.3.1.4 Since lysosomes are an essential and integral part of organellar communication, and the extensive expertise available, we propose to study lysosomal biogenesis using the invertebrate model systems including *Hydra* [protein-protein interaction studies will be carried out in order to decipher lysosomal biogenesis pathway (mannose 6-phosphate receptors/lysosomal enzymes) and role of other proteins like Sortilin in transport of lysosomal enzymes in invertebrate models will be studied. Furthermore, novel recombinant lysosomal enzyme antibodies will be produced a) for quantification of the enzymes from human sera and b) their potentiality as tools for Enzyme Replacement Therapy in lysosomal diseased conditions will be tested. Additionally, phosphorylated manno-oligosaccharides and lysosomal enzyme nanoparticles will be used as tools for targeted delivery into cells (normal versus diseased) mediated by the Mannose 6-phosphate receptor protein (NSK).

2.3.2 Sub-theme B: **Development and Differentiation:** What are the regulators that drives the cell fate decision and development in plants and animals?

2.3.2.1 We will propose to Investigate the transcriptional changes that regulate the development and differentiation of immune cells. Current efforts are focused to determine the cell-type-specific cis-regulatory interactions and their associated factors to build core transcriptional regulatory network by analyzing genome architecture. We will also analyze the transcription regulatory networks to understand the role of RUNX family of transcription factors which plays a critical role in differentiation of several lineages like MSCs, HSCs, neural development and GI tract formation. We also propose to look at organellar dynamics, function and ISR pathway as described in above sub-theme. These studies are anticipated to address fundamental questions about how multipotent progenitors govern the commitment to differentiation and how dysregulation of terminal differentiation can lead to disease condition such as cancer (JP, BM, SK, NBVS, KVAR).

2.3.2.3 We propose to study light signaling during tomato fruit development and ripening. We plan to use both untargeted and targeted mutagenesis strategies for genome engineering of tomato to create gain of function/loss of function alleles in the genome for improving fruit quality traits. Neural networks will be employed at systems level to identify the regulatory partners enhancing nutraceutical levels in tomato fruits (RPS, YSL).

2.3.2.4 Sexually dimorphic cell signaling pathways and regulation will be analyzed during development in bony fish models. Identification of these pathways would provide fundamental ideas to apply for aquaculture breeding practices. Proposed study will focus on identification of genes/factors that regulate gonadal differentiation and gamete maturation in a variety of bony fish models using functional genomics approaches (SB, JP, SK).

While some of the group members focus on retrograde signaling and mechanistic details of metabolites, the other members emphasize the epigenomic regulation of diverse cellular development and differentiation programs. Recent studies highlight that metabolites play a dynamic role in cellular differentiation and retrograde signalling. Importantly, how retrograde signaling causes fluctuations in metabolites, how changes in metabolites affect epigenetic events and how epigenetic changes influence the cellular differentiation gene expression programs. These studies will expand our capability to test how metabolite pathways affect cell development and function in normal and disease conditions.

2.4 Expected outcome: To understand the fundamental principles underlining the interplay between gene expression, stability and its epigenetic regulation during cellular differentiation and growth, how form and function are related at the organelle level and how inter-organelle and inter cellular communication can influence on cell status. These studies would pave the way for understanding developmental processes such as fruit ripening and plant growth, stress response, redox status and link them to understand diseases such as Alzheimer's and Parkinson's for better health. During the project period, MSc, PhDs, and post-doctoral researchers will get trained.

2.5 Technology Development: These studies would expect to eventually to yield or develop a) multiple high throughput genomic-technologies to understand the spatial features of genome organization, b) developing imaging tools to study cellular organelles and real-time assembly of organelle components, c) Enzyme replacement therapy and developing nanoparticles as specific tools for delivery into cells d) molecules to induce breeding in male fishes, e) pathway tools to identify the neurological disorders such as Alzheimer's and Parkinson's disease, and cancer, f) mutants screening technology for generation of novel variety of tomato plants having higher shelf life with nutrient quality g) development of stress tolerant algae.

2.6 Selected (recent) publications:

1. B. Sunil, D. Saini, R.B. Bapatla, V. Aswani and **A. S. Raghavendra**. 2018. Photorespiration is complemented by cyclic electron floe and alternate pathway to optimize photosynthesis and protect against abiotic stress. *Photosynth Res* (In press).
2. G. Gayatri, S. Agurla, K. Kuchitsu, K. Anil, A. R. Podile and **A. S. Raghavendra**. 2017. Stomatal Closure and Rise in ROS/NO of Arabidopsis Guard Cells by Tobacco Microbial Elicitors: Cryptogein and Harpin. *Frontiers Plant Sci*.**8:** 1096.
3. M. Hodges, Y. Dellero, O. Keech, M. Betti, **A.S. Raghavendra**, R. Sage, X.G. Zhu, D.K. Allen, and A.P. Weber. 2016. Perspectives for a better understanding of the metabolic integration of photorespiration within a complex plant primary metabolism network. *J. Exp. Bot.* **67:** 3015-3026.

4. A. Srinivas and **A. S. Raghavendra**. 2016. Convergence and divergence of signaling events in guard cells during stomatal closure by plant hormones or microbial elicitors. *Frontiers Plant Sci.* **7:** 1332. doi: 10.3389.
5. M.R. Puli, P. Rajsheel, V. Aswani, S. Agurla, K. Kuchitsu and **A.S. Raghavendra**. 2016. Stomatal closure induced by phytosphingosine-1-phosphate and sphingosine-1-phosphate depends on nitric oxide and pH of guard cells in *Pisumsativum. Planta***244:** 831-841.
6. J. Uppala, A.R. Gani and K. V. Ramaiah (2017) Chemical chaperone, TUDCA unlike PBA, mitigates protein aggregation efficiently and resists ER and non-ER stress induced HepG2 cell death, K. Scientific Reports-Nature, (2017), 7: *3831*, 1-13.
7. S. Medchalmi and K. V. Ramaiah (2015) Insulin treatment promotes tyrosine phosphorylation of PKR and inhibits polyIC induced PKR threonine phosphorylation, Arch.Biochem. Biophys., 585:98-108.
8. A.R. Gani, J.K, Uppala and K. V, Ramaiah (2015) Tauroursodeoxycholic acid prevents stress induced aggregation of proteins in vitro and promotes PERK activation in HepG2 cells (2015), Arch. Biochem.Biophys., 568,8-15.
9. Rakesh Kumar, Vajir Tamboli, **Rameshwar Sharma**, **Yellamaraju Sreelakshmi*:** **"**NAC-NOR mutations in tomato Penjar accessions attenuate multiple metabolic processes and prolong the fruit shelf life". **Food Chemistry** 2018 **259**: 234-244.
10. Himabindu Vasuki Kilambi, Kalyani Manda, Avanish Rai, Chaitanya Charakana, Jayram Bagri, **Rameshwar Sharma**, **Yellamaraju Sreelakshmi*** : "Green-fruited Solanum habrochaites lacks fruit-specific carotenogenesis due to metabolic and structural blocks". **J. Exp. Bot.** 2017 **68**: 4803–4819.
11. Gupta Prateek; Bodanapu Reddaiah; Salava Hymavathi; Upadhaya Pallawi; Tyagi Kamal; Sarma Supriya; Datta Sneha; Malhotra Bharti; Thomas Sherinmol; Sunkum Anusha; Devulapalli, Sameera; Till Bradley; **Yellamaraju Sreelakshmi*** ; **Sharma Rameshwar*** : "NGS-based identification of induced mutations in a doubly mutagenized tomato (Solanum lycopersicum) population" **The Plant Journal** 2017 **92**:495-508.
12. Upadhyaya P, Tyagi K, Sarma S, Tamboli, V. **Sreelakshmi Y**, **Sharma, R**: "Natural Variation in Folate Levels among Tomato (*Solanum lycopersicum*) Accessions". **Food Chemistry** 2017 **217:**610-619.
13. Bodanapu R, Gupta SK, Basha PO, Sakthivel K, Sadhna S, **Sreelakshmi Y** and **Sharma R**: Nitric oxide overproduction in tomato shr mutant shifts metabolic profiles and suppresses fruit growth and ripening. **Front. Plant Sci**. 2016 **7**:1714.
14. Chava S, Chennakesavulu S, Gayatri BM, **Reddy ABM*** (2018) Novel phosphorylation by AMP-activated kinase regulates RUNX2 from ubiquitination in osteogenesis over adipogenesis. ***Cell Death Dis,*** 9;9(7):754.
15. Bhamidimarri PM, Krishnapati LS, Ghaskadbi S, **Nadimpalli SK**. Mannose 6-phosphate-dependent lysosomal enzyme targeting in hydra: A biochemical, immunological and structural elucidation (2018) *FEBS Lett.* **592(8)**:1366-1377. doi: 10.1002/1873-3468.13030.
16. A. Ajith Kumar and **Nadimpalli Siva Kumar**[#] (2018) *Takifugu rubripes* cation independent Mannose 6-phosphate receptor: Cloning expression and functional characterization of the IGF-II binding domain. *Int. J. Biol. Macromolecules***, 113,** 59-65.
17. A. Venugopal, C. Sudheer Kumar, **Nadimpalli Siva Kumar**[#]**,** M. J. Swamy[#](2017) Kinetic characterization of a lysosomal α-L-fucosidase from *Lamellidens corrianus Int. J. Biological Macromolecules* **– 104**, 432-441.

18. Siva Kumar N[#] and Poorna Manasa B (2015) Lysosomal enzymes and their receptors in invertebrates: an evolutionary perspective – *Current Protein and Peptide Science, Thematic issue* on Molecular and Cellular Glyco-Sciences- **16** (1) 49-65, **Editor** – **N. Siva Kumar**
19. Ismail Khan and **Siva Kumar, N[#],** (2012) Mannose 6-Phosphate Containing Nanoparticles: Preparation,Characterization and Interaction with Cation Independent Mannose 6-Phosphate /IGF-II Receptor (MPR300) *J. of Bionanosciences***. 5,**1-9, 2012
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21. Lin MY, Cheng XT, **Tammineni P**, Xie Y, Zhou B, Cai Q, Sheng ZH (2017) Releasing Syntaphilin Removes Stressed Mitochondria from Axons Independent of Mitophagy under Pathophysiological Conditions. *Neuron* 94 (3): 595-610.e6.
22. **Tammineni P**, Jeong YY, Feng T, Aikal D, Cai Q (2017) Altered retromer trafficking contributes to lysosomal deficits in Alzheimer's disease neurons. *Human Mol. Genetics* 26 (22): 4352-4366.
23. Norris A, **Tammineni P**, Wang S, Murr A, Gerdes J, Kwan KY, Cai Q, Grant BD (2017). SNX-1 and RME-8 oppose the assembly of HGRS-1/ESCRT-0 degradative microdomains on endosomes. *Proc. Natl. Acad. Sci. U S A* 114(3): E307-E316.
24. Ye X, Feng T, **Tammineni P**, Chang Q, Jeong YY, Margolis D, Cai H, Kusnecov A, Cai Q (2017). Regulation of Synaptic Abeta Generation through BACE1 Retrograde Transport in Alzheimer's disease. *J Neuroscience* 37(10):2639-2655.
25. S.K. Madireddi, S. Nama, E. Devadasu, **R. Subramanyam** (2019) Thylakoid membrane dynamics and state transitions in *Chlamydomonas reinhardtii* under elevated temperature. *Photosynth. Res.* 139(1-3):215-226
26. S. Bujaldon, N. Kodama, F. Rappaport, **R. Subramanyam**, C.de Vitry, Y. Takahashi, F.A. Wollman (2017) The functional accumulation of antenna proteins in chlorophyll *b*-less mutants of *Chlamydomonas reinhardtii*. *Mol. Plant* **10**:115-130.
27. V. Yadavalli, C. Malleda, **R. Subramanyam** (2011) Protein-protein interactions by molecular modeling and biochemical characterization of PSI-LHCI supercomplexes from *Chlamydomonas reinhardtii. Mol Biosyst*. **7**: 3143–3151
28. Sornapudi et al., (2018). Comprehensive profiling of transcriptional networks specific for lactogenic differentiation of HC11 mammary epithelial cells. ***Scientific Reports***. 8:11777
29. Boya et al., (2017). Developmentally regulated higher order chromatin interactions orchestrate B cell fate commitment. ***Nucleic Acids Research***. 45 (19), 11070-11087
30. Zhou et al., (2013). Chromatin looping defines expression of *TAL1* and its flanking genes and regulation in T- ALL. ***Blood***. 122(26):4199-209
31. Sexton et al., (2012). Sensitive detection of chromatin co- associations using enhanced chromosome conformation capture on chip (e4C). ***Nature Protocols***. 7(7):1335-50
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33. Pongubala, JMR., Northrup, DL., Lancki, DW., Medina, KL., Treiber, T., Bertolino, E., Thomas, M., Grosschedl, R., Allman, D. and Singh, H. EBF restricts alternate lineage options and promotes B cell fate commitment independently of Pax5. ***Nature Immunology*** *9; 203-215, 2008*

34. Johnson, K., Hashimshony, T., Sawai, CM., Pongubala, JMR., Skok, JA., Aifantis, I. and Singh, H. Regulation of immunoglobulin light-chain recombination by the transcription factor IRF-4 and the attenuation of interleukin-7 signaling. ***Immunity*** *28; 335-345, 2008*

3. **Role of Post-Translational Modifications in Pathogen Biology and Pathogenesis**

3.1 Investigators: MS: Manjula Sritharan, MKB: Mrinal K Bhattacharyya, KM: Krishnaveni Mishra, RM: Ragiba Makandar, SB: Sharmistha Banerjee, KG: Gopinath Kodetham, KAK: Kota Arun Kumar, MV: Musturi Venkata-ramana, RM: Radheshyam Maurya, SB: Sunanda Bhattacharyya, NK: Nooruddin Khan

3.2 Overview: Pathogens, including bacteria, viruses, parasites, and fungi use different mechanisms to alter cellular processes during their interactions with the host. Since most of these interactions are mediated by proteins that were earlier thought to be a direct translation of the coding genome, it is increasingly evident that multiple post-translational modifications (PTMs) occur in both the infecting pathogen and the host. This can include proteolytic cleavage, as observed in several bacterial toxins or transfer of modifying groups to one or more amino acids of these proteins. Such PTMs may influence biological activity, compartmentalization, turnover, and/or interactions with other proteins. Under this proposal, we will study the PTMs in both the pathogens and the host to identify and characterize post-translationally modified proteins, PTM-modified protein interaction networks and associated post-translational modification host signaling interactive pathways. We will compare and contrast different PTMs associated with both the pathogens (represented by viruses, bacteria, parasites, and fungi) and the host to find if there are common PTMs in the host that have a mutual impact on the outcomes and responses to different infections. The study will lay the foundation information required in identifying PTMs with potential as candidate antigens for drug discovery, diagnostics, and vaccines paving the way for developing better control measures against various pathogens.

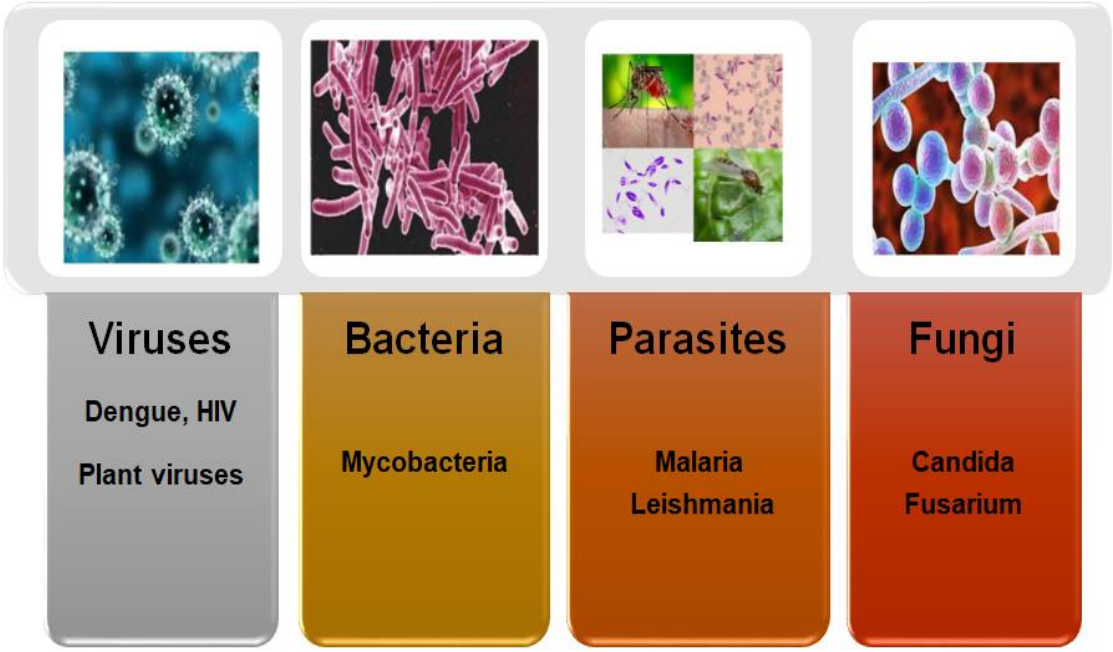
3.3 Hypothesis: Post-translational modifications (PTMs) of the pathogen and host proteins, by altering their activity and regulatory potential can orient the success of a pathogen in establishing infection or host-response for an elimination of infection. Studying of PTMs of critical pathogen / host proteins can, therefore, help in understanding pathogen biology and pathogenesis for designing intervention strategies. Using varied infection models, the long-term objective is to identify unifying and discrete PTMs specific to pathogen/host.

3.4 Objectives

1. Identification of PTMs of critical proteins in pathogen and their role in pathogen physiology
2. Identification of PTMs of critical proteins in the host and their impact on the outcome of infection

3.5. Proposed work plan: The group is working towards understanding the physiological importance of post-translationally modified proteins in pathogen physiology and map host-associated PTMs that are critical for host response and outcome of infections. Organisms shown below, representing various classes of pathogens have been selected to address the same.

Organisms selected for the study



3.6 The selection of pathogens is based on the available expertise within the group. The expertise of the eleven PIs comprising the group is provided in the table below.

Expertise of the Faculty

Viruses

- HIV: Sharmistha Banerjee (SB), Dengue: Venkataramana Musturi (VM), Plant viruses: Gopinath Kodetham (GK)

Bacteria

- Mycobacteria: Manjula Sritharan (MS), Sharmistha Banerjee (SB),
- Host response to viruses and bacteria: Nooruddin Khan (NK)

Parasites

- *Plasmodium*: Kota Arun Kumar (KAK), Mrinal Kanti Bhattacharyya (MKB), Sunanda Bhattacharyya (SBh), *Leishmania*: Radheshyam Maurya (RM)

Fungi

- *Candida*: Krishnaveni Mishra (KM), *Fusarium*: Ragiba Makandar (RM)

While critical proteins of these pathogens will be studied for their role in pathogen-biology, host cells with genetically modified backgrounds for various PTMs like sumoylation, ubiquitination, glycosylation, etc. will be tested for their permissiveness and responses to infections. As final validations, animal models will be used to study the response of genetically modified (for specific PTMs) pathogens for their pathogenesis and host responses. Alternately, transgenic cell lines/animals (for specific host PTMs) will be tested for their susceptibility or resistance to these pathogens.

3.7 The detailed objective-wise work plan is given below:

3.71 Objective 1: Identification of post-translational modifications of critical proteins in pathogen and their role in pathogen physiology

***3.711 Viruses (HIV)*:** It is proposed to perform a systematic analysis of post-transcriptional modifications of HIV regulatory proteins Rev and Tat and their implications in HIV cell tropism. Infection of three different host cell lines, namely, T-cells, macrophages and astrocytes, with HIV, isolation of Rev and Tat through immune-chromatography, Identification of post-translational modifications by LC-MS/MS, Generation of protein mutants to establish the significance of PTMs in pathogenesis and cell tropism (SB).

***3.712 Bacteria (Mycobacterium)*:** The intracellular iron levels regulate not only the expression of proteins involved in iron acquisition but also virulence determinants in bacteria. In this study, it is proposed to identify PTMs of iron-regulated proteins of the human pathogen M. tuberculosis, grown in axenic media and from experimental infections and an established virulence secretory factor. The work plan, in brief, includes cell-associated and secreted proteins of the pathogen will be isolated and analyzed by mass spectrometry for PTMs. Also, since transcriptome data is available with the group, selected candidates namely HupB, MmpL, MmpS, PapA3, and EsxR will be analyzed for PTMs (MS). Another M. tuberculosis protein, Zmp1, a secretory virulence factor, and a highly potent TB antigen, with a possible role in mycobacterial dissemination, will be studied to identify PTMs and their influence on Zmp1 activity and host response (SB).

***3.713 Parasites (Plasmodium, Leishmania)*:** Under this objective, the group will focus on PTMs of stage-specific plasmodium proteins (KAK), enzymes associated with recombination in Plasmodium (MKB) and Plasmodium topoisomerase (SBh).

In the validation of the functional role of post-transcriptional modification of proteins in mosquito and liver stages of Plasmodium, the proteome database of the mosquito and liver stages of Plasmodium will be analyzed, and selected candidate proteins will be subjected to extensive PTM analysis. Genetic approaches, using homologous recombination will be made to introduce mutations in target genes at residues where PTM occurs, and the KO mutants will be studied during the various stages of the life cycle for a probable phenotype.

Abrogation of homologous recombination (HR) pathway in malaria parasites compromises its virulence. It is proposed to characterize different PTMs (phosphorylation, sumoylation, and ubiquitination) of the key enzymes of the parasitic HR pathway and investigate their roles in regulating the HR pathway through mutants. This work would provide valuable insights on how to manipulate the HR pathway with small molecule inhibitors which might lead to avirulent parasites.

Type II topoisomerases are reported to be phosphorylated on the onset of DNA replication which stimulates its activity. It is proposed to address whether such post-translational modifications occur in Type II topoisomerases of *Plasmodium falciparum* with a special focus on *Plasmodium* TopoVI and how that regulates its intra cellular distribution as well as its role in DNA replication. The work plan in brief, involve co-immuno-precipitation of PfTopoVIB from the parasite-infected RBC at the Schizont - specific stage, identification of its PTM by mass spectrometry analysis, generation of mutant protein and studying its activity, generation of transgenic *P. falciparum* and studying its role in intra organelle distribution of PfTopoVIB and recruitment of the mutant protein to chromatin during the onset of replication of the parasite.

The human pathogen *Leishmania donovani* is an intracellular parasite that has adapted to the intracellular environment of the macrophages. Resistance to miltefosine, an anti-leishmanial drug is well known. In this study, it is proposed to perform comparative proteomics of miltefosine resistant and sensitive strains using 2D-gel electrophoresis, followed by mass spectrometry. PTMs of the differentially expressed proteins will be analyzed and characterized for their possible role in miltefosine resistance (RSM).

3.714 Fungi (*Candida, Fusarium*): The major focus here is to study the importance of protein SUMOylation in the pathobiology of *Candida glabrata* and *Fusarium graminearum*. The work plan includes a comprehensive analysis of SUMOylation of pathogen proteins in the context of infection. Enrichment of SUMOylated proteins from *C. glabrata* isolated from infected macrophages by affinity chromatography, followed by the identification of SUMOylated proteins by LC-MS/MS will be done. Functional characterization of the identified targets of SUMOylation by genetic manipulation of *C. glabrata* and *F. graminearum* will also be done (KM and RM).

3.72 Objective 2: Identification of post translational modifications of critical proteins in the host and their impact on the outcome of infection

***3.721 Viruses (Dengue and Plant viruses) infections of hosts*:** Dengue virus uses genome un-translated regions (UTRs) in replication and translation along with *trans*-acting host proteins. Such host proteins undergo certain post-translational modifications as a result of virus infection, which influences the outcome of the infection. Under this objective, dengue-infection induced host PTMs will be studied. The work plan includes a) development of dengue virus UTR - based replicative system, b) expression and purification of active dengue virus replicase, c) screening of different cell extracts (using the above developed replicative system) for the altered replication, d) identification of the protein(s) involved in replication alteration & analysis of their role in disease pathogenicity (VM).

Plant viral pathogenesis, specifically *Melon necrotic spot virus*, *Papaya Ring spot virus*, and *Peanut bud necrosis virus* have been short-listed to work on as a collection of clones for these are available with the group. The work plan includes analysis of clones (lab collection) for *Melon necrotic spot virus* and *Papaya Ring spot virus* for the role of PTMs in *Nicotiana benthamiana* (host system) to study the impact of host PTMs on infectivity of these pathogens (GK).

3.722 Fungal *(Candida, Fusarium*) infection of host: Fungal pathogens have demonstrated an ability to modify host mechanisms for successful pathogenesis *via* suppressing host defenses. The relevance of SUMOylation during plant-pathogen interactions shall be

explored using Arabidopsis-Fg and wheat-Fg interactions. The proposed study is to investigate whether *Fusarium graminearum* (Fg) compromises the SUMOylation pathway during the pathogenesis of the host plants, *Arabidopsis thaliana*, and wheat. The proteome profiling of (i) mutant and wild-type Fg strains and their interaction with Arabidopsis and (ii) proteome profiling of resistant and susceptible plant genotypes and their interaction with Fg would be carried through LC-MS/MS and MALDI-TOF assays to detect SUMOylated proteins. Functional characterization of candidate genes shall be carried through yeast-two-hybrid assays, gene complementation studies, pathogen assays for virulence, plant bioassays to detect host-susceptibility factors (RM).

In *Candida glabrata*, the work plan includes a comprehensive analysis of SUMOylation of host proteins during candida infection. In experimental infection of macrophages with *C. glabrata*, host proteins will be analyzed. Enrichment of SUMOylated proteins from infected macrophages by affinity chromatography, followed by the identification of SUMOylated proteins by LC-MS/MS will be done. Functional characterization of the identified targets of SUMOylation of *C. glabrata* by genetic manipulation of will also be done (KM).

3.8 Connectivity: MS, SB, KM, MKB, KAK, and SBh will begin exploring the respective pathogen proteins for PTMs, while VM, RSM, RM and, KM will simultaneously study the PTMs in the host and their alterations during infections. MS, SB, KM, RM, MKB, KAK, and SBh will generate the mutants for respective pathogens, while the information on the host-associated PTMs identified by VM, RSM, RM and, KM will be used to generate KO host cell lines to study the impact of these diverse types of infection. GK will facilitate the expression of some of the above proteins in the plant system using the clones developed in his lab. The entire group will use the transgenic cell lines by KAK to study infections of their wild type and PTM associated mutant pathogens. NK will perform animal experiments for the group. Animal model and GCN2 KO cell line will be studied by NK upon infection with pathogens by MS, SB, KM, MKB, KAK, SBh, VM, RSM and RM and assaying the immunological responses in terms of cytokines and chemokines.

3.9 Novelty: To the best of our knowledge, this is the first attempt towards a comparative study of PTMs in diverse types of pathogens and, correlate the same with the alterations in the host PTMs that eventually is decisive in the outcomes of these infections. A comparative study on the impact of host PTMs on infection outcome using the generated KO background will help in discovering common pathways that the host uses in response to different infections. At the same time, the study will also indicate the host PTMs which are specific for response to a specific kind of infection. The identification of pathogen-associated PTMs will help us identify leading PTMs significant for the pathogenesis of the specific pathogen.

3.10 Outcome: The study will identify common and specific PTMs associated with pathogen-biology and hosts responses to diverse infections.

3.11 Selected Publications

1. Chaurasia R, Thresiamma KC, Eapen CK, Zachariah BJ, Paul R, **Sritharan M**. (2018) Pathogen-specific leptospiral proteins in urine of patients with febrile illness aids in differential diagnosis of leptospirosis from dengue. ***Euro J Clin Microbiol Infect Dis***. 2018;37(3):423-433. doi: 10.1007/s10096-018-3187-9.

2. Yaseen I, Choudhury M, **Sritharan M**, Khosla S (2018) Histone methyltransferase SUV39H1 participates in host defense by methylating mycobacterial histone-like protein HupB. ***EMBO J*** 37: 183 – 200.
3. Divya M B, Vemula M, Balakrishnan K, **Banerjee S**, Guruprasad L. (2018) Mycobacterium tuberculosis PE1 and PE2 proteins carrying conserved α/β-serine hydrolase domain are esterases hydrolyzing short to medium chain p-nitrophenyl esters. ***Prog Biophys Mol Biol.*** pii: S0079-6107(18)30083-X. doi: 10.1016/j.pbiomolbio.2018.04.012. (**Impact Factor: 3.427**)
4. Asalla S, Mohareer K, **Banerjee S**. (2017) Small molecule mediated restoration of mitochondrial function augments anti-mycobacterial activity of human macrophages subjected to cholesterol induced asymptomatic dyslipidemia. ***Front. Cell. Infect. Microbiol***; 7: 439 doi: 10.3389/fcimb.2017.00439 (**Impact Factor: 4.3**)
5. Balakrishnan K, Mohareer K, **Banerjee S.** (2017) Mycobacterium tuberculosis Rv1474c is a TetR-like transcriptional repressor that regulates aconitase, an essential enzyme and RNA-binding protein, in an iron-responsive manner. ***Tuberculosis (Edinb).*** 103: 71–82 **(Impact factor 3.394)**
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7. Vemula MH, Ganji R, Sivangala R, Jakkala K, Gaddam S, Penmetsa S, **Banerjee S.** (2016). Mycobacterium tuberculosis Zinc Metalloprotease-1 Elicits Tuberculosis-Specific Humoral Immune Response Independent of Mycobacterial Load in Pulmonary and Extra-Pulmonary Tuberculosis Patients. ***Front Microbiol. 31st March 2016***doi: 10.3389/fmicb.2016.00418 **(Impact factor 4.019)**
8. Ganji R, Dhali S, Rizvi A, Rapole S, **Banerjee S.** (2016). Understanding HIV-Mycobacteria synergism through comparative proteomics of intra-phagosomal mycobacteria during mono- and HIV co-infection. ***Scientific Reports*** doi:10.1038/srep22060 **(Impact factor 4.12)**
9. Ganji R, Dhali S, Rizvi A, Sankati S, Vemula MH, Mahajan G, Rapole S, **Banerjee S.** (2016). Proteomics approach to understand reduced clearance of mycobacteria and high viral titers during HIV-mycobacteria co-infection. ***Cellular Microbiology***, 18:355-368. **(Impact factor 4.41)**
10. Pratima K, Goud N, Mohammed A, Ramamoorthy G, Ananthathatmula R, Doble M, Rizvi A, **Banerjee S**, Alvala R, Alvala M. (2018) An efficient and facile Green synthesis of Bisindole Methanes as potential Mtb FtsZ inhibitors. ***Chem Biol Drug Des.*** doi: 10.1111/cbdd.13363. (**Impact Factor: 2.328**)
11. Dev RR, Ganji R, Singh SP, Mahalingam S, **Banerjee S**, Khosla S. (2017) Cytosine methylation by DNMT2 facilitates stability and survival of HIV-1 RNA in the host cell during infection. ***Biochem J***. 474: 2009-2026 (**Impact Factor: 4.396**)
12. Reddy ER, Yaseen AM, Rizvi A, Deora GS, **Banerjee S**, Sevilimedu A, Rajadurai M. (2017) Antibacterial Nanoparticles Based on Fluorescent 3-Substituted Uridine Analogue ***Chemistry Select***, 2, 557 –561**(Impact factor 1.505)**
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14. Sharma A, Rustag T, Mahajan G, Kumar A, Rao Kanury V. S, **Banerjee S,** Sherman DR and Mande SC (2016). Towards understanding the biological function of the unusual chaperonin GroEL1 of Mycobacterium tuberculosis. ***Tuberculosis (Edinb). 2016 97:137-146*** **(Impact factor 3.394)**

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16. **Sritharan, M.** (2016) 'Iron homeostasis in *Mycobacterium tuberculosis*: mechanistic insights into siderophore-mediated iron uptake' ***J Bacteriol***, doi:10.1128/JB.00359-16

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4. Molecular Cancer Therapeutics

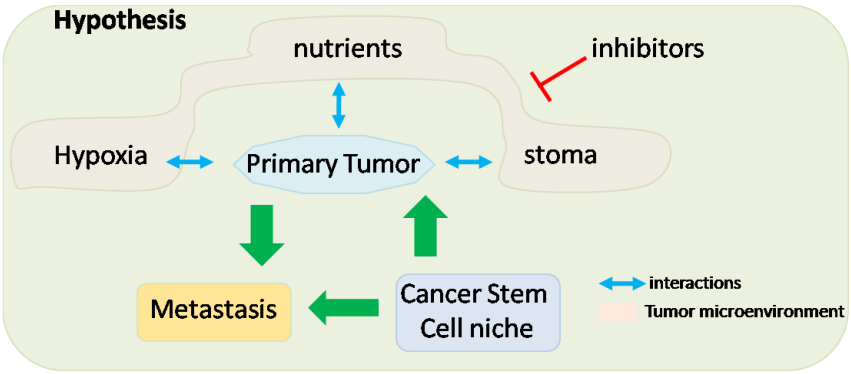
4.1 Investigators: AKK: Anand Kumar Kondapi, PPB: P Prakash Babu, BM: B Manavathi, RKG: Ravi K Gutti, YS: Y. Suresh, MKA: MK Arunasree, PAK: P. Anil Kumar, KR: K. Roy, GHP: G. Hari Prasad and PR: P. Reddanna

4.2 Overview: Cancer is a heterogeneous disease. Heterogeneity is of two types: Inter-tumor heterogeneity, in which the primary tumors originated from the same tissue/site in genetically different patients display heterogeneity; whereas in intra-tumor heterogeneity heterogeneity arises due to diverse cancer clones within the tumor. It is an important clinical determinant of patient outcomes (Hinohara and Polyak, 2019). Due to its nature, most effective therapy for each individual cancer patient remains the Holy Grail in cancer treatment. Because of these factors, cancer continues to increase among global mortality factors. Among several, breast, glioma and leukemia are category of high mortality and high-risk cancers and are also prevalent in India. Conventional therapy designed to treat various cancers were failed partially or completely in several occasions as these drugs exhibit resistance, tumor recurrence, side effects etc. Particularly no specific treatments are available to treat cancers such as triple negative breast cancers, fostering the need for alternative therapies to treat these cancers (Bianchini et al., 2016). Glioblastoma multiform (GBM) is another such aggressive cancer type which is also diagnosed at modest frequency in India. It is a highly invasive form of glioma that covers 55.4% of the malignant glioma with least (5.5%) five-year post-diagnostic survival (Ostrom et al. 2016). The probable reason for low GBM survival is resistance against the currently available standard of care owing to its complex genetic and phenotypic heterogeneity making it globally one of the most noted malignancies. Chronic neutrophilic leukemia (CNL) and atypical chronic myeloid leukemia (aCML) are myeloproliferative neoplasms arise due to missense mutations in several oncogenes, yet the exact pathogenic basis of CNL remains elusive. Accumulating evidence suggest that mmicroenvironment drives the tumor heterogeneity, aggressiveness and metastasis. Therefore, targeting tumor microenvironment which includes hypoxia, reduced nutrients and stromal cells will be an effective approach to treat cancers such as TNBC, glioma and leukemia. With this background, we are proposing the following specific aims and objectives:

1) Identification and characterisation of molecular regulators of tumor microenvironment and novel signaling pathways
2) Design, development and Targeted delivery of bioactive molecules:
3) Evaluation *in vitro* and *in vivo*

4.3 Rationale: Identification and characterisation of molecular regulators of tumor microenvironment and novel signaling pathways

The tumor microenvironment to mitigate tumor initiation and metastasis in Triple Negative Breast Cancer (TNBC) and glioblastoma (GBM) and novel signaling pathways:



Breast cancer- (TNBC) – common cancer in India
Highly metastatic
No specific therapy
only ***10-15%*** survival rates

Glioblastoma (GBM) – Deadly cancer and prevent in India
Highly metastatic
No specific therapy
only ***5 %*** survival rates

Leukemia– Common childhood cancer
Drug resistance

Figure 2: Microenvironemnt drives the tumor heterogeneity, aggressiveness and metastasis. Therefore, targeting tumor microenvironment which include hypoxia, reduced nutrients and stromal cells will be an effective approach to treat cancers such as TNBC, glioma and leukemia.

4.4 Hypothesis:

The tumor acidic/ hypoxia-associated microenvironment facilitates immune cells recruitment, epithelial to mesenchymal transition (EMT) and NF-κBsignaling that are pivotal for cancer progression, malignancy and drug resistance (Aggarwal 2004; Chen et al. 2016; Fearon and Vogelstein 1990; Gatenby and Gillies 2004; Marcucci et al. 2016; Ramirez et al. 2013). Suggesting targeting microenvironment of glioma, breast cancer and leukaemia may modify cancer metastasis and drug resistance and related disease progression. Analysing and targeting pathways that tumor microenvironment and tumor progression would throw light on the novel strategies for molecular therapeutic development.

4.5 Technical Approach:

4.5.1 Identification and characterisation of molecular regulators of tumor microenvironment and novel signaling pathways

4.5.1.1 Targeting acidic microenvironment of Glioma: Proposed project we are proposing to modify acidic microenvironment through targeting pH regulators such as V-ATPase, Na+/H+Exchanger or proton pumps. Specifically identifying mechanism of

microenvironment-mediated induction of reactive oxygen species (ROS), epithelial to mesenchymal transition (EMT) and NF-κB signaling (PPB)

4.5.1.2 Targeting TNBCs: We have identified HPIP-HIF1a pathway is deregulated in triple negative breast cancer (TNBC) and may be considered as a novel therapeutic target in TNBCs (Khumukcham et al., unpublished). In the current proposal we would like to investigate and understanding the role of multifaceted protein TRIM28 in molecular regulators of tumor hypoxic environment is needed to further target these pathways/genes to treat drug resistant cancers. Given its physiological significance, the regulation of TRIM28 gene expression under metabolic stress is largely unknown. Furthermore, although TRIM28 has been considered as a transcriptional factor, the role of epigenetic marks on its transcriptional activity under hypoxic microenvironment, a major cause for the development of drug resistance and aggressiveness of many solid tumor types, is scarce. We believe that TRIM28 is a complex epigenetic regulator that may be involved into both establishments of DNA methylation signatures and in translation them into gene silencing (BM)

4.5.1.3 Targeting ZEB-Natural Antisense Transcript to Prevent Metastasis of mammary Tumor cells: We found GH induces zinc-finger E-box Binding homeobox 2 (ZEB2) in mammary tumor cells. ZEB2 is a transcription factor orchestrates epithelial-mesenchymal transition (EMT) via suppressing E-cadherin. ZEB2 expression is regulated by a natural antisense transcript (NAT), which is transcribed by the same gene in an antisense manner. Understanding the regulation of NAT expression in mammary cells and investigating the possible modes for suppressing the NAT expression could be a promising therapeutic strategy to attenuate ZEB2 expression and to combat GH-dependent metastasis of mammary tumor cells. We made a serendipitous observation that GH increases expression of Smad Interacting Protein 1 (SIP1; also known as ZEB2, for zinc finger E-box-binding protein 2 and *ZFHX1B*). We also demonstrated that this induction of SIP-1 is in part due to a novel action of GH with induction of a SIP1 natural antisense transcript (SIP1-NAT). We also observed decreased E-cadherin and increased N-cadherin (a mesenchymal cell marker) expression in GH treated T47D breast cancer cells. EMT compromises intercellular adhesion and enhances motility. EMT confers invasive properties to breast cancer cells and contributes to the malignant phenotype of mammary carcinoma (Hazan, RB et al., 2000, Logullo AF et al., 2010, Creighton CJ et al., 2010, Beltran M et al, 2008). We propose to investigate its role in promoting malignant phenotype for identification of potential targets (BM)

4.5.1.4 Targeting CSF3R mutant specific pathways in Leukemia: In our previous studies, oncogenic mutations in JAK2, FIP1L1-PDGFRA, c-Kit and FLT3 mediated myeloproliferative neoplasms identification of mutant specific signaling pathway lead to development of novel therapeutic targets (SP Gorantla et al.2011, 2015). *CSF3R* gene is located on chromosome 1p34.3, codes the trans-membrane receptor for granulocyte colony-stimulating factor (G-CSF), which plays a major role in proliferation and survival of granulocytes and also contributes to their differentiation and function. In our preliminary studies, we could clearly demonstrate that JAK family kinases are dispensable for membrane proximal mutations mediated CNL. Based on these results understanding the mutant specific signaling pathway will be a novel therapeutic approach in CSF3R mutations mediated leukemia and solid tumors. In this study, we will generate

the Ba/F3 cells stably expressing the CSF3R wild type and T618I CSF3R and measure the unfolded protein response by checking the activation of inositol-requiring enzyme 1alpha (IRE1α and IRE1β), protein kinase RNA-like ER kinase (PERK), and activating transcription factor 6 (ATF6). To further evaluate the role of these sensory proteins in CSF3R mutation mediated signaling and transformation we will systematically down regulate these proteins in Ba/F3 cells using shRNA against these proteins and measure their transformation ability. Finally, we will develop CSF3R mediated CNL by retroviral syngeneic mouse model and evaluate the role of unfolded protein response and crucial target molecule in these mouse model. At the end, we will treat our mouse model with UPR inhibitors and evaluate the disease outcome (KR, GHP).

4.5.1.5 Targeting inflammatory pathways in leukemic Cancer stem cells: Cancer stem cells contribute majorly for the recurrence of the cancer. Hence there is need for understanding the molecular mechanisms behind the resistance of the cancer stem cells towards the chemotherapy and the factors responsible for stem cells proliferation and differentiation. Previous studies have suggested that eicosanoids play a key role in the cancer stem cells proliferation and differentiation of many types of cancers, including haematological malignancies. Our previous studies have shown eicosanoids pathway is involved in drug resistance mechanisms and inhibitors of these pathways may overcome drug resistance (Roy KR et al., 2010; Arunasree KM et al., 2008). Studying the role of specific eicosanoids (metabolites of LA, ALA, AA, EPA, DHA etc) and pathways (LOX/COX/EPOX pathways) involved in leukaemia stem cells proliferation and differentiation (Dolinska M et al., 2017; Wu L et al., 2018) will help in identification of novel targets for the treatment of cancers, specifically leukaemia. The studies will mainly focus on Chronic Myeloid Leukaemia (CML) employing K562 cells and CML patient samples (KR, GHP, PR, MKA, PAK).

4.5.1.6 Targeting megakaryopoiesis in acute megakaryoblastic leukemia (AMKL): Dami cell line differentiates into megakaryocyte-like cells. The ability of phorbol esters to induce differentiation of leukemic cells suggests that these can be used for the treatment of human leukemia. PMA-induced differentiation regulates several proteins that are essential for megakaryocytopoiesis through long-non-coding RNAs (lncRNAs) mediated regulation. Several studies show that lncRNAs play important role in the biological processes, including differentiation and development of the blood cells. However, lncRNA expression has not yet been comprehensively characterized in megakaryocytes (MKs). In this study, we will study the PMA-induced differentiation of lncRNAs associated with different stages of MK development. For this, megakaryoblastic cell line Dami (ATCC Cat # CRL-9792) which are derived from the peripheral blood of a patient with megakaryoblastic leukaemia will provide perfect model to study the process of

megakaryopoiesis(RKG,PAK).

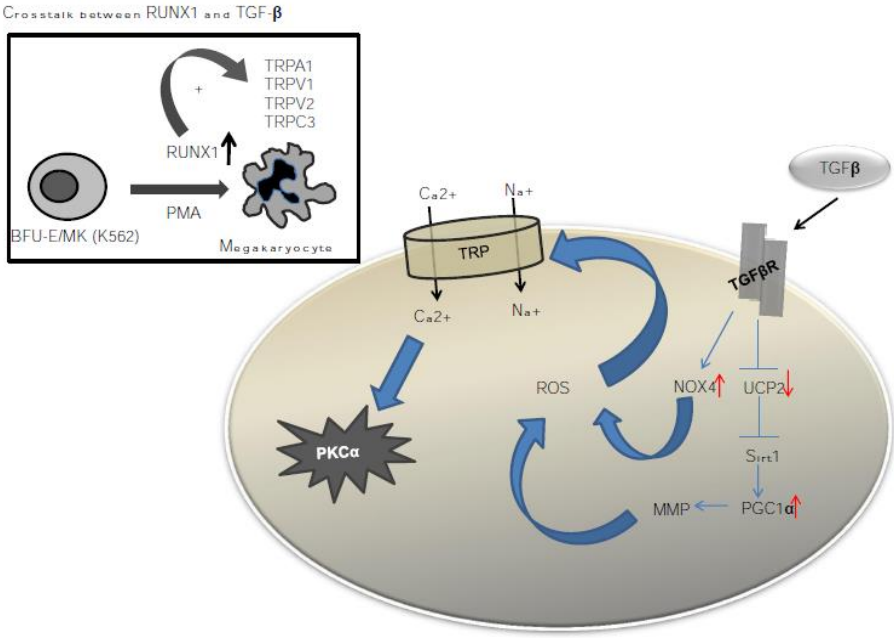


Figure 3. PMA mediated pathways

4.5.1.7 Targeting Ang2-Tie2 Pathway to control tumour growth and angiogenesis, a target for TNBC: Tumour angiogenesis is mediated by glycoproteins, Angiopoietins. Angiopoietin 2 has been reported to induce destabilization in the endothelium of host vessels, followed by generation of VEGF that promotes new vessel sprouting and tubule formation. Blocking the activity of ang2 demonstrated a decrease in growth and angiogenesis of tumours, in preclinical models. The interference with the angiopoietin-Tie2 axis might be effective as a part of multimodal treatment to inhibit tumours in humans (Moss 2013, Mazzieri. 2010). Ang2 signals primarily through Tie2, a 150 kDa transmembrane receptor tyrosine kinase. The extracellular domain of Tie2 binds the angiopoietins, it consists of a short transmembrane region, and an intracellular kinase domain that promotes for intracellular signalling. We propose to develop small molecule inhbitors against Ang2-Tie2 pathway and affect Ang2 function and tumor invasion and metastatic phenotypes development (AKK).

4.5.2 Design, Development and Targeted delivery of Bioactive molecules

A team of 4 scientists would be working on developing various therapeutic strategies targeting the already known targets or novel targets identified by the collaborating teams. The team would be involved in developing and screening the potential drug candidates and finally identify the lead molecules which can further be tested for their safety, efficacy and delivery systems using in vitro and in vivo models. The molecular therapeutics include but not limited to small molecule inhibitors, drug repositioning, epigenetic modulators such as miRNA etc.

4.5.2.1 Small molecule inhibitors: Novel small molecules would be designed and developed for various targets identified to be responsible for the development of glioma, breast cancer and leukaemia. Natural-product inspired and natural-product based small

molecules would be designed using several *in silico* methods. Validated targets identified under objective 1, will be studied further using (a) structural studies, (b) molecular docking, (c) QSAR to develop various small molecule and peptide-based inhibitors. Predicted inhibitors will be synthesized, based activity studies in vitro, active pharmacophores will be identified using docking and bioactivity studies. Further, the groups, Hexahydroquinazoline thione derivatives, Heteroaryl coumarins, Dihydropyrazole Curcumin derivatives , Epoxy- Dicoumarin Derivatives were tested in the lab and showed high cytotoxicity and hence the derivatives would further be tested for anti-cancer activity Based on such studies a series of inhibitors will be synthesised and activity will be determined (AKK, MKA)

4.5.2.2 Drug Repositioning: In light of the recent success in the drug repurposing, using already known drug prescribed for an indication to treat another indication, we also aim at evaluating the existing drugs to be used for glioma, breast cancer and leukaemia. For example, we have clearly demonstrated that a non-steroidal antiinflammatory drug (NSAID), Celecoxib, can effectively be repurposed to treat drug-resistant leukemia (MKA)

4.5.2.3 Epigenetic modulators: Epigenetics has been the major focus of basic research and targeted drug discovery. Epigenetic modulators such as HDACs, miRNA, DNMTs have been identified as the culprits behind cancer development, progression and chemoresistance. We would also like to focus on developing therapeutic strategies targeting these epigenetic modulators (MKA).

4.5.2.4 Targeted delivery: Potent molecules significant activity in vitro, may show low activity in vivo. Further, some molecule may undergo inactivation due to low stability or non-specific degradation caused by the acidic microenvironment. One can overcome these limitation in use of inhibitors in vivo, by encapsulating such inhibitors with highly basic compounds and peptides like, Protamine, Polyamine compounds, poly-histidine peptides in nanoparticles. Small molecules, peptides, antibodies, SiRNA, DNA etc., will be encapsulated in protein nanoparticles for delivery of bioactive molecules to target cancers namely glioma, breast cancer and leukaemia. Target direction will be achieved by further modification on the surface of nanoparticle using specific ligands against tissue-specific receptor and other cancer microenvironment-specific drug release (AKK).

4.5.3 Evaluation *in vitro* and *in vivo*

4.5.3.1 Efficacy in cell lines: The molecules would be screened using various biochemical and cell-based assays to determine the target inhibitory affects and identify the lead molecules. Efficacy will be evaluated using a panel of sensitive and resistant cells lines. Effect of bioactive molecules will be studied for anti-proliferation, cell invasion and mechanism of action of bioactive compound against cancer type will be assessed. Cell proliferation (CK8/MMT assay); Cell migration/invasion (transwell assay); Anchorage

independent growth (soft agar assay); Clonal propagation (clonogenic assay) Assayed for Nucleofection, Microscopy, ROS, Mito potential Cell lines to be used in the study are Dami, K562, T47D, MDA-MB231, 4T1 cells, MCF7, Mostly glioma cell lines, C6-rat glioma cell line, and U87or LN18 human-derived glioma (GBM) cell lines (AKK, PPB, BM, RKG, YS, PAK, MKA, KR, GHP)

4.5.3.2 Proton pump inhibitors: After targeting proton pumps or its specific target using chemical inhibitors or siRNA in-vitro, several molecular and functional assays but not limited to PCR, Immunoblots, confocal imaging, MTT, clonogenic, dye exclusion test, Tunel, FACS, migration and invasion assays, can be done (MKA).

4.5.3.3 Efficacy in animal models: Appropriate cancer model will be developed for evaluation of bioactive molecules. IHC, Biomarkers will be used for monitoring prognosis of cancer. tumor xenograft assay in mude mice. Calcium and TRP Channel analysis in mice. Tumor xenograft assay -Human breast cancer cells engrafting onto Nude mice. The results in-vitro will be confirmed in Orthotropic rat glioma model (Pandey V, and Babu PP et al. 2019) in-vivo study using glioma model can be done. We can evaluate anti-tumor effects through histopathological staining, and molecular alteration using immunoblot or confocal can be assessed. Survivability can also be assessed (PPB; BM).

4.5.3.4 Bioavailability of bioactive molecules: Tissue distribution and pharmacokinetics/pharmacodynamics (PK/PD) studies will be carried out to identify half-life, Cmax, AUC etc., these studies will augment in optimization of structure of bioactive molecule (AKK)

4.5.3.5 Safety of Bioactive molecules: Initial in silico ADME will be carried out at the time of initial selection. Bioactive molecules will be assessed for organ specific toxicity using specific markers and histochemistry. Further, safety advantage of delivery system also will be evaluated. Reproductive toxicity will be evaluated wherever it is mandated (AKK, YS, MKA).

4. 6 Contributions of investigators in the proposed research area

It was demonstrated the anticancer efficacy of proton pump inhibitor-pantoprazole. Further showed that pantoprazole Induces mitochondrial apoptosis and attenuates NF-κB Signaling in Glioma Cells (Geeviman K, Babu D, Prakash Babu P., et al 2018). This initial study indicates by using pH modulator, the tumor acidity can be compromised resulting apoptosis cell death (Pandey V, et al. Sci Rep. 2019 Mar 21;9(1):5012. Geeviman K et al., Cell Mol Neurobiol. 2018 Nov;38(8):1491-1504; Deshpande RP et al., Mol Neurobiol. 2017 Dec;54(10):8162-8169). Research studies have demonstrated that cancer cells utilize a complex signalling pathway involving HPIP, FAK, Calpain2 and Talin to reulate cell migration; HPIP-PI3K/AKT-Snail signalling pathway to control epithelial to mesenchymal transition, a critical step in tumor metastasis, etc. Also, his laboratory identified HPIP-HIF1a pathway is deregulated in triple negative breast cancer (TNBC) and may be considered as a novel therapeutic target in TNBCs (Khumukcham et al., unpublished). This work provided a clear mechanistic frame work for

tumor metastasis and is a major milestone. This observation has inroad implications for interpretation of an even increasing wealth of malignancy (Nakuluri K et al., J Cell Physiol. 2019, 234(5):6503-6518; J Cell Biochem, 2018 doi: 10.1002/jcb.28041; Kumar PA et al., Archives of Biochem Biophys. 2016. 590: 10-19; J Physiol Biochem. 2014; 70:433-40; J Bio Chem 2010:285:31148-56; Kumukham SS et al. J Biol Chem (under revision); Guntuku L et al., Oncogene 2018 Aug 30. doi: 10.1038/s41388-018-0446-2.; Bugide S et al., Cell Oncol, 2017, 40(2):133-144. Gajulapalli VR et al., Biochemical Journal, 2016, 473(8):1047-61; Bugide S et al., Oncogene, 2015, 34(35):4601-12;). Several mutant specific Leukemia models were established, namely JAK2V617F which is involved in MPNs, BCR-ABL in CML, FLT3-ITD in AML and FIP1L1-PDGFRA in CEL. We have recently initiated studies on CSF3R mutations mediated Leukemia. Recent studies showed that the co-expression of miR-125b and miR-99a contributed to the Vincristine resistance (VCR) to CMK cells due to actively transcribed miR99a/miR-125b locus on chromosome 21q21.1. Since miR-99a and miR-125b are located on chromosome 21, an additional copy in Down syndrome correlates to the overexpression of these miRNAs and co-expression of these leads to VCR resistance. Further studies to establish the role of these miRNAs as a therapeutic strategy in leukemia need to be explored (Kandi et al., 2015, Hematol Oncol Stem Cell Ther. 2015 Jun;8(2):95-7; Karnati HK et al., . Tumor Biology 2014 Oct;35(10):9505-21). Drug desing and development has been extensively carried out (Sai Krishna AD et al., Arch Biochem Biophys. 2005;438(2):206-160; Kammari K et al., Future Med Chem. 2017;9(14):1597-1609.). A novel protein nanoparticles were developed for delivery of drugs and DNA. Effective in drug delivery anti-cancer drug in hepatocellular carcinoma (Krishna AD et al., PLoS One. 2009;4(10):e7240; Golla K, et al., J Cancer. 2013 Sep 14;4(8):644-52; Drug Deliv. 2013, 20(3-4):156-67; PLoS One. 2012;7(12):e51960), glioma (Kumari et al., Sci Rep. 2017,;7(1):6602); Nanomedicine (Lond). 2018, 13(20):2579-2596); Melanoma (Kumari S et al., Int J Biol Macromol. 2017 Feb;95:232-237); Colon Adenocarcinoma (Farhan A et al., Pharm Res. 2018;35(9):178) and Retinoblastoma (Ahmed F et al., Int J Biol Macromol.2014;70:572-82). Indeed, were also effective in delivery of Biologicals like DNA (Kumari and Kondapi, Int J Biol Macromol. 2018;108:401-407). Experience in extensively characterizing the systemic toxicity of anti-HIV drug loaded nanoparticles (Mdugulla L et al. Syst Biol Reprod Med. 2018 Sep 27:1-9).

4.7 Expected Outcome:

4.71 Research productivity: Proposed studies would help in understading pathways associated with above communicable and non-communicable diseases along with disease signatures and sensitive targets for drug action. Further, evaliuate potential of nanoparticle delivery system for tissue localization for effective treatment

4.72 Manpower training: 30 Doctoral and 25 Post-Doctoral research fellows will be trained along with Masters Students during their project work.

4.73 Technology development: This study will help in identifying new and robust therapeutic targets and novel therapeutics.

5. Structural, Computational and Systems Biology (SCSB group)

5.1 Investigators: HAN: Nagarajaram, HA, SR: Rajgopal, S, VV: Vindal, Vaibhav, NPP: Prabhu, NP, SM: Mishra, Seema, PS: Padhi, S, MA: Akif, Md, IAQ: Insaf Qureshi; PSD: Singh, Pankaj D, VT: Thakur, Vivek, MK: Manjari Kiran, PM: Parul Mishra,

5.2 Overview: In the era of post-genome research, it has become quintessential to investigate in detail functions, expression pattern, regulation, post-translational modifications, high resolution 3D structures and pathways of expressed products (RNA and proteins) of genes and their mutational variants along with the other biomolecules such as metabolites, sugars etc. With these knowledges in hand, to further investigate interactions among various biomolecules as a means to discern the fact that the emergent properties of biological systems are not simply the sum of their parts but more than the sum, and further to correlate the emergent properties to different phenotypes as a function of environmental impacts on organisms. The current and emerging trends in biological research in this direction, involve judicious application of multidisciplinary approaches involving various biophysical techniques, genetics, genomics, proteomics, bioinformatics, computational biology and systems biology. In this respect, SCSB group aptly comprises of structural biologists, computational biologists, data scientists and systems biologists who intend to involve in inter and intra-group collaborations by means of integrating their individual domain expertise to gain insights into structural and spatio-temporal organisation of different biomolecular components, their regulation and interactions that give rise to different emergent properties (disease and health) of biological systems in different milieu and niches. The accrued knowledge will be useful for understanding the molecular mechanisms and further developing disease models. These models can be utilized for drug discovery as well as identifying disease diagnostics and prognostics markers.

5.3 Objectives

1. To study the structure, function, dynamics and interactions of proteins and nucleic acids of key importance to cellular function

2. Research support to the other groups

5.4 Technical approach/work plan:

5.41 To study the structure, function, dynamics and interactions of proteins and nucleic acids of key importance to cellular function

5.411.Solving crystal structures of candidate proteins: It is anticipated that the research proposed by the other four groups is going to identify certain protein targets requiring both structural and functional characterization. We propose to use both computational as well as experimental techniques such as X-ray crystallography/NMR for unravelling the structural details of such protein targets that are essential for understanding their

biological roles. We will also employ biochemical approaches for elucidating their activities. These findings will fuel further studies by the other groups toward biological characterisation of those target proteins.

5.412. In-silico drug discovery: Discovery and synthesis of lead molecules New lead molecules will be designed and synthesized for the identified targets. This demands extensive computational search of candidate molecules for a particular target. Molecules from existing databases will be scanned for drug repositioning/repurposing.

5.413. Enzyme engineering: Engineering candidate proteins especially enzymes to enhance catalytic properties: Catalytic activity of wild type enzymes for unnatural reactions are often found to be low. We will engineer industrial enzymes to increase their catalytic properties and develop a sustainable process for the production of value added chiral molecules.

5.42 Research Support to other research groups

5.421 Multi 'omics' data analysis support:

5.4211 Analysis of mass-spectrometry data generated for identification of common post-translational modification (PTM) during infection (Group C: Infectious Diseases)

5.4212 Analysis of cancer transcriptomic data to identify differentially expressed genes involved in establishment of tumor microenvironment (Group D: Molecular cancer therapeutics)

5.4213 Metataxonomic and metagenomic data analysis for finding microbes having plant growth promoting properties meant for formulation development (Group A: Bio-resources and Innovations)

5.4221 Construction and analyses of bimolecular networks:

5.4221Construction of protein network and/or post-translational modification network during infection (Group C: Infectious Diseases)

5.4222 Deciphering development biology by constructing and analyzing network of interacting DNA in 3D chromatin (Group B: Cell Signaling and Intra-organelle communications)

5.4223 Delineating the differences in protein interaction networks in normal versus cancer (Group D: Molecular cancer therapeutics)

5. 43 Mathematical modeling: Mathematical models will be developed to understand dynamics of retrograde signaling in complex biological processes such as, circadian rhythm, diseases (both communicable and non-communicable) and development (fruit and immune system) (Group D: Molecular cancer therapeutics)

5.44 Enzyme engineering: Enzyme based technology and enzyme engineering plays important role in improving the function of enzymes. These technologies will be applied

to enhance the required functions of chitinases and relevant enzymes specified by other groups (Group A: Bio-resources and Innovations) as per the requirement.

Expected outcomes: It is expected that the investigations carried out by SCSB group yield the following

- High resolution X-ray and NMR structures of different proteins and their variants in human host and in various pathogens including viruses, bacteria, fungi etc.The structures will be deposited in PDB.
- Biochemical characterization of the activity and enzyme-inhibitor interactions
- Studying structure-dynamics-function relation of the essential proteins.
- Development of engineered enzymes for industrial applications such as enzymes with increased catalytic activities.
- Functional characterisation of genes and the factors that regulate them in prokaryotic and eukaryotic models systems
- Resolving host-pathogen interactions at molecular as well as at systems levels
- Understanding the role of chromatin folding as a spatial regulator of gene expression, during different developmental stages of different cell types

5.6 Technology development:

- Development of computational pipeline for automated annotation of NGS epigenome datasets
- Highly annotated bacterial, plant and other genomes of interest
- Development of plant metabolites as candidate drug molecules
- Development of databases and web servers in the related areas

5.7 Selected publications

1. Bramhini, A., Prabhu, N. P. (2018) Glutamate induced thermal equilibrium intermediate and counteracting effect on chemical denaturation of proteins. ***J. Phys. Chem. B***, **122 (3)**, 1132-1144.
2. Haque, N., Baratam, K., Prabhu, N. P. (2017) Analysing the microenvironment of 2-p-toluidinylnaphthalene-6-sulfonate (TNS) in solvents and in different conformational states of proteins in relation to its fluorescence properties: a computational study. ***Phys. Chem. Chem. Phys.***, **19**, 24656-24666.
3. Haque, N., Prabhu, N. P. (2016) Lid closure dynamics of porcine pancreatic lipase in aqueous solution. ***Biochim. Biophys. Acta*** (*Gen. Subjects*), **1860 (10)**, 2313.
4. Manjari Kiran and H.A. Nagarajaram (2016) Interaction and Localization Diversities of Global and Local Hubs in Human ProteinÂProtein Interaction Network, ***Molecular Biosystems*** , **12**, 2875-2882.
5. Rachita Halehalli and H.A. Nagarajaram(2015) Molecular principles of human virus protein-protein interactions , ***Bioinformatics*** , **31**, 1025-1033.

6. Ravindra Taware, Khushman Taunk, Jorge Pereira, Amey Shirolkar, Dharmesh Soneji, Jose Camara, H A Nagarajaram, Srikanth Rapole (2018) Volatilomic insight of head and neck cancer via the effects observed on saliva metabolites , ***Scientific Reports*** , **8:17725**

7. Starr TN*, Flynn J*, **Mishra P*,** Bolon DN^{+}, Thornton JW^{+}. 2018, Pervasive contingency and entrenchment in a billion years of Hsp90 evolution. ***Proceedings of the National Academy of Sciences USA***, **115(17)**:4453-4458 *(* equal contribution)*
8. **Mishra P*,** Flynn J*, Starr TN, Bolon DN. 2016, Systematic mutant analyses elucidate general and client-specific aspects of Hsp90 function. ***Cell reports,*****15(3)**: 588-98. *(* equal contribution)*
9. **Mishra P**, Bolon DN. 2014, Designed Hsp90 heterodimers reveal asymmetric ATPase-driven mechanism *in vivo*. ***Molecular Cell,*** **Vol 53**; Issue 2,344-350.
10. KRD Sagara NS Gurusinghe, Aanchal Mishra and Seema Mishra (2018) Glucose-regulated protein 78 substrate-binding domain alters its conformation upon EGCG inhibitor binding to nucleotide-binding domain: Molecular dynamics studies. Scientific Reports (Nature Publishing Group) 8:5487, DOI:10.1038/s41598-018-22905-6.
11. A. Saleembhasha and Seema Mishra (2017) Novel molecules lncRNAs, tRFs and circRNAs deciphered from Next Generation Sequencing/RNA Sequencing: computational databases and tools. **Briefings in Functional Genomics, 1-11**
12. Rituparna Bhattacharjee, Arpita Devi and **Seema Mishra** (2015). Molecular docking and molecular dynamics studies reveal structural basis and selectivity of inhibitors EGCG and OSU-03012 towards Glucose Regulated Protein-78 (GRP78) overexpressed in Glioblastoma. **Journal of Molecular Modeling** 21:272.
13. Kiran M, Chatrath A, Xiwei T, Keenan DM, Dutta A (2018) A prognostic signature for gliomas based on expression of long noncoding RNAs. ***Molecular Neurobiology*** 1-13
14. Shibata E, Kiran M, Shibata Y, Singh S, Kiran S, Dutta A (2016) Two subunits of human ORC are dispensable for DNA replication and proliferation. ***eLife***, **5**: e19084
15. Nisha Jangir, Santosh Kumar Padhi, 2019, Immobilized Baliospermum montanum hydroxynitrile lyase catalyzed synthesis of chiral cyanohydrins. ***Bioorg. Chem.***, **84**, 32-40.
16. D.H. Sreenivasa Rao, Santosh Kumar Padhi. 2019, Production of (*S*)-β-nitro alcohols by enantioselective C-C bond cleavage with an (*R*)-selective Hydroxynitrile lyase. ***ChemBioChem.***, **20**, 371-378.
17. Nisha Jangir, Dheeraj Sangoji, and Santosh Kumar Padhi, 2018, Baliospermum montanum hydroxynitrile lyase catalyzed synthesis of chiral cyanohydrins in a biphasic solvent. ***Biocatal Agric Biotechnol.***, **16**, 229-236.
18. Kakade A, Kumari B, Dholaniya PS. (2018). Feature selection using logistic regression in case-control DNA methylation data of Parkinson's disease : A comparative study. ***J Theor Biol.*** **2018**; **457**:14-18. doi:10.1016/j.jtbi.2018.08.01
19. Bollimpelli VS, Dholaniya PS, Kondapi AK. (2017). Topoisomerase IIβ and its role in different biological contexts. ***Arch Biochem Biophys***.; **633:** 78-84.

6. Time lines and Milestones

Milestones>	Objective-1					Objective-2			
Year >	1	2	3	4	5	1	2	3	4
Bio-resources and Innovations									
Intra- and Inter-Cellular Communications									
Post-Translational Modifications: Role in Pathogen Biology and Pathogenesis									
Molecular Cancer Therapeutics									
Structural, Computational and Systems Biology									

h. Financial requirements for achieving the objectives

Summary **(In Rupees)**

Sl. No	Description	Recurring	Non-Recurring	Total
i.	Sophisticated instruments proposed to be used in Central Facilities infrastructure support for state-of-art post-graduate laboratories along with numbers of M.Sc / PhD to be accommodated	—	60000000	60000000
ii	Consumables	6900000 x 5 = 34500000	—	34500000
iii	Workshops	500000 x 5	—	25,00,000
iv	Contingency (Secretarial Assistance and miscellaneous expenditure)	500000x 5	___	25,00,000
v	Travel	100000 x 5	___	5,00,000
Sub Total		40000000	60000000	100000000
Overheads to University (10%)		40,00,000_____	6000000	10000000
Total		**44000000**	**66000000**	**110000000**

Justification for Consumables and Contingency

The project requires consumables grant of ₹3,45,00,000/- to successfully implement the objectives. The contingency grant of ₹25,00,000/- is required for secretarial assistance and miscellaneous expenditure such as filing the records, ordering and maintanenance of grant records, etc.

1. (a) Details of equipment proposed: Rs. 60000000

Sl. No.	Name of the requested equipment	Justification of the requested equipment	Budgeted cost			
			Quotation details (Please compulsorily enclose copies of quotation(s))	Cost in foreign currency (if applicable)	Cost in Indian currency	Requested Cost
Infrastructure						
(a)	Animal house requires, cages, cage holders, transportation trolleys, Surgical microscopes, Balances, pH meters, Water purification system,	Given below	(1) Racks for mice and rat	—	72,95,872.50	17443867
			(2) Cage bins and water bottles	—	34,82,667.00	
			(3) Anaesthesia machine with accessories	—	4,24,720.00	
			(8) (–)20 freezer (2 no.)	—	2,99,250.00	
			(9) Horizontal rectangular	—	41,34,900.00	

	Aquarium for Fresh water fishes and Zebrafish.		fully automatic PLC based double door sterilizer			
			(10) Refrigerator	—	1,29,150.00	
			(11) Aquarium	—	10,12,540.00	
			(12) Balance pH and RO system	—	6,64,768.65	
(b855)	Greenhouse constructed under CREBB requires renovation and upgradation especially for transgenic studies.	Given below	(1) Bore-well and electrical work	—	15,08,305.80	11788855
			(2) AC	—	2,74,575.00	
			(3) New transgenic greenhouse	—	53,90,700.00	
			(4) UPS	—	4,15,275.00	
			(5) Greenhouse and nethouse	—	42,00,000.00	
(c)	Computer server and work stations and network facility are required for conducting BigData analysis, mathematical modelling and biological system simulations by Computational group.	Given below	Computer Server and Work Stations and network	—	75,00,000	75,00,000

Justification for Animal House equipment:

University of Hyderabad, requires an infrastructure for “a state-of-art” research laboratory animal house with breeding facility. Towards this end, the University has provided 5.2 Cr funds towards establishment of New Animal House. With these funds an animal house has been built in a total area of 1501 Sqm hourbouring 66 rooms. These rooms include housing for mice, rats, rabbits, squirrels and immune compromised animals. In addition, special facility has been created for rearing insect models like Anopheles, Drosophila and silk worm and a fish breeding facility for fresh water wishes and zebra fishes.

To complement the efforts of UoH and make the animal facility a fully functional, we are in requirement of several research equipment that we are proposing in DBT BUILDER program. We are therefore proposing equipment like animal housing cages, cage racks, IVS system for maintaining immune compromised mice, autoclaves, water purification system and surgical microscope. Procurement of

these research equipment are highly required to execute the research work proposed in DBT BUILDER program.

Justification for Green House Maintenance:

The existing green house facility was sponsored CREBB of DBT. The proposed new installation and renovation of the existing facility is required to upgrade its usage for transgenic plant culture in the green house facility. The existing facility does not cater to the increased number of faculty and students working in the area of transgenic plant culture. The existing bore-well has dried up and a new one required to maintain the greenhouse facility. Further, electric panels, controller, timer, pipes, fan motor and other miscellaneous items need to be installed. Further, a dedicated RO plant systems is required to prevent frequent blockage of water pipes and cooling pads. Further, laying of new underground cables is also required to meet additional power demands and prevent frequent disruption in power supply. To maintain the temperature in the green house, we need air-conditioners. Upgradation of tissue culture hydroponic growth rooms with racks, ACs, UPS, electrical fitting and dedicated incubator shakers, cold cabinets are required to support transgenic work and store related reagents. The proposed budget will be utilized to upgrade and install the green house facility.

Justification for Computer Server and Work Station:

Existing Bioinformatics Infrastructure Facility (BIF) is not been able to support the computing demand of the SLS researchers because the servers are old and obsolete. The current and the proposed research works involving computational works such as NGS data analyses, Data modelling, Biological network modelling, mathematical modelling of biological systems, etc require hardware as mentioned in the previous column. The HPCF infrastructure at Centre for Simulation, Modelling and Design (CMSD) is a common facility to the entire university and is heavily used by various schools and departments. The proposed research and developmental activities in this program requires a dedicated HPC support in order that the objectives are met in a time bound manner.

Sl. No.	Name of the requested equipment	Justification of the requested equipment	Budgeted cost			
			Quotation details (Please compulsorily enclose copies of quotation(s))	Cost in foreign currency (if applicable)	Cost in Indian currency	Requested Cost
Equipment						
(i)	Seahorse XFp Analyzer is required for metabolic flux analysis of all groups.	Given below	Labmate Seahorse System	—	99,67,241.00	99,67,241.00
(ii)	IMARIS software for microscopic 3/4D image analysis in cells and tissues by all groups.	Given below	Towa	42,785	36,36,725.00	50,00,000.00

(v)	Single cell DLS is required for analysis of drug and particle evaluation in cells and tissues in the experiments proposed by three groups.	Given below	Almil DLS System	£70,851	67,30,845.00	67.30,845.00
(vi)	Stereotaxic Apparatus with accessories such as microscope is required for analysis of ion transport and signaling processes in cells, organelles and tissues by all groups.	Given below	Zeiss Microscopic Camera for Microinjection	€25,069	21,30,865.00	21,30,865.00

Justification for Seahorse XFp Analyzer:

Seahorse XF Analysers measure oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) of live cells in a multi-well plate, interrogating key cellular functions such as mitochondrial respiration and glycolysis. XF Analysers perform compound addition and mixing, label-free analytical detection, and automatic measurement of OCR and ECAR in real time.

Justification for IMARIS software

A lot of work in the School of life Sciences involves collecting large amounts of imaging data from fluorescence microscopes including confocal, super-resolution microscopes, transmission electron microscopes and then analysing them for detailed information. A sophisticated software for image analysis that has multiple packages for specific applications spanning visualization and measuring shapes of various objects including organelles such as nuclei, nucleoli, mitochondria, biofilms, cells, tissues, organs, embryos, tissues as well as whole organisms would be very useful. It can also be used to detect protein clusters, vesicles, autophagic material. The software encompasses interactive processing, analysis of 3D and 4D microscopic images. It is especially suited for imaging facilities where there are multiple users with varied needs. It can integrate data from the high content and high-resolution imaging systems.

IMARIS software will be used for proper functioning and analysing images of high content and high throughput imaging system and hence both IMARIS quote and Imaging system quote are requested to be considered as combined quote.

Justification for Single-Cell DLS

Measuring size of molecules, molecular weight, stability and affinity between molecules at different physicochemical conditions is an essential part of biomolecules research. The proposed dynamic light scattering instrument will be able to measure molecular size in the range of 1 nm to 10 microns, molecular weight in the range of 1 kDa to 10,000 kDa and zeta potential, at different temperatures ranging

from 10 to 90 deg. This instrument will help to investigate wide range of biological reactions such as protein-protein interactions, protein-DNA interactions, and protein aggregation. With size and molecular weight measurement stoichiometry and the strength of binding can be evaluated. Also, temperature-induced changes in bio-macromolecules such as self-aggregation can be examined. In addition, DLS will be useful to measure the size of different nanoparticles used in drug formulation and delivery. Evaluating surface charges is essential to understand the formation and interaction of nano particles. Therefore, the proposed DLS will be inclusive of zeta potential measurement which will enable us to simultaneously measure the charge distribution and size at different temperature and pH conditions.

Justification for Patch-Clamp Accessories:

Electrophysiological studies using patch clamp technique would be used to study single or multiple ionic currents in individual isolated living cells, tissue sections, or patches of cell membranes. Subsequent analysis of the data from these studies would be applied to the analysis of structure-function relationships.
The microscope that will be purchased will be useful in establishing the patch clamp setup in the School.

(b) Please enclose a certificate duly forwarded by your head of institution(s)/ University that requested equipment is/are not available in the institute. If requested equipment are already available in the institute, then adequate justification is to be submitted for requesting another set of the equipment.

Enclosure 1

vii. Workshops and training programs for UG, PG students and Technicians
Facilities and research propograms proposed under the program will service periodical programs as given under:

DBT-UoH Skill development six weeks Cenrtificate courses (20 participants for UG/PG students/ Technicians)
Training in Biosafety Level III Facility

The certificate course is designed to train graduate and postgraduate students with the techniques that are commonly used in the area of plant and microbial technology. Both basic and advanced techniques offered in this course will help students to get jobs in the industry.

The specific modules of the course are

1. Techniques in Plant and Microbial biotechnology

a) Isolation and analysis of macromolecules from plants and microbes
b) Spectroscopic and chromatographic coupled mass spectrometry techniques for secondary metabolite profiling
c) Plant and microbial culturing techniques for enhanced production of bioactive molecules
d) Screening techniques of enzymatic and non-enzymatic assays with plants and microbes of medicinal and other commercial value
e) Molecular cloning and gene expression studies

f) Protein engineering

2. Cell biology and Biochemical techniques:

a) Cell biology techniques like isolation of organelles (mitochondria, peroxisomes, nucleus, ER, chloroplast and lysosomes) from mammalian, plant cell cultures and animal or plant model systems.
b) Basic methodology in usage of regular and confocal microscopy. Immunofluorescence studies.
c) Functional enzymatic studies with isolated organelles (mitochondria, chloroplast, ER, nucleus and lysosomes)

3. Molecular Diagnostics and Therapeutics

a) Phenotypic and Genotypic assays,
b) Blood and Tissue analysis
c) Receptor-based assays for drug screening
d) Cell-based assays for drug evaluation
e) In vitro PK and Toxicology assays

4. Bioinformatics and structural biology

1) Drug potency and stability studies
2) Bioinformatics training
3) Animal handling and toxicology studies
4) Facility design, sample labelling, storage and management,
5) IPR, inventory management and data & record archiving and storage.

5. Training in BSL-III Facility

Faculty of the school are actively involved in collaboration with various Industries, members of regulatory committees and scientific bodies of industry and Institutes. Expertise of faculty members will be invested in conducting training of students from local colleges. On completion of the course, it is expected that students will be well prepared for practical-ready to take-up a job in Industries.

viii. Contribution of University in terms of building, infrastructure and equipment

i. **Building**: (a) University would provide construction cost of Rs.5.5 crores for Animal House measuring 6000 sft. (b) An equipped lab of 2000 sft with equipment worth of 1.25 crores for conducting workshop, training program and finishing school,
ii. **Infrastructure**: University would provide basic infrastructure including facilities for animal and plant cell culture, radiation safety facility, microscopic facility etc.
iii. **Equipment:** Basic equipment are available, additional equipment are required for increased strength of manpower under the program.

iv. **Sophisticated equipments:** SPR, High resolution single cell imaging system, multipurpose reader to the extent of Rs. 3 crores.

xi. Details of public-private partnership envisaged

i. BIONEST is established by the BIRAC, University proposes to initiate private-public partnerships involving faculty and students in BIONEST and other local companies for technology development of commercial importance.

ii. Industries located in Hyderabad will be involved in Finishing school and internship program

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Enclosure -1

GENOMICS FACILITY

The genomics facility at the School of Life Sciences, University of Hyderabad, is one of the core facilities of the school. It provides infrastructure and services to support research needs of high-throughput genomicsto scientists. The facility was established in the year 2007 from the grant support of DBT- CREBB.

At Genomics Facility, the services provided are as follows:

1. Microarray gene expression and microarray printing
2. QC for RNA, DNA, and high-throughput sequencing libraries
3. Real-time PCR and gene expression, genotyping, melt, etc.
4. Sample preps: DNA and RNA extractions, plasmid preps.
5. BTX Electroporation unit
6. Focused Ultra Sonicator
7. Access to instrumentation and software

This facility provides access to instruments, equipment and software utilized within the microarray field and supports Agilent, Illumina, and other microarray platforms. In addition, the facility can also print custom microarrays utilizing cDNA, oligonucliotides, proteins, peptides, antibodies, cell lysates, siRNAs, and other types of biological materials. The latest addition of real-time PCR machine is equipped with latest HRM technology which helps in single base mutation detection. Quality control analysis of RNA/DNA is done with the help of bio analyzer that is useful for several downstream applications such as microarray and next generation sequencing (NGS). In addition to this, qualitative and quantitative analysis for proteins and DNA can also be done. The provision for automated DNA/RNA extractions is also available in the facility. Focused Ultra Sonicator can be used for mechanical shearing for NGS, DNA /RNA extraction from formalin-fixed, paraffin-embedded (FFPE) tissue samples, dried blood spots (DBS) and whole blood for NGS, chromatin mechanical shearing for ChIP-Seq, biomarker extraction for research and clinical microbiology, tissue disruption & homogenization. BTX Electroporation unit can be used for cell fusion assays, *in vivo* electroporation and large volume transfection assays that are a pre-requisite for formulating any transgenic experiments.

The genomics facility provides services for gene expression and genotyping studies utilizing microarray and real time PCR, and other related services to researchers within the university and is also open for other institutes, state universities and companies with minimal user charges. The facility also provides training and research support to international students who regularly visit UoH under exchange programs such as IRTG, DAAD etc. Furthermore, the facility can be used for conducting practical training programs for the postgraduate students in the school as well as for the integrated masters students of the university.

PROTEOMICS FACILITY

The mission of our Proteomics Facility is to provide protein analysis services along with consultation not only for University of Hyderabad community at large, but also for other academia, research organizations and industries. The facility routinely conducts training and workshops for faculty & students apart from refresher courses for undergraduate college lecturers every year. Proteomics facility is equipped with state of the art mass spectrometers;
MALDI TOF/TOF and ESI-LCMS Q-TOF. Also, we have AKTA Pilot Protein Purification System which are flexible and intuitive chromatography system to meet your purification challenges in research applications and scale up industrial level. The facility is equipped with robust bioinformatics tools to identify and characterize proteins. The facility has been upgraded with the latest Surface Plasmon Resonance (SPR) system for protein-protein, protein-small molecules and protein nucleic acid interactions. This facility was created CREBB grants which was obtained from DBT in 2007. However, still there are lapses as the technology is improving, we were not able equip to analyse the post translational modification of proteins. Hence, we require further the Quadrupole mass spectrometry to
analyse the posttranslational and quantification of proteins.

Our services include protein identification and protein quantitation from a wide variety of sample types, from simple mixtures (gel spots and bands) to complex mixtures (protein complexes, cell lysates, and plasma). Our principal approach for the analysis of proteins is 'bottom-up' proteomics, where all proteins are proteolytically digested, producing peptide surrogates (signature peptides) of the original proteins. Protein or peptide molecular weight determination by MALDI TOF/TOF or LCMS-ESI Q TOF.

METABOLOMICS FACILITY

Metabolomics facility is one among the three core "omics" facilities established by the school of life sciences to chatter the needs of high-through-put metabolite analysis. This facility was started with a,

Mission: To provide an excellent analytical platform catering the needs of metabolite analysis and data interpretation.

Vision:

Develop state-of-the-art facility, meeting international standards for high-through-put metabolite analysis.

Metabolomics, as the name indicates the study of chemical processes involving metabolites, the small (<1000 Dalton's) molecule intermediates and product of metabolism. This speaks to the major extant of functional genomics, however not completely, because some of the reactions are non-gene coded involving simple or complex chemical reactions which remain unexplained through genomic or transcriptomic or proteomic studies. Metabolomics helps in all areas of biological research and the school of life sciences is rapidly growing and expanding in metabolite analysis. We would like to expand the metabolomics facility from simple metabolite analysis and data interpretation to emerging areas like "chemomics" and "metabolite repository". Chemomics, is an interdisciplinary study using approaches from chemoinformatics, bioinformatics, synthetic chemistry and other related disciplines. On the other hand, "metabolite repository" is a novel concept housing biological and synthetic molecules under one umbrella and becomes a hub for many users.

Requirements:

Facilities:

1. High resolution LC-NMR - 4 Crore

   Justification: Today we realise that vast majority of metabolites are unidentified. Some of the gustimates indicated that only 1-2% of the metabolites are known while a large (approximately, 98%) number of metabolites are yet to be characterised. Characterization of metabolites is fastidious since the quantities are limited and purity becomes an issue. To have the best fit combination to characterise metabolites, the centre proposes an high resolution LC-NMR which helps in the structural analysis of the metabolite.
2. High (100 ml/min) flow rate preparative HPLC - 1 Crore

   Justification: Helps in extraction and purification of metabolites in large quantities.
3. Flash Chromatography – 0.6 Crore

   Justification: Helps in extraction and purification of metabolites in large quantities.

4. Metabolomics soft wares - 0.5 Crore

   Justification: Helps in data interpretation.

5. Metabolomics computer facility – 1.5 Crore

   Justification: Helps in establishing chemomics facility

6. An exclusive metabolomics chemistry laboratory – 2Crore

Justification: Metabolite analysis requires special laboratories which help in avoiding chemical contamination. We propose this facility where a biological sample is given to a chief scientist, who will further process the sample and prepare for analysis. This facility requires ultra clean room to gather with some of the minor instruments for sample preparation. The proposed laboratory will also host the chemical repository.

Manpower:
Instrument technical officers: 2 No
Chemists – 2 No

MICROSCOPIC FACILITY

There are three microscopes housed in the common facility of the School of Life Sciences that cater to the imaging needs of the research projects. A trinocular upright fully motorized fluorescence microscope (Leica DM6B), a Zeiss Confocal and a STED-based super-resolution microscope (Leica TCS-SP8 based). The STED is also equipped with live-cell imaging capability. The trinocular and confocal are used extensively. The usage of STED is limited due to lack of technical support.

Requirements:
a) a trained operator for STED who can work with students to develop methods for specific requirements as Super-resolution microscopy requires sample based development of staining method and image analysis
b) funding for maintenance (AMC, UPS, air conditioner, LASER upkeep)

c) To strengthen the imaging facility it would be important to add an AIRY scan set-up to the Zeiss confocal microscope. This upgradation will allow fast acquisition of multicolor images with super-resolution and high sensitivity at 120 nm laterally and 350 nm axially. Especially for low expressed proteins, this will allow us to gain speed, sensitivity and resolution. In addition, it allows usage of a better range of dyes. Together with the STED and regular confocal, the Airy scan can cover the entire range of resolution. (require 1.50 crores for this upgradation)

In Vivo Imaging Facility

School name	**: School of Life Sciences**
Equipment name	**: *In Vivo* Imaging System**
Model	**:** In vivo MS FX Pro
Make	**:** Kodak system; Aquired by Carestream Health Inc, USA and now with Bruker, Germany.
Distributer	**:** Inkarp Instruments Pvt Ltd.
Purchased Cost	**: US $ 2,15,880.00**
Date of Purchase	**: June 2011.**
Date of Installation	**: Jan 2012.**
Name of the Incharge	: Dr Bramanandam Manavathi, Asst Professor, Biochemistry, PhNo: 040-23134546
Utilization rate	: Less
Log Book details	: Copied attached

Remarks regarding break down: At the beginning itself, we got a problem with the camera which was under warranty. So the company has replaced with the new one. Now it is functioning.

Research carried out/Application:*In vivo* imaging of live/dead animals/plants or plant parts (Small in size) (transgenic plants or animals). Fluorescent labeled or luminescent samples can be imaged in the samples.

Any patents claimed **:** None.

- Light Source: 400 W Xenon
- Monochrome interlined, fixed lens (10x), cooled (-29 C, absolute) CCD camera (13.8 x 13.8 cm / 2048 x 2048 px, 67 μmpx, 16 bit)
- Imaging Modalities: Bioluminescence, Multi-wavelength fluorescence, X-ray, Reflected Light, Radioisotopic
- Excitation Filters: 28 automated bandpass excitation filters available (410 nm - 760 nm)
- Emission Filters: 6 automated wide angle emission filters available (535 nm - 830 nm)
- Isoflurane vaporizer for anesthesia during imaging
- Animal warming (20°C – 40°C) for longer-term anesthesia
- Computer command center running Windows 7 Pro with Carestream MI acquisition and analysis software

PLANT CELL CULTURE FACILITY

The existing Plant Cell Culture Facility with 3 Culture Rooms is catering to the teaching and research requirements of the faculty in School of Life Sciences. The facility is being used for M.Sc. students of Plant Biology and Biotechnology and M.Sc. Biotechnology students for carrying out various experiments which has helped them to gain practical experience in different aspects of in vitro studies. The facility is being used by research scholars and post doctoral fellows of School of Life Sciences working in the area of in vitro plant biology and plant functional genomics studies. The facility established with the support of DBT-CREBB in 2007 has made a lot of impact on the quality of teaching and research activities at the School of Life Sciences which is evident by the papers published by the faculty in reputed International journals. Due to continuous use of the facility for teaching and research purposes, the Air Conditioners, Temperature Controllers/Photoperiodic Controllers and Incubator shakers have become obsolete and repeatedly breaking down. Hence, there is a need to renovate/upgrade the facility for smooth running of the teaching/research activities of the Department/School.

It is proposed to renovate/upgrade the facility by procurement of Incubator Shakers, Split Air-Conditioners, Temperature Controllers, Culture racks with Photoperiodic Controllers for which an amount of Rs. 25 lakhs is being requested.

ANIMAL HOUSE

School of Life Sciences, University of Hyderabad is one of the top rated schools within the university and also across the universities in India. The school is rigorously training and promoting quality education at the level of post-graduation and PhD level by constantly updating their faculty skills, infrastructure and training their students in the emerging areas of current biology. The 57 faculty members and more than 400 research scholars in the school of life sciences here have been engaged in the research pertaining to wide areas of modern biology such as stem cell biology, regenerative medicine, cancer, inflammation, infectious diseases, metabolic disorders, genomics & proteomics, chemical biology & drug discovery, Endocrinology, Chrono and Neurobiology, bioinformatics and environmental biology addressing both **basic biology as well as translational research**. In order to maintain the quality education in research, research output and also to attract industry academic collaborations, having state-of-art animal research facility is imperative. The school is currently lacking such facility that has shown significant setback in attracting industry-academic collaborations, outstanding research publications, where proving every research findings from in vitro analysis requires in vivo confirmation. Thus, **University of Hyderabad, requires to construct "a state-of-art" research laboratory animal house with breading facility in the campus**. In addition, to truly translate the cancer biology findings from the laboratory to the humans, the state of the art animal facility to house the nude

mice/NOD/SCID mice and also knockout and transgenic animals is essential. Existing animal house lacks several facilities and also cannot accommodate wide range of animals for experimentation. Considering the large expertise and CPCSEA approval for various studies pertaining to different projects sanctioned SLS faculty, in the new animal house, animal facilities will be established for fish breeding and rearing for performing transgenics and early development and maturation related studies. In addition, mosquito rearing facilities will be established for studying malarial parasite and vaccine development by targeting potential biomarkers. In addition, animal facility for performing chronobiology experiments will be established. Further, the proposed animal house not only strengthen in house infrastructure facilities, but will also provides rigorous training programs & workshops related to animal handling, procedures, development of transgenic animals along with ethical issues pertaining to animal handling and usage for students.

PLANT CULTURE FACILITY

Proposal to up-grade existing infrastructure of Plant Culture Facility to strengthen prospective plant-based research of School of Life Sciences

The Plant Culture Facility of School of Life Sciences (SLS) is one of the core-infrastructural facilities of the School, serving the needs of the research community involved in carrying out plant-based research at SLS, UoH.

Existing infrastructure of the facility:

The facility houses four independent green house chambers each with a separate electric control panel to regulate temperature for growth of plants. Each chamber is subdivided into a set of six cabins with a total number of 24 temperature controlled green houses. The status of most of these green houses presently are in unusable conditions, with lack of functional motors, temperature controllers, filter pads, broken water pipes and storage tanks. With increasing number of users, which include graduate students, research scholars, project fellows, post doctoral fellows and the faculty, the existing facility is insufficient to meet their research needs and demands for additional installations of green houses, especially those to carry transgenic work, insect-plant interaction chambers and net houses to protect plants from pests and animals.

The proposed budget of Rs. One Crore Twenty Five Lakhs (Rs. 1,25,00,000/-) to meet the costs of renovation and up-gradation of existing facility with new installations; bore well (Rs.25,00,000), transgenic rooms (Rs.48,00,000) and renovation costs of existing green houses (Rs.48,00,000), manpower (Rs.8,00,000) and the remaining amount for plumbing, civil, electrical work and maintenance cost is justified reasonably as given below:

Proposed new installations in the facility:

- The existing bore-well frequently dries with no water to draw and pump motor also breaks down many a time with no back up supply for growing plants. An installation of an additional bore well as a backup for the existing water supply source is required.
- Construction of transgenic rooms, net houses, insect-plant testing chambers is also proposed.
- Since animal culture facility is housed within the premises, it necessitates fencing to prevent infestations from rodents, snakes and other predators in the facility.
- Proper lighting of the facility is mandatory for safety concern of the users.
- A water pipeline bordering the premises is required to prevent incidents from fire outbreaks.
- Installation of an underground sump, pump motors, laying of pipelines will maximise utilization of the open land to conduct field-based trials as well as growing live-plant herbarium for first-hand practical experience for graduate research training.

- A sunken composting micro-plant is also proposed to utilize effluents and animal house organic wastes to prepare manure for plant culture.
- There is dearth in man power to maintain the facility. Two Field Assistants and two daily wage-labourers are required to constantly monitor and maintain the facility throughout the day.

Sl. No	Existing Infrastructure	Proposed New Installations
1	One bore -well which dries up in summer season	Installation of an additional bore well
2	Four independent green house chambers with six cabins each- Mostly unusable with non-functional electrical equipment	Transgenic rooms, net houses and plant-pest chambers, room for soil preparation, an auto-clave
3	A broken fence partially encumbering electricity supplying board and a run-down motor	Fencing, lighting and a water pipeline encumbering the facility to prevent fire break-outs
4	Lack of functional motors, temperature controllers, filter pads, broken water pipes and storage tanks.	Underground sump, pump motors, laying of pipelines
5		A sunken composting micro-plant for manure
6	Manpower is NIL	Manpower- Two field Assistants and two daily wage-labourers
7		**Annual maintenance costs (10% installation costs)**

BSL3 Facility

University of Hyderabad houses a spacious, state-of-art, BSL3 facility with animal BSL3 laboratory providing safe working environment for high-risk and high-security BSL3 grade pathogens. It is a standalone self-sufficient facility which is third party validated.

Location
It is located on the North campus, beside CR Rao Advanced Institute of Mathematics, Statistics and Computer Science building. BSL-3 is built in a vast area of about one acre.

The common essential feature of BSL-3 laboratory is the unidirectional air flow using room pressure gradient of negative pressure, exhaust air being HEPA (high efficiency particulate air) filtered and proper procedures for disposal of biomedical waste. Measures of waste disposal and effluent decontamination are followed as per the guidelines of bio-safety of containment laboratories. The air discharged from the facility is passed through exhaust HEPA filters which are capable of filtering 0.3 micron air-borne particles with very high efficiency. The personnel are well protected with PPE as per

standard guidelines of BSL3 facility. All the users are trained and hold a BSL3 users certificate before initiation of their proposal. The researchers intending to use the facility submit their proposals along with detailed methodology involving high-risk pathogens to BSL3 user committee and then to University IBSC committee for approval before initiation of their work in the BSL3 facility.

BSL-3 facility is comprised of

- **Main BSL-3 laboratory**
- **Pre-culture room**
- **Animal BSL-3**

THE MAIN BSL-3 LABORATORY

The main BSL-3 lab maintains a negative pressure of -55pa. It contains two Bio safety cabinets of level -II category. The main BSL-3 lab is well equipped with all the basic equipment including Co2 incubator, Centrifuge, orbital shaking incubator, Spectrophotometer, PCR machine, Ph meter ,-80degrees freezer,4 degrees refrigerator etc. Each Bio safety cabinets are equipped with microfuge and vortex. The main BSL-3 lab is connected through one way pass box for separate man and material movement and is internally connected to Pre culture room, Animal BSL-3 facility and to central autoclave facility.

THE PRE CULTURE ROOM (NON-INFECTIOUS MATERIAL)

Pre culture room is meant for handling non-infectious material and to maintain cell lines, cell cultures. The pre culture room is maintained at about -45pa and is equipped with all the required equipment such as Trinocular Inverted microscopy, Centrifuge, 4degrees refrigerator and CO2 incubator. The Pre culture room has one Bio safety cabinet of level-II category. The room is adequately connected to Animal BSL-3(ABSL-3) and main BSL-3 lab through pass boxes.

ABSL-3 (ANIMAL BSL-3) LAB

The main strength of BSL-3 facility of University of Hyderabad is the availability of well-equipped and functional Animal BSL-3 facility. Animal BSL-3(ABSL-3) consists of an Animal acclimatization room, ABSL-3 lab and Challenge/Dissection room. The Animal acclimatization room is maintained at a negative pressure of about -10pa. The ABSL-3 lab is maintained at negative pressure of -60pa and is equipped with Individually Ventilated cages, Arsol injection chamber or Inhalation exposure system. The ABSL-3 lab also has one level-II bio safety cabinet for animal treatments and infections work. A part of ABSL-3 is Animal Challenge /dissection room which is again connected to main BSL-3 lab. The Animal Challenge /dissection room is maintained at a negative pressure of about -55pa. The ABSL-3 facility is also well connected to Pre culture room, main BSL-3 lab and Autoclave facility via pass boxes.

The BSL-3 Facility has an uninterrupted power supply with DG set with a capacity of 500KVA.Each room is monitored by BMS, Emergency Alarms, Emergency Exits, Emergency Showers, CCTV, Door interlocking and Intercom connections.

LIST OF MAJOR EQUIPMENT

1	**Centrifuge**	**02 No**
2	CO2 Incubator	02 No
3	Bio-Safety Cabinet class II	05 No
4	-80 Freezer	01 No
5	Autoclaves	03 No
6	Inhalation Exposure system	01 No

7	Trinocular Inverted microscopy	01 No
8	Co2 cylinder	01 No
9	Vortex	01 No
10	Centrifuge(microfuge)	01 No
11	Spectrophotometer	01 No
12	Orbital Shaker incubator	01 No
13	Microwave	01 No
14	Electropor5ator	01 No
15	Weighing balance	01 No
16	pH meter	01 No
17	-20° freezer	01 No
18	4°c fridge	01 No
19	PCR machine	01 No
20	Gradient PCR machine	01 No
21	Microfuge	01 No
22	Individually Ventilated cages	96 Nos

FUNDS RELATED:

The facility, though is ready, in order to be functional for pathogenic organisms and usage of ABSL-3 has a recurring cost of about Rs. 36 lakhs per year and would be made operational once this recurring fund is allotted and manpower recruited. The details on funding required to support the same is provided below.

1. Manpower:
    Director (Technical Officer)-1: Rs. 7,60000/- per year
    Technical Assistant-1: Rs. 3,60000/- per year
    Non-technical staff-1: Rs. 2,40000/- per year

2. Annual Maintenance: About Rs. 200000/- per year
3. Miscellaneous (waste disposal, horticulture, diesel etc): Rs. 2,20000/- per year
Total: Rs 36,00000/- per year
Faculty-in-charge: Dr. Noorudin Khan
Coordinator: Dean, School of Life Sciences

Bioinformatics Infrastructure Facility (BIF):

Facility coordinator: Prof. H.A.Nagarajaram

Bioinformatics Infrastructure Facility (BIF) is a computational facility setup by DBT at the School of Life Sciences (SLS), UoH. This infrastructure has been setup as a part of Biotechnology Information System Network (BTISNET) program of DBT, Government of India, to support Bioinformatics educational and research programs of the school. Every year the school receives a small grant to support BIF in terms of salary for one systems administrator and for procurement of computer related consumables.

Currently the BIF hardware comprise of a linux grid cluster which has reached its end of support from its manufacturer. The laboratory has been populated with about 40 desktops and are nearing their end of support. BIF has been falling severely short of support to the on-going research and education activities. It is, therefore, urgently required to upgrade the infrastructure with high end servers

and workstations to support the on-going and near-future research goals of the school which is invariably dependent on the state of the art computational infrastructure without which the modern research cannot sustain. Both hardware as well as software need to be upgraded.

Enclosure-2

List of Ongoing Projects

Year	Tittle	PI	Agency Tenure	Amount
2019	Toll-like Receptor Signalling: Significance in Megakaryocyte Development and Platelet Production	Ravi Kumar, Gutti	DST-SERB	46.2 lakhs
2019	From small to big: microRNAs as new players in developmental megakaryocytopoiesis	Ravi Kumar, Gutti	ICMR	46.6 lakhs
2019	Long non-coding RNA Regulation: Role in Megakaryocyte Development and its Significance in Platelet Disorders	Ravi Kumar, Gutti	CSIR	18 lakhs
2019	Biochemical investigation of endosomal targeting proteins and functional analysis of lysosomal enzymes and their receptors in Hydra	Nadimappli Siva Kumar	DST-SERB 3 years	57 lakhs
2019	Quantitative proteomics of Protein Body components (lectins and glycosidases), from the Trichosanthes anguina seeds: elucidation of protein-protein interactions in the protein body biogenesis	Nadimappli Siva Kumar	UGC-BSR midcareer fellowship 2 years	10 lakhs
2019	Role of MIA40 in ETC biogenesis and Fe-S cluster Export	Naresh V Sepuri	DST-SERB 3 years	49.8 lakhs
2018	Environmental stress responses in protein structure and metabolism of plant and algal chloroplasts.	S Rajagopal &Nathan Nelson, Tel Aviv Univ. Biochemistry	UGC-ISF 3 years	1.74 crores
2018	Characterization of Epap-1 bound epitopes of gp120: Development of novel entry inhibitors	Anand K Kondpai	DBT	62 lakhs
2018	Development of Novel Bioactive glass and glass ceramics- *In vitro and In vivo* evaluation.	Brahmanandam Manavathi (as CoPI)	DST SERB 3 Years	37 Lakhs
2018	- SERB-DST: Deacetylation meets deadenylation in control of tumor metastasis. (25 lakhs)	Brahmanandam Manavathi	DST SERB 3 years	25 Lakhs

2018	Development of Novel Bioactive glass and glass ceramics- *In vitro and In vivo* evaluation.	Brahmanandam Manavathi (as CoPI)	DST SERB 3 Years	37 Lakhs
2018	SERB-DST: Deacetylation meets deadenylation in control of tumor metastasis. (25 lakhs)	Brahmanandam Manavathi	DST SERB 3 years	25 Lakhs
2018	JC Bose Fellowship	P. Appa Rao	DST 5 years	90 lakhs
2018	Bacterial sporulenes and insights into sporulenes of *Lysinibacillus acetophenoni* JC23^{T}	Ch Venkata Ramana	CSIR	18 lakhs
2018	Enzyme cascade biocatalysis in the stereoselective synthesis of chiral intermediates	Santhosh Kumar Padhi	CSIR	NA
2018	Modulation of photorespiration by oxidative stress: Role or reactive oxygen and reactive nitrogen species	A.S. Raghavendra	DST, 3 years	36 lakhs
2018	Membrane associated organophosphate (OPH) hydrolase complex in Sphingobium fuliginis: determination of inter subunit interactions and elucidation of its role in acquisition of phosphate or iron	S. Dayananda	SERB, DST 3 years	56 lakhs
2018	Isolation and taxonomic characterization of drug resistance bacteria from the effluent and soil samples collected from the bulk drug manufacturing units located in Hyderabad	S. Dayananda	BDMA: Bulk Drug Manufacturers Association (India) 2 years	15 lakhs
2018	Isolation and taxonomic characterization of drug resistance bacteria from the effluent and soil samples collected from the bulk drug manufacturing located in Hyderabad	S. Dayananda	BDMA: Bulk Drug Manufacturers Association (India) 2 years	15 lakhs
2018	Structural and functional studies of glucose 6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase to understand their role in leishmaniasis	Insaf Qureshi	DST-SERB 3 years	40.328 Lakhs

2018	Development and application of high resolution genome confirmation capture technology to investigate genome architecture in space and time	Srinivasulu, K	DBT 3 years	72.2 Lakhs
2018	Molecular characterization of genes/factors promoting testis growth and sperm maturation using teleost fish models	B. Senthilkumaran	DST-SERB 3years	77,89,800
2018	Unraveling the role of FGFs and signalling during gametogenesis in teleosts	B. Senthilkumaran	CSIR 3years	19,00,000
2017	A combined approach of metabolomics, proteomic, transcriptomic and organization of photosynthetic apparatus from Chlamydomonas reinhardtii under various light intensities with different growth conditions.	S. Rajagopal	DBT 3 years	70 Lakh
2017	A combined approach of metabolomics, proteomic, transcriptomic and organization of photosynthetic apparatus from Chlamydomonasreinhardtii under various light intensities with different growth conditions.	S. Rajagopal	DBT 3 years	70 Lakh
2017	12R-Lipoxygenase as a Target for Development of Drugs against Psoriasis	P. Reddanna	DST-DRL 3 years	135.83 lakhs
2017	Members of the phylum *Planctomycetes* as source for anammox (anaerobic ammonia oxidation) bacteria: The "bugs" for removal of ammonia from sediment and waste	Ch Venkata Ramana	DBT-TATA Innovation 5 years	45 lakhs
2017	Understanding the mechanism of protein kinase C mediated functional regulation of protein arginine methyltransferase 5	B K Santhosh	DST SERB 3 Years	52 lakhs
2017	Structural Characterization and epitope mapping of multi-domain host interacting outer membrane proteins from Leptospira	Akif Mohammad	DST-SERB	Rs.48.6 lakhs
2017	Effect of Ionic Liquids on Different Phases of Protein Fibril Formation	N.Prakash Prabhu	DST-SERB	Rs.20.74 lakhs
2017	Enzyme engineering for efficient synthesis of diastereoselective Henry products	Santhosh Kumar Padhi	DST-SERB	Rs.63lakhs

2017	Discovery of missing components of gene regulatory network underlying C_4 pathway/anatomy for translational research	Vivek Thakur	DBT	Rs.88 lakhs
2017	Redox constraints regulate photorespiration	A.S. Raghavendra	India-Isreal 3 years	93 lakhs
2017	Engineering photosynthesis in mulberry for resilience to climate change: A C4 approach	A.S. Raghavendra	CSTRI, Mysore 3 years	23 lakhs
2017	Expression and purification of L1 proteins and vlp's of human papiloma virus and use of vlp's as potent vaccine candidate	S. Dayananda	Biological E Ltd 3 years	25 lakhs
2017	Expression and characterization of cofactor regeneration systems used for enzyme biocatalysis	S. Dayananda	Aurobindo Pharma Ltd. 3 years	26 lakhs
2017	Comprehensive omics studies on a versatile sphingomonad strain to establish theoretical basis for in situ bioremediation of recalcitrant environmental pollutants	S. Dayananda	Indo-Japan, SERB, DST 3 years	5 lakhs
2017	Role of non-coding small RNAs (sRNA) in regulation of carbon catabolic pathways in E. coli: Investigations into regulation of sRNA, Seco 10054a Expression and it's interaction with lipoamide dehydrogenase (*Lpd*) mRNA	S. Dayananda	CSIR, 3 years	25 lakhs
2017	Understanding the role of aminopeptidases in leishmaniasis through structural and functional studies (CSIR)	Insaf Qureshi	CSIR 3 years	19.9 Lakhs
2017	Epigenetic mechanisms in embryonic stem cell pluripotent and differentiation	Srinivaulu, K	ICMR 3 years	47.7 Lakhs
2017	Regulation of Prion Formation in vivo	Parul Mishra	DST-SERB	32.5 Lakhs
2017	Bio-prospecting for anti-osteroporotic collagen peptides derived from fish bones	B. Senthilkumaran	DBT 3years	23,41,800

2016	India-UK Nitrogen Fixation Centre (IUNFC)	P. Appa Rao	DBT 3 years	90 lakhs
2016	Structure-function studies of fungal or bacterial lytic polysaccharide monooxygenases	J. Madhuprakash	DST-INSPIRE 5 years	35 Lakhs
2016	NCDs-CAPomics: Exploring the Volatome of NonCommunicable Diseases as a Promising Non-Invasive and Integrating Approach for its Rapid Diagnostics. The Case Study of Cancer and Neurodegenerative Diseases	H.A.Nagarajaram (Co-PI)	INNO-IN-DIGO, DST 3 years	Rs.30 lakhs (share of grant)
2016	Effect of molecular crowding on the kinetics and mechanism of protein fibrillation: studies under isostable and isoviscous conditions	N.Prakash Prabhu	CSIR	Rs.15.8 lakhs

Enclosure-3 (Biodata of PI & CIs)

PART VI: PROFORMA FOR BIOGRAPHICAL SKETCH OF INVESTIGATORS

Provide the following information for the key personnel in the order listed on PART II. Follow this format for each person. **DO NOT EXCEED THREE PAGES**

Principal Investigator: Prof. S. Dayananda

Name : Dayananda Siddavattam
Designation : Professor

Department of Animal Biology, School of Life Sciences, University of Hyderabad, Hyderabad -500046, India.

Date of Birth: 01.07.1957 Sex: M

Education (Post-Graduation onwards & Professional Career)

S. No.	Institution Place	Degree Awarded	Year	Field of Study
1	S.V. University, Tirupathi	Ph.D.	1985	Zoology
2	S.K. University, Anantapur	M. Sc	1981	Biosciences

Position and Honors

Position and Employment **(Starting with the most recent employment)**

S. No.	Institution Place	Position	From (Date)	To (date)
1.	University of Hyderabad	Senior Professor	2019	till date
2	University of Hyderabad	Professor	2004	2019
3	SK University, Anantapur	Professor	1998	2004
4	SK University, Anantapur	Reader	1990	1998
5	SK University, Anantapur	Lecturer	1985	1990

Honors/Awards

- UGC National Visiting Associate: (1985 to 1988 – three months in a year)
- DAAD Fellow (1988-90)
- BMFT Visiting Scientist (1992-93)

- Commonwealth Academic Staff Fellow (1995-1996)
- Fellow, National Academy of Sciences, Allahabad, India (NASI)
- Fellow, Indian Academy of Sciences, Bangalore, India
- Fellow Indian National Science Academy, New Delhi. India
- Recipient of Andhra Pradesh Scientist Award-2008 – by The State Council of Science and Technology, Govt. of Andhra Pradesh, India
- Fellow, Andhra Pradesh Academy of Sciences (FAPAS), 2006.
- International Research Development Award – by The Welcome Trust, UK
- JC Bose Fellowship 2020 (DST)

Professional Experience and Training relevant to the Project

B. Publications (Numbers only) 64
Books: Nil Research Papers - 55 Reports: Nil General articles: 3
Patents: 2 Others (Please specify):
Total citations: 895 h-index: 16 i10-index: 28

Selected peer-reviewed publications (Ten best publications in chronological order)

1. Hari Parapatla, Ramurthy Gudla, Guruprasad Varma Konduru, Elsin Raju Devadasu, Hampapathula Adimurthy Nagarajaram, Manjula Sritharan, Rajagopal Subramanyam and Dayananda Siddavattam (2020) Organophosphate Hydrolase interacts with ferric-enterobactin and promotes iron uptake in association with TonB dependent transport system. Biochemical Journal (In Press)

2. Ramurthy Gudla, Guruprasad Varma Konduru, HampapathaluAdimurtyNagarajaram and **Siddavattam D** (2019) Organophosphate hydrolase interacts with Ton components and is targeted to the membrane only in the presence of the ExbB/ExbD complex. **FEBS Letters.**593(6):581-593

3. Parthasarathy, S., Parapatla, H., and **Siddavattam D.** (2017) Topological analysis of the lipoprotein organophosphate hydrolase from *Sphingopyxis wildii* reveals a periplasmic localisation. **FEMS Microbiol. Lett. 364: 187-192.** 10.1093/femsle/fnx187.

4. Parthasarathy, S., Parapatla, H., Nandavaram, A., Palmer, T., and **Siddavattam D.** (2016) Organophosphate Hydrolase Is a Lipoprotein and Interacts with Pi-specific Transport System to Facilitate Growth of *Brevundimonas diminuta* Using OP Insecticide as Source of Phosphate. **J. Biol. Chem.**291, 7774–85

5. DeviprasannaChakka, Ramurthy Gudla, Ashok Kumar Madikonda, Emmanuel Vijay Paul Pandeeti, Sunil Parthasarathy, AparnaNandavaram, and Dayananda Siddavattam. (2015) The Organophosphate Degradation (*opd*) Island-borneEsterase-induced Metabolic Diversion in *Escherichia coli* and Its Influence on *p*-Nitrophenol Degradation. **J. Biol. Chem.**290, 29920–29930.

6. Sunil Parthasarathy, Sarwar Azam, Y, AnnapoorniLakshmanSagar, VeeraNarasimha Rao, Ramurthy Gudla, Hari Parapatla, HarshitaYakkala, SujanaGhantaVemuri, and **Dayananda Siddavattam**. (2017) Genome-Guided Insights Reveal Organophosphate- Degrading Brevundimonasdiminuta as *Sphingopyxis wildii* and Define Its Versatile Metabolic Capabilities and Environmental Adaptations. **Genome Biol. Evol. *9:*** 77–81.

7. Pandeeti EV, Longkumer T, Chakka D, Muthyala VR, Parthasarathy S, Madugundu AK, Ghanta S, Medipally SR, Pantula SC, Yekkala H**, Siddavattam D** (2013) Multiple mechanisms contribute to lateral transfer of an organophosphate degradation (*opd*) island in *Sphingobium fuliginis ATCC 27551*.***G3: Genes Genomes and Genetics*** (Genetics Society of America: Bethesda) 2(12):1541-54.1.

8. Longkumer T, Parthasarathy S, Vemuri SG, **Siddavattam D** (2014) OxyR-dependent expression of a novel glutathione S-transferase (Abgst01) gene in *Acinetobacterbaumannii* DS002 and its role in biotransformation of organophosphate insecticides. **Microbiology**. 160:102-12.
9. Gorla P, Pandey JP, Parthasarathy S, Merrick M, **Siddavattam D**. (2009) Organophosphate hydrolase in Brevundimonas diminuta is targeted to the periplasmic face of the inner membrane by the twin arginine translocation pathway. **J Bacteriol**. 6292–6299.
10. **Siddavattam D,** Khaja Mohiddin S, Manavathi B, Suresh Babu P and Merrick MJ (2003) Transposon-like organisation of the plasmid-borne organophosphate degradation (*opd*) gene cluster found in *Flavobacterium* sp. **Appl. Environ. Microbiol.** 2533 – 2539.

Co-Investigator: Prof. N. Siva Kumar

Name: NADIMPALLI SIVA KUMAR
Designation : Senior Professor

Department/Institute/University: Biochemistry/University of Hyderabad

Date of Birth: 23-11-1958 Sex (M/F) M SC/ST: - General

Education (Post-Graduation onwards & Professional Career)

Sl No.	Institution Place	Degree Awarded	Year	Field of Study
1	Andhra University,Waltair	M.Sc	1980	Biochemistry
2	CFTRI, Mysuru	Ph.D.	1986	Biochemistry
3	Indian Institute of Science	Post doc	1986 Jan-Sept.	Biochemistry

Position and Honors

Position and Employment (Starting with the most recent employment)

Sl No.	Institution Place	Position	From (Date)	To (date)
1	Biochemistry Department, University of Hyderabad	Senior Professor	01-03-2019	To date
2	--------do----------	Professor	01-11-2004	28-02-2019
3	--------do----------	Reader	01-08-1998	31-10-2004
4	---------do----------	Senior Lecturer	11-09-1991	31-07-1998
5	---------do----------	Lecturer	10-09-1986	10-09-1991

Honors/Awards
National – 9 and International -12

National

5. UGC Mid Career Award – 2018: Given to Professors who guided more then 15 Ph.D. students as single supervisor. I guided 19 already.

4. Awarded the Andhra Pradesh Scientist Award 2012 in Biological Sciences for the outstanding **teaching and research** contributions made in the field of Glycobiology

3. Awarded the DBT, Overseas associateship, 2008 to carryout research for 6 months (March-September, 2009) in the University of Goettingen, Goettingen, Germany. Collaborator – Dr. Bernhard Schmidt. (This fellowship is given by the DBT for scientists to carryout short term research work outside India and selection is made through an open advertisement by the DBT).

2. Awarded the Prof. M. Sadhaksharaswamy Endowment Lecture Award 2007, by the Society for Biological Chemists (India) for outstanding contributions in **teaching and research** in the field of biological chemistry and allied sciences. (This is given by the SBC (India) once in three years to eminent teachers of the Universities who have proven their scientific and teaching abilities also by an open call).

1. Elected Fellow of the Andhra Pradesh Akademi of Sciences, India, March, 2006

International

5. DAAD Visiting Professorship to teach for one semester in an international Program Masters in Biochemistry and Molecular Biology (March to July, 2019) in University of Bremen, Germany

4. Award for Teaching Excellence – 2015 - INDUS Foundation Indo-Global Education Summit 2015 (14-15th November, 2015), Hyderabad

3.Three of my Ph.D. students were awarded the DAAD Fellowship to work in German Universities.

2. Recipient of an International Research Grant supported by the Volkswagen research Foundation, Germany (2000-2006 I/78096., I/78193). Only Principal investigator from India Prof. N. Siva Kumar: German collaborators: Prof. Dr. Dr. h. c. K. von Figura, Goettingen University, Prof. Dr. Regina Pohlmann, University of Muenster, Germany. Total amount (2000-2005) about Rs. 58 lakhs (Completed). (These projects are highly competitive in nature internationally and only the best would get the funding)

1. Awarded the DAAD Postdoctoral fellowship (1998-1990< University of Wurerzburg, University of Goettingen including 4 months' language course) and 3 months DAAD re-invitation (1994 at EMBL, Heidelberg).

Professional Experience and Training relevant to the Project

N. Siva Kumar has about 33 years of teaching and research at the University of Hyderabad. He was actively involved in teaching various courses at Masters Level in the School of Life Sciences and more courses for the M.Sc. Biochemistry students. He is currently a Senior Professor in the Biochemistry Department and has so far supervised 19 Ph.D.'s and Mentored 3 postdocs including one DST WoS. He has successfully completed 14 research projects including one prestigious International Project supported by the Volkswagen research Foundation. His research specialization is Glycobiology and Nanobiotechnology (working on both plant and animal systems). He also coordinated the First International research Training Group in Molecular and Cellular Glycosciences with the University of Hyderabad and University of Muenster, Germany for 7 long years. During this program he was instrumental in organizing winter and summer workshops for Ph.D. students under the project both in UoH and in Muenster Germany (in collaboration with German counter parts).

He is currently the Director of International Affairs at the University of Hyderabad and is instrumental in organizing workshops at the UoH and visits of foreign delegations in organizing workshops at the UoH in collaboration with some foreign Universities that would lead

to the development of MoUs which will facilitate student and faculty exchange. He is also the Coordinator of the New Passage to India program at the University of Hyderabad, being monitored by the University of Goettingen, Germany. I have also organized an International Meeting at UoH (Asian Community of Glycoscience and Glycotechnology during December, 2014).

Research Papers: 86; Citations: 836; h-index: 17; i10-index: 29

Selected peer-reviewed publications (Ten best publications in chronological order)

1. Kavyashree, S.R, Venugopal, A and **Siva Kumar, N**[#] (2019) Class II α-mannosidase from *Trichosanthes anguina* (Snake Gourd) seeds: Purification and biochemical characterization. **I.J. Biol.Macromolecules** 131, 734-743
2. Bhamidimarri PM, Krishnapati LS, Ghaskadbi S, **Nadimpalli SK**. Mannose 6-phosphate-dependent lysosomal enzyme targeting in hydra: A biochemical, immunological and structural elucidation. (2018) **FEBS Lett**. 592(8):1366-1377. doi: 10.1002/1873-3468.13030.
3. A. Ajith Kumar and **Nadimpalli Siva Kumar**[#] (2018) *Takifugu rubripes* cation independent Mannose 6-phosphate receptor: Cloning expression and functional characterization of the IGF-II binding domain. **Int. J. Biol. Macromolecules,** 113, 59-65.
4. A. Venugopal, C. Sudheer Kumar ,**Nadimpalli Siva Kumar**[#]**,** M. J. Swamy[#](2017) Kinetic characterization of a lysosomal α-L-fucosidase from *Lamellidens corrianus* **Int. J. Biological Macromolecules –** 104, 432-441.
5. **Siva Kumar N**[#] and Poorna Manasa B (2015) Lysosomal enzymes and their receptors in invertebrates: an evolutionary perspective – **Current Protein and Peptide Science, Thematic issue** on **Molecular and Cellular Glyco-Sciences**- 16 (1) 49-65, **Editor** – **N. Siva Kumar**
6. Gnanesh Kumar, B.S, Pohlentz,A, Mona Schulte, Mormann,M and **Siva Kumar, N** (2014) N-glycan analysis of mannose/glucose specific lectin from *Dolichos lablab* seeds **Int. J. Biol. Macromolecules – 69,** 400-407
7. Gnanesh Kumar, B.S., Pohlentz, G, Schulte Mona, Mormann, M and **Siva Kumar, N** (2014) Jack bean α mannosidase:Amino acid sequencing and N-glycosylation analysis of a valuable glycomic tool - **Glycobiology** 24(3) 252-261.
8. Kartika N Shetty, Vakada Lavanya Latha, Rameshwaram Nagender Rao, **Siva Kumar Nadimpalli** and K Suguna[#](2013) Affinity of a galactose- specific legume lectin from *Dolichos lablab* to adenine revealed by X-ray crystallography **IUBMB Life,**65 (7), 633-644.
9. Mohammad Mansour Saleh Saif, **N. Siva Kumar** and M.N.V.Prasad[#](2012) Binding of aqueous cadmium to *Strychnos potatorum* seed proteins: adsorption kinetics and relevance to water purification **– Colloids & Surfaces B: Interfaces –** Volume 94, 1 June 2012, Pages 73-79
10. Ismail Khan and **Siva Kumar, N**[#]**,** (2012) Mannose 6-Phosphate Containing Nanoparticles:Preparation,Characterization and Interaction with Cation Independent Mannose 6-Phosphate /IGF-II Receptor (MPR300) **J. of Bionanosciences.** Vol.5,1-9, 2012

Coordinator & Coinvestigator II: Prof. Naresh Babu V. Sepuri, PhD (Cell Signalling and Intra-organelle communications)

Name: NARESH BABU V. SEPURI.
Designation: Professor

Department/Institute/University: Biochemistry, School of Life Sciences, University of Hyderabad

Date of Birth: 22/11/1966 Sex (M/F) M SC/ST : N/A

Education (Post-Graduation onwards & Professional Career)

Sl No.	Institution Place	Degree Awarded	Year	Field of Study
1	University of Hyderabad	PhD	1997	Biochemistry and Molecular Biology
2	Department of Physiology, University of Pennsylvania	PDF	1996-1999	Biochemistry, Molecular Biology and Mitochondrial Biology
3	Johns Hopkins University	PDF	1999-2002	Yeast genetics, MB
4	Dept Biochemistry and Pharmacology, Thomas Jefferson University	PDF	2002-2004	Human physiology, Human genetics, mitochondrial disorders
5	Dept Animal Biology, University of Pennsylvania	RA	2004-2007	Mitochondrial Biology

Position and Honors
Position and Employment (Starting with the most recent employment)

Sl No.	Institution Place	Position	From (Date)	To (date)
1	University of Hyderabad	Professor	April 2015	--
2	University of Hyderabad	Associate Professor	November 2010	April 2015
3	University of Hyderabad	Reader	November 2007	Noovember 2010

Honors/Awards
American Heart Association Fellowship in the year 2002
CSIR Junior and Senior Research Fellow, 1990-1996
Member of American Association of Cell Biologists
Visiting Scientist at University of Pennsylvania in 2015 (May-July) to implement a collaborative project on the role of mammalian TOM40 in import of Cytochrome P450s in Dr. Avadhani's lab at Dept of Animal Biology.

Visiting Scientist at Thomas Jefferson University in the year 2010 (April-July) to implement a collaborative project on development of in vitro mitochondrial translation system in Dr. Michael P.King's lab.

Collaborative project with Prof. Hatzoglou MDepartment of Pharmacology, Case Western Reserve University, Cleveland, Ohio, USA on stress induced tRNA fragments and their role in apoptosis.

Collaborative project with Dr. Sagar Sen Gupta (NII, New Delhi) on mitochondrial REQL protein.

Research Papers: 31; Patents: 2; Citations: 2471; h-index: 20; i10-index: 24

Selected peer-reviewed publications (Ten best publications in chronological order)

1. Gandikota C, Mohammed F, Gandhi L, Maisnam D, Mattam U, Rathore D, Chatterjee A, Mallick K, Billoria A, PrasadVSV, Sepuri NBV*, Venkataramana M*. (2020). Mitochondrial Import of Dengue Virus NS3 Protease and Cleavage ofGrpEL1, a Cochaperone of Mitochondrial Hsp70. Journal of Virology.17;94(17): e01178-20. doi: 10.1128/JVI.01178-20.

2Karri S, Singh S, Paripati AK, Marada A, Krishnamoorthy T, Guruprasad L, Balasubramanian D, **Sepuri NBV** (2018). Adaptation of Mge1 to oxidative stress by local unfolding and altered Interaction with mitochondrial Hsp70 and Mxr2. **Mitochondrion**. 2018 Apr 9. pii: S1567-7249(17)30346-X. doi: 10.1016/j.mito.2018.04.003.

3. Allu PK, Boggula Y, Karri S, Marada A, Krishnamoorthy T, **Sepuri NBV** (2018). A conserved R type Methionine Sulfoxide Reductase reverses oxidized GrpEL1/Mge1 to regulate Hsp70 chaperone cycle. **Sci Rep**. 2018 Feb 9;8(1):2716. doi: 10.1038/s41598-018-21083-9.

1. **Sepuri NBV**, Angireddy R, Srinivasan S, Guha M, Spear J, Lu B, Anandatheerthavarada HK, Suzuki CK, Avadhani NG (2017). Mitochondrial LON protease-dependent degradation of cytochrome c oxidase subunits under hypoxia and myocardial ischemia. **Biochim Biophys Acta.** 2017 Jul;1858(7):519-528.
2. Marada A, Karri S, Singh S, Allu PK, Boggula Y, Krishnamoorthy T, Guruprasad L, **Sepuri NBV (**2016). A Single Point Mutation in Mitochondrial Hsp70 Cochaperone Mge1 Gains Thermal Stability and Resistance. **Biochemistry**. 7065-7072.

6. Murari A, Thriveed VT, Mohammad F, Tammineni P, Gorla M, Krishnamoorthy T and **Sepuri NB** (2015). Mitochondrial Mia40 is a component of FE-S cluster export machinery. **Biochemical Journal**. 471, 231-41.

7. Allu PK, Marada A, Boggula Y, Karri S, Krishnamoorthy T, **Sepuri NB** (2015). Methionine sulfoxide reductase 2 reversibly regulates Mge1, a cochaperone of mitochondrial Hsp70, during oxidative stress. **Mol Biol Cell**. 1; 26(3):406-19.

8. Gorla, M and Sepuri NB (2014). Perturbation of apoptosis upon binding to tRNA to the heme domain of Cytochrome c. **Apoptosis.** 19 (1) 251-68.

9. Marada A, Allu PK, Murari A, PullaReddy B, Tammineni P, Thiriveedi VR, Danduprolu J, **Sepuri, N.B** (2013) Mge1, a nucleotide exchange factor of Hsp70, acts as an oxidative sensor to regulate mitochondrial Hsp70 function. **Mol Biol Cell**. (6):692-703.

10. Tammineni P, Anugula C, Mohammed F, Anjaneyulu M, Larner AC, **Sepuri NB** (2013).The import of the transcription factor STAT3 into mitochondria depends on GRIM-19, a component of the electron transport chain. **J Biol Chem**. 288(7):4723-32. (featured in Science signaling as an Editorial choice)

Biodata of Team Leaders

Prof. Ch. Venkata Ramana (Bio-resources and Innovations)

Name : Dr. Ch. Venkata Ramana
Designation : Professor

Department/Institute/University : Plant Sciences, School of Life Sciences, University of Hyderabad

Date of Birth : 18th July, 1962 Sex (M/F) Male SC/ST : No

Education (Post-Graduation onwards & Professional Career)

Sl No.	Institution Place	Degree Awarded	Year	Field of Study
1.	M.S University Vadodara	M.Sc.	1985	Botany
2.	Osmania University	Ph.D	1989	Cyanobacteria diversity and Hydrogen production

Position and Honors

Position and Employment (Starting with the most recent employment)

Sl No.	Institution Place	Position	From (Date)	To (date)
1.	University of Hyderabad	Professor	2008	Continuing
2.		Reader	2000	2008

Honors/Awards

a) TATA Innovative Fellow 2016 given by the Dept. of Biotechnol. Gov. of India
b) Recipient of the prestigious Dr. E.K. Janaki Ammal life time achievement award in microbial taxonomy – 2016 given by the Ministry of Environment, Forestry & Climate change, Govt. of India.
c) Elected as member of International Committee on systematics of prokaryotes: Subcommittee of phototrophic bacteria.
d) Refereed papers for
International Journal of Hydrogen Energy (Elsevier Science Publishers, Amsterdam, Netherlands),
Int. J. Syst. Evol. Microbiol.
Indian Journal of Microbiology (Springer,New York, USA)
Indian Journal of Experimental Biology (NISCOM, India)
Indian journal of Experimental Biology & JSIR (NISCAIR, India)
Current Science of National Academy of Science, India
Journal of General and Applied Microbiology (CAP, Japan)
Antonie Van Leeuwenhoek journal of microbiology (Springer,USA)
International journal on plant physiology and biochemistry (Elsevier),
Journal of Applied microbiology and many others

e) Life Member of Association of Microbiologists of India.
f) Resource person for evaluation of DBT and MoES and MoEF projects
g) Top five prolific publishers in Microbiology from India for the year 2013-2014 and 2014-2015: Scopus report
h) Recipient, CSIR Research associateship
i) Recipient of CSIR Pool-scientist

Professional Experience and Training relevant to the Project

- Leading bacterial taxonomist of our country
- About 30 years of PG teaching experience

Research Papers: 217; Patents: 4; Monographs: 2; Citations: 3067; h-index: 29; i10-index: 98

Selected peer-reviewed publications (Ten best publications in chronological order)

01. Sasikala, K., **Ramana, Ch.V**., Raghuveer Rao, P. & Kovacs, K.L. (1993). Anoxygenic phototrophic bacteria : Physiology and advances in hydrogen production technology. *Adv. Appl. Microbiol.* **38**, 211-295.

02. Sasikala, K., **Ramana, Ch.V.** & Raghuveer Rao, P. (1991). Environmental regulation for optimal biomass yield and photoproduction of hydrogen by *Rhodobacter sphaeroides* OU 001. *Int. J. Hydrogen Energy* **16**, 597-601.

03. Sasikala, K., **Ramana, Ch.** & Raghuveer Rao, P. (1994). 5-Aminolevulinic acid : A potential herbicide/insecticide from microorganisms. *Biotechnology Progress* **10**, 123-126.

04. Pankaj Kumar Arora, Ch. Sasikala & **Ramana, Ch.V. (2012).** Degradation of chlorinated nitroaromatic compounds. *Appl. Micorbiol. Biotech.* **93**, 2265-2277.

05. Sasikala, Ch. & **Ramana, Ch.V. (1998).** Biodegradation and metabolism of unusual carbon compounds by anoxygenic phototrophic bacteria. *Adv. Microbiol. Physiol.* **39**, 339-377.

06. Srinivas, T.N.R., Ani Kumar, P., Sasikala, Ch. & **Ramana, Ch.V. (2007).** *Rhodovulum imhoffii* sp. nov., *Int. J. Syst. Evol. Microbiol.* **57**, 228-232.

07. Subhash, Y., Tushar, L., Sasikala Ch. & **Ramana Ch.V. (2013).** *Erythrobacter odishaensis* sp. nov. and *Pontibacter odishaensis* sp. nov. isolated from a dry soil of a solar saltern. *Int. J. Syst. Evol. Microbiol.* **63**, 4524-4532.

08. Venkata Ramana, V., Sasikala, Ch., Takaichi, S. & **Ramana, Ch.V. (2010)**. *Roseomonas aestuarii* sp. nov., a bacteriochlorophyll-a containing alphaproteobacterium isolated from an estuarine habitat of India. *Syst. Appl. Microbiol.* **33**, 198-203.

09. Tushar D. Lodha, Sasikala Ch. & **Ramana Ch.V. (2014)**. Draft genome sequence of *Rhodomicrobium udaipurense* JA643^T with special reference to hopanoid biosynthesis. *DNA Research* doi: 10.1093/dnares/dsu026, pp 1-9.

10. Mujahid, Md., Lakshmi Prasuna, M., Sasikala, Ch. & **Ramana, Ch.V. (2015).** Integrated metabolomic and proteomic analysis reveals systemic responses of *Rubrivivax benzoatilyticus* JA2 to aniline stress. *J. Proteom. Res.* **14**, 711-727.

Prof. Manjula Sritharan (Role of Post-Translational Modifications in Pathogen Biology and Pathogenesis)

Name : .....…… Dr. Manjula Sritharan.....
Designation :…… Professor,

Department/Institute/University : Department of Animal Biology, University of Hyderabad

Date of Birth : .....2nd July 1957..... Sex (M/F) .....F..... SC/ST : No.....
Education (Post-Graduation onwards & Professional Career)

Sl No.	Institution Place	Degree Awarded	Year	Field of Study
1	JIPMER, (Faculty of Medicine) University of Madras	M.Sc	1980	Biochemistry
2	University of Hull, Hull, United Kingdom (UK)	Ph.D.	1988	Microbial Biochemistry

Position and Honors

Position and Employment (Starting with the most recent employment)

Sl No.	Institution Place	Position	From (Date)	To (date)
1	Department of Animal Biology, University of Hyderabad	Professor	2008	To Date
2	Department of Animal Biology, University of Hyderabad	Professor & Head	2010	2012
3	Department of Animal Biology, University of Hyderabad	Reader	2000	2008
4	Department of Animal Biology, University of Hyderabad	Guest Faculty	1998	2008
5	Centre for Biotechnology Anna University	Reader	1994	1997
6	Centre for Biotechnology Anna University	Visiting Faculty	1992	1994
7	Harvard School of Tropical Public Health, Boston, USA	PDF	1989	1992
8	University of Delhi, South Campus	CSIR Scientific Pool Officer	1988	1989
9	Lady Hardinge Medical College, New Delhi	Demonstrator	1981	1984

Honors/Awards

2016 Fellow of Telangana Academy of Sciences Telangana Academy of Sciences
2007 Commonwealth Faculty Fellow Tuberculosis Research Group, Veterinary Laboratories Agency, Surrey, United Kingdom on "Functional Genomics and Transcriptomics"
2010, 2006 Commonwealth Split-Site Fellowship, Collaborative work with Tuberculosis Research Group, Veterinary Laboratories Agency, Surrey, United Kingdom for two of my doctoral students
2010 Nehru-Fulbright Fellowship Collaborative work with University of California, Los Angeles (UCLA) for a doctoral student for work in leptospirosis
2001 Visiting Scientist in the lab of Prof. Robert Gilman International Health at Johns Hopkins University, USA & Universidad PeruanaCayetano Heredia, Peru, South America
2000 Prof. K. P. Sinha & Prof P. S. Krishnan Award for the best original research paper Association of Clinical Biochemists of India.
Kamatchiammalet al. 2000. Diagnosis of pulmonary TB in HIV - infected patients by direct detection of M. tb in blood samples using a simple sample processing and Polymerase Chain Reaction Ind J Clin Biochem 2000, 15 (2), 76-82
1996 Fellow of Association of Biomedical Scientists (FABMS) Association of Biomedi cal Scientists
1989-1992 Post-Doctoral Fellow Harvard University
1985-1988 LEPRA Graduate Research fellowship, United Kingdom For doctoral studies in University of Hull, UK
1980 Rank holder M.Sc Biochemistry, Faculty of Medicine, JIPMER, Pondicherry
Member of the American Society of Microbiology (ASM), USA, International Leptospirosis Society, Society of Biological Chemists, Indian Association of Medical Microbiolo-gists, Association of Bio-Medical Scientists of India, Indian Leptospirosis Society (ILS)

Member of the Biosafety Committee, RCC Labs, Institutional Ethical Committee, CCMB, Institutional Biosafety Committee, NIN, Institutional Biosafety Commit-tee, Indian Immunologicals Pvt. Ltd

B. Publications

Research Papers: 49

Selected peer-reviewed publications (Ten best publications in chronological order)

1. Chaurasia et al. (2018) Pathogen-specific leptospiral proteins in urine of patients with febrile illness aids in differential diagnosis of leptospirosis from dengue. ***Euro J Clin Microbiol Infect Dis***. 2018;37(3):423-433. doi: 10.1007/s10096-018-3187-9.
2. Yaseen et al (2017) Histone methyltransferase SUV39H1 participates in host defense by methylating mycobacterial histone-like protein HupB. ***EMBO J*** 37: 183 – 200.
3. Sritharan, M. (2016) 'Iron homeostasis in *Mycobacterium tuberculosis*: mechanistic insights into siderophore-mediated iron uptake' ***J Bacteriol***, doi:10.1128/JB.00359-16

4. Narayanavari et al.(2015) Role of *sph2* Gene Regulation in Hemolytic and Sphingomyelinase Activities Produced by *Leptospira interrogans*. ***PLoS Neglected Tropical Diseases 9(8):*** e0003952. doi:10.1371/journal. pntd.0003952.
5. Sritharan et al M. 2014. Highly immunoreactive antibodies against rHup-F2 fragment (aa 63-161) of the iron-regulated HupB protein of *Mycobacterium tuberculosis* and its potential for the serodiagnosis of extrapulmonary and recurrent tuberculosis. ***Eur J Clin Microbiol Infect Dis***, 34:33–40.
6. Pandey et al (2014). Transcriptional regulation of the *Mycobacterium tuberculosis hupB* gene expression. ***Microbiology***, 160, 1637–1647.
7. Pandey et al (2014). Iron-regulated protein HupB of *Mycobacterium tuberculosis* positively regulates siderophore biosynthesis and is essential for growth in macrophages ***J Bacteriol***, 196:1853.
8. Dandawate et al (2014). Synthesis, characterization and anti-tubercular activity of ferrocenylhydrazones and their β-cyclodextrin conjugates. **Carbohydrate Polymers**, 108:135-144**.**
9. Sivakolundu et al (2013). Serum iron profile and ELISA-based detection of antibodies against the iron-regulated protein HupB of *Mycobacterium tuberculosis* in TB patients and household contacts in Hyderabad (Andhra Pradesh), India. ***Trans R Soc Trop Med Hyg***, 107: 43-50(8).
10. Jamadar et al (2012). Synthesis, characterisation and antitubercular activities of a series of pyruvate-containing aroylhydrazones and their Cu-complexes ***Dalton Trans, R Soc Chem, UK***. 41: 9192-9201

Prof. Anand K. Kondapi (Molecular and Cancer Therapeutics)

Name : Prof Aanand K. Kondapi
Designation : Senior Professor

Department/Institute/University: Dept Biotechnology and Bioinformatics University of Hyderabad, HYDERABAD - 500 046, India.

Tel: Office: +91-40-2313 4571; Res: +91-40-2300 0654; Mob: +91-9246212654

Email: akondapi@gmail.com, akondapi@uohyd.ac.in

Date of Birth : . August 20, 1963.. Sex (M/F) .....M..... SC/ST : .....No.....

Education (Post-Graduation onwards & Professional Career)

Sl No.	Institution Place	Degree Awarded	Year	Field of Study
1.	Andhra University	Ph.D	1990	Chemistry
2	Andhra University	M.Sc	1985	Chemistry

Position and Honors

Position and Employment (Starting with the most recent employment)

Sl No.	Institution Place	Position	From (Date)	To (date)
	University of Hyderabad	Senior Professor	Feb, 2019	To Date
	University of Hyderabad	Professor	Dec, 2006	Feb, 2019
	University of Hyderabad	Reader	Oct, 2000	Dec, 2006
	University of Hyderabad	Lecturer	Jun, 1993	Oct, 2000

Fellowships/Honours:

- Fellow of Telangana Akademy of Sciences
- Fellow of AP Akademi Of Sciences
- Biotechnology Overseas Associateship (LT), Department of Biotechnology, Govt of India
- NBTB Research Associateship, Department of Biotechnology, Govt of India
- Dr. K. S. Krishnan DAE Fellowship

Representation in National Bodies:

- Member in Review Committee on Genetic Manipulation (RCGM), Department of Biotechnology, Govt. of India.
- Member, Research Advisory Committee, National Institute of Nutrition, Hyderabad
- Member, Expert group of Scientific Expert Committee for Recombinant Products and Therapeutic Monoclonal Antibodies, National Institute of Biologicals, Delhi

- Member, Expert group of Molecular Biology, National Institute of Biologicals, Delhi
- Member, TEC on Infectious Disease Biology, DBT.

B. Publications

Research Papers: 85; Patents: 13; Citations: 1863; h-index: 26; i10-index: 44

Patents:

- Kondapi, A. K., University of Hyderabad & Secretary, Department of Biotechnology. A process for purification of anti-HIV active glycoprotein (90 KDa) from human placenta. Indian patent, Patent Filed in March 1999, Granted in 2004 (191075, 21/Del/1999).
- Kondapi, A. K. University of Hyderabad & Secretary, Department of Biotechnology. A process for purification of A 60 KDa. anti-HIV active glycoprotein from human placenta Indian patent, Patent Filed in 2000, Granted in 2005 (191822, 496/Del/2000).
- Kondapi, A. K. University of Hyderabad & Secretary, Department of Biotechnology. Anti-HIV-1 active bacterial and baculovirus recombinant Epap-1 United States Patent. 7,927,831, April 19, 2011.
- Kondapi, A. K. University of Hyderabad & Secretary, Department of Biotechnology. Anti-HIV-1 active bacterial and baculovirus recombinant Epap-1 Indian Indian patent (#3477/DEL/2005) Granted Application, Patent Number : 226541
- Kondapi, A. K. University of Hyderabad & Secretary, Department of Biotechnology. Anti-HIV-1 active bacterial and baculovirus recombinant Epap-1 PCT # PCT/IN06/00204 Filed on December 28, 2005.
- Kondapi, A. K. University of Hyderabad. Novel nanoparticles of apotransferrin/transferrin pharmaceutical composition containing them and their process for preparation (1572/CHE/2006). Indian Product and Process Patent No. 275797 on 31 st August, 2006.
- Kondapi, A. K. University of Hyderabad. Novel nanoparticles of apotransferrin/transferrin pharmaceutical composition containing them and their process for preparation. PCT #14433-P1-PCT in Aug. 2007.
- Kondapi, A. K. University of Hyderabad. Novel nanoparticles of lactoferrin useful for preparing a pharmaceutical composition facilitating easy delivery of the drug and a process for preparing the same. Indian Patent Appln No. 4657/CHE/2011 dated Dec 30, 2011.
- Kondapi, A. K. University of Hyderabad. Novel Nanoparticles of Lactoferrin Useful for Preparing a Pharmaceutical Composition Facilitating Easy Delivery of the Drug and a Process for Preparing the Same. US Patent Appln No. 13729214; EFS ID: 14575179; Confirmation Number: 6937 dated Dec 28, 2012. Published on 5th December, 2013 and bears Publication No. US-2013-0323314-A1.
- Methods and compositions to treat sexually ytansmitted infections (STIs) and sexually transmitted infections medicated inflammation, Anand K. Kondapi. University of Hyderabad, Indian Patent Provisional; Temp/E-I/11084/2016-E date 7/4/2016. Complete Complete filed: 201641012389 (Ref No. E- -2/373/2017/CHE)

- High active antiretroviral combination drugs loaded lactoferrin nanoparticles for first line and second line therapy. Anand K. Kondapi, University of Hyderabad, Indian Patent Application No. 201641015363, Date of Entry 7th May 2016.
- Novel formulation cotaning native or recombinant apotranferrin or lactoferrin nanopartcile loaded with biological alone or in combination with chemotherapeutic agent for targteed therapy. Anand K. Kondapi. University of Hyderabad. Indian patent Appln No. 201741017576 dt.19/5/2017
- Novel anti-HIV-1 heteroaromatic compounds targeted to HIV-1 associated Topoisomerase II beta kinase. Anand K. Kondapi. University of Hyderabad. Indian patent Appln No. 201741017390 dt 18/5/2017

Selected 10 peer-reviewed publications (2015 to Date):

1. Analysis of gene expression during aging of CGNs in culture: Implication of SLIT2 and NPY in senescence, K. Preeti Gupta, Pankaj Singh Dholaniya, Anil Chekuri, Anand K. Kondapi, Age (Dordr). 2015 Jun;37(3):9789. Erratum Kondapi AK. Age (Dordr). 2015 Aug;37(4):9810
2. Neuroprotective effect of Curcumin-loaded lactoferrin nano particles against rotenone induced neurotoxicity. Bollimpelli VS, Kumar P, Kumari S, Kondapi AK.Neurochem Int. 2016 May;95:37-45.
3. TopoisomeraseIIβ in HIV-1 transactivation. Chekuri A, Bhaskar C, Bollimpelli VS, Kondapi AK.Arch Biochem Biophys. Arch Biochem Biophys. 2016 Feb 11;593:90-97
4. Triple combination MPT vaginal microbicide using curcumin and efavirenz loaded lactoferrin nanoparticles. Lakshmi YS, Kumar P, Kishore G, Bhaskar C, Kondapi AK. Sci Rep. 6:25479, 2016,
5. Efavirenz loaded lactoferrin nanoparticles oral formulation with improved bio-distribution and pharmacokinetic profile. Prashant Kumar, Yeruva Samrajya Lakshmi and Anand K Kondapi, HIV Medicine. 2017, 18 (7), 452-462 (IF: 3.341)
6. Development of Pyridine Dicoumarols as potent anti HIV-1 leads, targeting HIV-1 associated TopoisomeraseIIβ Kinase. Kurumurthy K, Akhila B, Kiran Kumar D A, Future Medicinal Chemistry, 2017, 9 (14), 1597-1609
7. Overcoming blood brain barrier with a dual purpose Temozolomide loaded Lactoferrin nanoparticles for combating glioma, Sonali Kumari, Saad Ahsan, Jerald Mahesh Kumar, and Rao Nalam, Scientific reports, 2017, 7, 6602 (IF: 4.259)
8. Receptor-mediated targeted delivery of DNA using Lactoferrin nanoparticles. S Kumari, AK Kondapi, Int J Biol Macromol; 2018,108:401-407 (IF: 3.138)
9. Evaluation of Antiproliferative Activity, Safety and Biodistribution of Oxaliplatin and 5-Fluorouracil Loaded Lactoferrin Nanoparticles for the Management of Colon Adenocarcinoma: an In Vitro and an In Vivo Study. Ahmed F, Kumari S, Kondapi AK. Pharm Res. 2018, 35(9):178.
10. Aurora kinase B siRNA-loaded lactoferrin nanoparticles potentiate the efficacy of temozolomide in treating glioblastoma. Kumari S, Bhattacharya D, Rangaraj N, Chakarvarty S, Kondapi AK, Rao NM. Nanomedicine (Lond). 2018 Oct;13(20):2579-2596..

Prof. HA Nagarajaram (Structural, Computational and Systems Biology)

Name : H. A. Nagarajaram

Designation : Professor

Department/Institute/University : Department of Systems and Computational Biology, School of Life Sciences, University of Hyderabad

Date of Birth : 09th February 1964 Sex (M/F) M SC/ST : No

Education (Post-Graduation onwards & Professional Career)

Sl No.	Institution Place	Degree Awarded	Year	Field of Study
1	Bangalore University	M.Sc.	1987	Solid State Physics
2	Indian Institute of Science	Ph.D.	1995	Molecular Biophysics and Computational Biology

A. *Position and Honors*

Position and Employment (Starting with the most recent employment)

Sl No.	Institution Place	Position	From (Date)	To (date)
1	School of Life Sciences University of Hyderabad	Professor	Feb 2017	Till now
2	Centre for DNA Fingerprinting & Diagnostics (CDFD), Hyderabad	Staff Scientist and Group Leader	Jan 2000	Feb 2017
3	Biochemistry, Cambridge University, Cambridge	Research Associate	Aug 1996	Jan 2000
4	Birkbeck College, London	Research Associate	Feb 1996	Aug 1996
5	Astra Research Centre, Bengaluru	Research Associate	June 1995	Jan 1996

Honors/Awards

Name of body, society, Academy	*A. Position*	**Year**	**Validity**
International Protein Society	Member	2012	2012
European Molecular Biology Net work (EMBnet)	National Node Manager, India	2000	2005
National Academy of Sciences, Allahabad	Member	2002	Still valid
Indo-Malaysian Cooperation in Bioinformatics	Visited Malaysia as one of the member of five member Indian delegation to discuss the cooperation in bioinformatics	2003	2003
SUN-Special Interest Group in Computational Biology	Member	2004	2006
Executive Committee, Asian Pacific Bioinformatics Network (APBioNet)	Elected Member	2005	2010
Biophysical Society, Baltimore, MD, USA	Member	2007	2014

International Society for Computational Biology (ISCB)	Life Member	Since 2012	Still valid
Andhra Pradesh Akademy of Sciences	Elected Associate Fellow	Since 2010	
Society of Biological Chemists (India)	Life Member	Since 2012	

Books: 1 (Edited) Research Papers: 71; Patents: 1; Citations: 1790; h-index: 22; i10-index: 38

Selected peer-reviewed publications (Ten best publications in chronological order)

1. Ravindra Taware, Khushman Taunk, Jorge Pereira, Amey Shirolkar, Dharmesh Soneji , José S Câmara, **H A Nagarajaram**, Srikanth Rapole (2018) Volatilomic insight of head and neck cancer via the effects observed on saliva metabolites ***Scientific Reports*** 8:17725 | DOI:10.1038/s
2. Manjari Kiran and **H.A.Nagarajaram** (2016) Interaction and Localization Diversities of Global and Local Hubs in Human Protein-Protein Interaction Network ***Molecular Biosystems*** **12,** 2875 – 2882
3. Jorge Pereira, Priscilla Porto-Figueira, Carina Cavaco, Khushman Taunk, Srikanth Rapole, Rahul Dhakne, **Hampapathalu Nagarajaram**, José Câmara (2014) Breath analysis as a potential and non-invasive frontier in disease diagnosis. A metabolomic approach**.** ***Metabolites*** 5, 3-55
4. Rachita Halehalli and **H.A.Nagarajaram** (2014) Molecular principles of human virus protein-protein interactions ***Bioinformatics*** **31**, 1025-1033
5. Anupam Sinha and **H.A. Nagarajaram** (2014) Nodes occupying central positions in human tissue specific PPI networks are enriched with many splice variants. ***Proteomics*** 14, 2242-2248
6. Rachita Halehalli and **H.A.Nagarajaram** (2014) Viral proteins that bridge unconnected proteins and components in human PPI network ***Mol.Bio.Sys***. **10**, 2448-2458
7. Manjari Sinha and **H.A.Nagarajaram** (2013) Global versus local hubs in human protein-protein interaction network ***J.Proteome Res.*** 12: 5436–5446
8. Anupam Sinha and **H.A.Nagarajaram** (2013) Effect of Alternative Splicing on the Degree Centrality of nodes in PPI networks of *Homo sapiens* ***J.Proteome Res.*** 12: 1980–1988
9. Vishal Acharya and **H.A.Nagarajaram** (2012) Hansa: An automated method for discriminating disease and neutral human nsSNPs ***Hum Mutat*** **33** 332-337
10. Md. Tabrez Anwar Shamim, Mohammad Anwaruddin and **H. A. Nagarajaram** (2007) Support Vector Machine based classification of protein folds using the structural properties of amino acid residues and amino acid residue pairs. ***Bioinformatics*** 23:3320-3327