BIOGRAPHICAL SKETCH

NAME: RAMASWAMY SUBRAMANIAN

eRA COMMONS USER NAME: RamaswamyS

POSITION TITLE: PROFESSOR OF BIOLOGY AND BIOMEDICAL ENGINEERING, DIRECTOR BINDLEY BIOSCIENCE CENTER.

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Bharathidasan University, Tiruchirapalli, India	B. Sc	06/1985	Physics
Bharathidasan University, Tiruchirapalli, India	M. Sc	07/1987	Physics
Indian Institute of Science, Bangalore, India	Ph.D	06/1992	Molecular Biophysics

A. Personal Statement

My research has focused on elucidating molecular mechanisms of how biological molecules function. We work on a number of systems. We started with Rieske oxygenases where, my laboratory not only did some of the initial structural work, but we also were involved in brining structural understanding to the mechanism, and the *regio*- and *stero*- selectivity of product formation. My interest has also been in understanding weak protein-protein interactions and how they control signaling, and in collaboration with the other groups, we help tease out the details of the interaction of ubiquitin (when not ubiquitinylated) in regulation of protein function. In recent years significant contribution has been in systematically dissecting the structure and function of proteins involved in sialic acid scavenging, assimilation and use by pathogenic gram negative bacteria. My laboratory has constantly taken unconventional paths that have led to unexpected discoveries, which include our work on 'cockroach milk' and 'blue walleye'. The laboratory collaborates widely, where we both contribute our expertise in the use of biophysical tools, but also take help in validating (with phenotypic information) the hypothesis we generate from our molecular work. The support of a significant amount of the work in the laboratory has been from public funds, and we have been aware of creating return to investment by constantly pursuing, translational work based on our discoveries, leading to a number of patents. In recent years a significant amount of the work has been on a class of proteins that are involved in 9-carbon sugar transport and nucleotide sugar transports in hosts and infectious pathogens. We use cryo-EM and X-ray crystallography for most of the work. As my laboratory transitions from Bangalore to Purdue, I expect the number of people in the lab doing structural work increase.

B. Positions and Honors

Research and Professional Experience:

2019- Professor of Biology and Biomedical Engineering, Director, Bindley Bioscience Center, Purdue University, West Lafayette, Indiana.

2009-2019 Senior Professor and Dean, Institute for Stem Cell Biology and Regenerative Medicine, Bangalore, India.

2009-2016 Chief Executive Officer, Center for Cellular and Molecular Platforms, Bangalore, India.

2006-2009 Assistant Dean for Scientific Affairs/Director of Core Research Facilities, Carver College of Medicine, University of Iowa, Iowa City, Iowa.

2003-2009 Associate Professor, Department of Biochemistry, Carver College of Medicine, U of Iowa
2003-2009 Adjunct Associate Professor, Department of Chemical and Biochemical Engineering, U of Iowa
2000-2003 Assistant Professor, Department of Biochemistry, Carver College of Medicine, U of Iowa
2000-2006 Director, Protein Crystallography Facility, University of Iowa.
2001-2003 Adjunct Assistant Professor, Department of Chemical and Biochemical Engineering, U of Iowa
1995-2000 Research Scientist (Docent from 1996), Department of Molecular Biology, Swedish University of Agricultural Sciences, Uppsala, Sweden.
1992-1994 NFR Post-doctoral Fellow, Department of Molecular Biology, Swedish University of Agricultural Sciences, Uppsala, Sweden.

Memberships in Professional Societies

Life member International Union of Crystallography.
Member American Society of Biochemistry and Molecular Biology.
Member, American Chemical Society.
Member, American Association for the Advancement of Science.
2018-. Life Member, Electron Microscopy Society of India.

Awards and Honors

Fellow of the Electron Microscopy Society of India.
University of Iowa Foundation – Innovator of the year award, 2016.

Boards and committees (last 5 years)

Co-Chair of the Department of Biotechnology Task Force on BioFuels (2016-2019)
Co-Chair of the Board of Governors of TransDisciplinary University (2014-2019)
Member of the Board of Trustees of Foundation of Revitalization of Local Health Traditions (2017-2019)
Member, Executive Committee, Electron Microscopy Society of India (2018-)
Founding Board member – Center for Cellular and Molecular Platforms (2009-)
Int. Union of Crystallography, Member, Commission on Synchrotron Radiation & XFEL – 2017.
Founding Society Member – Institute for Stem Cell Science and Regenerative Medicine (2009-)
Chair, Genome Engineering Task Force, Department of Biotechnology, Government of India (2014-2016).

C. Contributions to Science

My research program combines my training in structural biology and biochemistry, with the work of my collaborators who are cell biologists, developmental biologists, microbiologists among others. The overall goal of the research program has been in trying to understand biology from the first principles, by understanding structure function relationships in a variety of systems.

1. A long term interest in the lab has been metal enzymes catalysis. While the focus of the program has been on Rieske oxygenases and alcohol dehydrogenase, the laboratory has worked on a number of different enzymes all towards elucidating the molecular basis of catalysis by enzymes. One of the major findings was the demonstration of side on binding of oxygen to iron. The work has also contributed significantly towards fundamental understanding of molecular basis of catalysis, by connecting detailed enzyme kinetics studies with structural studies. A few recent and few selected papers are listed below.

a. Guntupalli S, Li Z, Chang L, Plapp B, **Subramanian R**. Cryo-Electron Microscopy Structures of Yeast Alcohol Dehydrogenase. Biochemistry. 2021 February; 60(9):663-677. doi: 10.1021/acs.biochem.0c00921
b. Arya CK, Yadav S, Fine J, Casanal A, Chopra G, Ramanathan G, Vinothkumar KR, **Subramanian R**. A 2-Tyr-1-carboxylate Mononuclear Iron Center Forms the Active Site of a Paracoccus Dimethylformamidase. Angew Chem Int Ed Engl. 2020 Sep 21;**59**(39):16961-16966. doi: 10.1002/anie.202005332. Epub 2020 Jun 30. PubMed PMID: 32452120; PubMed Central PMCID: PMC7686228
c. Sathyanarayanan N, Cannone G, Gakhar L, Katagihallimath N, Sowdhamini R, **Ramaswamy S**, Vinothkumar KR. Molecular basis for metabolite channeling in a ring opening enzyme of the phenylacetate degradation pathway. *Nat Commun.* 2019 Sep 11;10(1):4127. doi: 10.1038/s41467-019-11931-1. PubMed PMID: 31511507; PubMed Central PMCID: PMC6739347.
d. Plapp, B. V., Savarimuthu, B. R., Ferraro, D. J., Rubach, J. K., Brown, E. N., and **Ramaswamy, S.** (2017) Horse Liver Alcohol Dehydrogenase: Zinc Coordination and Catalysis. *Biochemistry*. **56**, 3632–3646.
e. Karlsson, A., Parales, J. V., Parales, R. E., Gibson, D. T., Eklund, H., and **Ramaswamy, S.** (2003) Crystal structure of naphthalene dioxygenase: Side-on binding of dioxygen to iron. *Science (80-.).* **299**, 1039–1042

2. Studies on Sialic Acid uptake and metabolism by gram negative bacteria: We and our collaborators have been involved in understanding the structure function studies of protein involved uptake and use of Neu5Ac by pathogenic gram negative bacteria. The long term goal has been to first understand then design molecules that can inhibit this pathway. We have pursued these studies by X-ray crystallography, electron cryo-microscopy and biochemical characterization. To date we have determined structures of the periplasmic binding components of the Sialic acid transport proteins, two of the membrane transporters (one published), all the enzymes involved in the conversion of Neu5Ac into fructose-6-phosphate.

a. Gangi Setty T, Mowers JC, Hobbs AG, Maiya SP, Syed S, Munson RS Jr, Apicella MA, **Subramanian R.** Molecular characterization of the interaction of sialic acid with the periplasmic binding protein from *Haemophilus ducreyi*. J Biol Chem. 2018 Dec 28;293(52):20073-20084.
b. Kumar JP, Rao H, Nayak V, **Ramaswamy S.** Crystal structures and kinetics of N-acetylneuraminate lyase from Fusobacterium nucleatum. Acta Crystallogr F Struct Biol Commun. 2018 Nov 1;74(Pt 11):725-732.
c. Manjunath, L., Guntupalli, S. R., Currie, M. J., North, R. A., Dobson, R. C. J., Nayak, V., and **Subramanian, R.** (2018) Crystal structures and kinetic analyses of *N* -acetylmannosamine-6-phosphate 2-epimerases from *Fusobacterium nucleatum* and *Vibrio cholerae*. *Acta Crystallogr. Sect. F Struct. Biol. Commun.* **74**, 431–440
d. Wahlgren, W. Y., Dunevall, E., North, R. A., Paz, A., Scalise, M., Bisignano, P., Bengtsson-Palme, J., Goyal, P., Claesson, E., Caing-Carlsson, R., Andersson, R., Beis, K., Nilsson, U. J., Farewell, A., Pochini, L., Indiveri, C., Grabe, M., Dobson, R. C. J., Abramson, J., **Ramaswamy, S.**, and Friemann, R. (2018) Substrate-bound outward-open structure of a Na+-coupled sialic acid symporter reveals a new Na^+ site. *Nat. Commun.* **9**(1), 1753.

3. Another major interest of the laboratory has been in identifying unusual biological phenomena and finding molecular explanations underlying these. Our work on *in vivo* crystals obtained from gut of the cockroach embryo is one of the most read articles (over 50,000 downloads) published in the last 5 years. Interestingly, the work also has led to development of yeast strains that are now being developed commercially for nutritional purposes. Another

significant work was the work on the blue walleye (walleyes are normally yellow). Our work resulted in the discovery of a new fluorescent protein that emits in the infra-red region. The idea of collaborating with colleagues to work on carry out biophysical experiments that when correlated with biological data has been a constant theme. A few recent papers are below.

a. Subramanian, S. P., Babu, P., Palakodeti, D., and **Subramanian, R.** (2018) Identification of multiple isomeric core chitobiose–modified high-mannose and paucimannose N-glycans in the planarian Schmidtea mediterranea. *J. Biol. Chem.* **293**, 6707–6720
b. Ghosh, S., Yu, C.-L., Ferraro, D. J., Sudha, S., Pal, S. K., Schaefer, W. F., Gibson, D. T., and Ramaswamy, S. (2016) Blue protein with red fluorescence. *Proc. Natl. Acad. Sci.* **113**, 11513–11518.
c. Mishra, A., Sriram, H., Chandarana, P., Tanavde, V., Kumar, R. V, Gopinath, A., Govindarajan, R., **Ramaswamy, S.**, and Sadasivam, S. (2018) Decreased expression of cell adhesion genes in cancer stem-like cells isolated from primary oral squamous cell carcinomas. *Tumour Biol.* **40** (6), 1010428318780859
d. Sahadevan, S., Antonopoulos, A., Haslam, S. M., Dell, A., **Ramaswamy, S.**, and Babu, P. (2014) Unique, polyfucosylated glycan-receptor Interactions are essential for regeneration of *Hydra magnipapillata*. *ACS Chem. Biol.* **9**, 147–155

For a complete list of publications see:
https://www.ncbi.nlm.nih.gov/labs/bibliography/1HqJeCMKcfJ/bibliography/public/

D. Research Support

Ongoing

Elanco Animal Health June 2020-Dec 2021.
Structure function studies of Calcium Sensitive Potassium Channels.

Department of Biotechnology (GOI) 12/2013 – 2021 (once renewed)
Characterization & Structure Function Studies of Proteins, Transporters and Enzymes of the Sialic Acid Scavenging- and LOS/LPS Sialyation Pathways: Putative Targets for New Antimicrobial Agents.
This is an Indo-Swedish collaborative grant to first elucidate the molecular basis of sialic acid uptake and catabolism by gram negative pathogens and then use them to determine specific inhibitors. We have now completed most of the structure function work and are currently screening for drugs both computationally as well as by design methods.
Role: PI (Indian part)

Competed (last 3 years)

Department of Biotechnology (GOI)
01/2015-04/2019
Molecular Form and Function Laboratory at Bangalore Life Science Cluster.
The grant is a large infrastructure grant to set up and manage a National Structural Biology Facility at the campus in Bangalore. The grant also provides the support for creating a large data facility to store mesoscale data from ecological research to atomic resolution structural information.
Role: Coordinator and one of the PIs at the Institute for Stem Cell Science and Regenerative Medicine, Bangalore.

Department of Science and Technology (GOI)08/2017-07/2020
Structure-function studies of Nucleotide Sugar Transporters.
The goal is to determine the structure of *Eukaryotic* Nucleotide sugar transporters and correlate them to molecular function. Several developmental disorders are caused due to mutations in these genes.

Role: PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Dhabaleswar Patra

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Postdoctoral fellow.

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Utkal University, Bhubaneswar, India	B. Sc B.Ed.	06/2003	Chemistry, Botany, Zoology & Education
Goa University, Goa, India	M. Sc	07/2005	Marine biotechnology
Indian Institute of Science, Bangalore, India	Ph.D	03/2015	Molecular Biophysics

A. Personal Statement:

My long-term research interests involve the structural and functional understanding of key proteins involved in human disease using single particle cryo-electron microscopy. My academic training and research experience have provided me with an excellent background in multiple biophysical techniques including structural biology (X-ray crystallography and Cryo-EM). As a graduate student, I was able to conduct research on novel mycobacterial lectins involved in host-pathogen interactions. As a predoctoral fellow, my research focused on structural and functional characterization of proteins involved in cardiovascular diseases. I gained expertise in the structural characterization of GPCRs and their signaling partners using cryo-electron microscopy. Among other work, I was also involved in LCAT-HDL interactions a key event in reverse atherosclerosis. Structural biology is a mainstay of my research. To complement this further, I am developing new methods of sample preparation for micro-ED experiments where my crystallography and cryo-EM knowledge come together.

B. Positions and Honors:

Research and Professional Experience:

2018- Post-doctoral fellow, Purdue University, West Lafayette, Indiana.
2015-2018 Post-doctoral fellow, University of Michigan, Ann Arbor, Michigan.

Memberships in Professional Societies

Life member Indian Crystallography Association. Member of Indian Biophysical Society. Reviewer of journal Annals of Glycomics & Lipidomics.

Awards and Honors

Recipient of IUPAB travel award for young scientists 17th International Biophysics Congress held in Beijing, China 2011
Recipient of the Junior/Senior Research fellowship from Council of Scientific and Industrial Research (CSIR), Government of India 2006
Successfully qualified the national level Graduate Aptitude Test Examination conducted by MHRD (Ministry of Human Resource and Development, Govt. of India)
Successfully qualified the national level entrance examination for admission to Ph.D. (2006) programme conducted by Indian Institute of Science, Bangalore, India

Qualified the national level entrance examination for admission to Master of Science degree (2003) conducted by Department of Biotechnology, Ministry of Science & Technology, Govt. of India, New Delhi
Recipient of silver medal in mathematics for senior level National Talent Search Contest 1996

C. Contributions to Science

I am currently involved on COVID 19 research (JBC 2020) after the pandemic. I am using X-ray crystallography and cryo-EM (single particle analysis) as structural biology tools to study some of the key proteins from SARS2 virus and host-SARS2 protein interactions. Also, I am involved on structural investigation of virus like particles (VLPs) from SARS2 using cryo-EM.

In university of Michigan, I was involved in G-protein coupled receptor (GPCR) mediated signal transductions research which are associated with cardiovascular diseases (JACS 2017). The phosphorylation of agonist occupied GPCRs by GPCR kinases (GRKs) functions to turn off G-proteins signaling and turn on arrestin mediated signaling. The structural understanding of GPCR/G-protein and GPCR/arrestin complexes has emerged in recent years, however the molecular architecture of GPCR/GRK complex is poorly defined. I was involved on GRK5 interactions with the β-adrenergic receptor (β2-AR) (Cell 2017). GRK5 is potentially inhibited by calcium sensing protein calmodulin (CaM), which leads to nuclear translocation of GRK5 and promotes cardiac hypertrophy. I recently investigated the complex formation of Ca^{2+}.CAM/ GRK5 using single particle electron microscopy (PNAS 2019). I am also involved in rhodopsin/GRK1 interaction as another model system for GPCR/GRK interactions (Nature 2021).

I am also involved in the study of lecithin-cholesterol acyltransferase (LCAT)/High-density lipoprotein (HDL) mediated reverse cholesterol transport, which is the key event in reducing plaque formation in arterial wall. LCAT esterifies cholesterol on HDL which promotes HDL maturation in reverse cholesterol transport- the process by which cholesterol is moved from arterial plaque to the liver. In this effort I was looking into the LCAT/HDL interaction using electron microscopy (Nature communication biology 2020).

I was also involved in Fab screening for structural and functional studies of a-secretase ADAM10 using electron microscopy, which eventually led into solving X-ray crystal structure of ADAM10-11G2$_{fab}$ complex structure (Cell 2017).

For a more complete list of publications see:
https://pubmed.ncbi.nlm.nih.gov/?term=dhabaleswar+Patra