

# CENTRE OF BIOMEDICAL RESEARCH

## Curriculum Vitae

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**Education:**

1980	<b>B.Sc.</b>	Lucknow University
1982	<b>M.Sc.</b>	Lucknow University
1992	<b>Ph.D.</b>	Central Drug Research Institute (CDRI) Lucknow, registered at Meerut University

**Postgraduate Training and Fellowship:**

January 1985 - January 1987     **Junior Research Fellow (CSIR)**, CDRI, Lucknow, India.

January 1987 - April 1988     **Senior Research Fellow (CSIR)**, CDRI, Lucknow, India.

**Faculty Positions:**

May 1988 – April 1991	<b>Scientist B</b> , Central Drug Research Institute
May 1991 – April 1996	<b>Scientist C</b>
May 1996 – April 2001	<b>Scientist E1</b>
May 2001 – April 2006	<b>Scientist EII</b>
May 2006 – April 2007	<b>Scientist F, Deputy Director</b>
16 <sup>th</sup> April 2007 onwards	<b>Professor</b> , Centre of Biomedical Research (CBMR), formerly known as Centre of Biomedical Magnetic Resonance (CBMR), Lucknow.
2 <sup>nd</sup> February 2019 onwards	<b>Director</b> (Additional charge), CBMR, Lucknow

#### **Awards, Honors:**

1993	<b>Bruker Young Scientist Award</b>
2000	<b>Fellowship under Indo-Italian Programme September to October 2000</b>
2001	<b>Fellow of National Academy of Sciences, F.N.A.Sc (Allahabad 2001)</b>
2013	<b>E. K. Zavoisky Stipend, ISMRM 2013</b>
2015	<b>Member of Editorial Advisory Board of the Journal, <i>Metabolomics</i> (Springer)</b>

#### **Membership in Professional and Scientific Societies:**

International Society of Magnetic Resonance in Medicine (since 2007)  
National Magnetic Resonance Society (since 1989)

#### **Administrative Responsibility:**

Incharge, NMR Laboratory at Central Drug Research Institute, Lucknow (1988-2007).

Head, Department of Molecular Diagnostic and Phenome Research, CBMR, SGPGIMS campus, Lucknow (2015 onwards).

Chairperson of Purchase Committee, Safety Committee and Appealing Officer RTI, Estate Manager of Residential area and Guest House, of CBMR (till 2<sup>nd</sup> Feb 2019), SGPGIMS campus, Lucknow.

### **ACADEMIC ACTIVITIES**

## Scientific and Academics:

- Supervised four research projects (6 monthly) of BITS, Pilani for partial fulfilment of graduate and post-graduate courses.
- Co-supervised seven M.D. and twenty four M.S. Thesis
- Supervised Ph.D thesis entitled “**Application of Modern NMR Techniques in Chemistry (Structure Elucidation, Dynamics, Mixture Analysis and Reaction Monitoring)**” thesis submitted by Mr. B.S.Joshi at Lucknow University, September 2002. The Ph.D degree has been awarded in the month of July, year 2003.
- Supervised Ph.D thesis entitled “**MODERN NMR APPLICATIONS IN MEDICINAL CHEMISTRY: Synthesis, Structure and Mechanistic Studies of Bioactive Molecules**” thesis submitted by Mr. Rajesh Kumar Grover at Lucknow University, March 2004. The Ph.D degree has been awarded in the month of July 2004.
- Supervised Ph.D thesis entitled “**NMR Structural Aspects in Biological Systems: Analysis in Leishmaniasis, Tuberculosis and Meningitis**”, thesis submitted by Mr. Subramanian A.R. at Birla Institute of Technology and Science, Pilani, May 2006 and awarded in the month of October 2006.
- Supervised Ph.D thesis entitled “**NMR Based Mechanistic Evaluation in Synthesizing Analogues of Bio-Active Molecules: Preferentially Anti-Cancer Agents**”, thesis submitted by Mr. Abhijeet Deb Roy at Benaras Hindu University, Varanasi, January 2007 and awarded in the month of May 2007.
- Supervised Ph.D thesis entitled “**Precise Quantitation and Structural Characterization of Various Chemical Components in Biological Samples by NMR Spectroscopy**” thesis submitted by Mr. Santosh Kumar Bharti at Lucknow University, September 2011 and awarded in the month of May 2012.
- Supervised Ph.D. thesis entitled “**Analysis of Tissues and Body Fluids in various Cancer Diseases by NMR Spectroscopy**” thesis submitted by Ms Shatakshi Srivastava at Lucknow University, October 2012 and awarded in the month of February 2014.
- Supervised Ph.D Thesis entitled “**Design and Synthesis of MRI Contrast Agents for Neurodegenerative Disorders**” thesis submitted by Mr. Neeraj Rastogi at Lucknow University, March 2014 and awarded in the month of December 2015.

- Visiting Faculty and consultant of **Center of Biomedical Magnetic Resonance, now known as Centre of Biomedical Research (CBMR)** at SGPGIMS Lucknow till April 2007.
- Jointly supervised two Ph.D. students one from KGMU Ms Alka Singh and the other from RMLIMS Lucknow., Ms Tanushri Chatterji,
- Presently supervising two Ph.D. students and one Research Associate.

### **Other Scientific and academic Activities:**

- Program Advisory Committee Member (PAC), of National Facility for High Field NMR at Tata Institute of Fundamental Research, Bombay (2002-2005).
- Conducted an NMR workshop at RRL Jammu (26<sup>th</sup> March to 30<sup>th</sup> March 2001).
- Convener and Faculty of a “National Summer School on NMR in Chemistry: From molecules to Human Behaviour”, at IHBT Palampur (25<sup>th</sup> June to 5<sup>th</sup> July 2002), jointly conducted by CBMR, SGPGIMS, CDRI Lucknow and IHBT Palampur.
- Secretary of National Magnetic Resonance Society (2008-2009).
- Faculty of National Summer School in NMR from molecules to Human Behaviour (2003 to 2008). Sponsored, by DST.
- Convener of one-year M.Phil course in Magnetic Resonance (MRI/MRS) during the year 2008-2010. This course was carried out at our Centre in collaboration with Lucknow University.
- Organizing Secretary of **16<sup>th</sup> Conference of National Magnetic Resonance Society**, February 21<sup>st</sup> to 24<sup>th</sup> 2010, at Centre of Biomedical Magnetic Resonance, Sanjay Gandhi Post Graduate institute of Medical Sciences campus, Lucknow.

### **Extramural Projects:**

- Co-Investigator for the DST project entitled, “National Summer School in NMR from molecules to Human Behaviour”, (2003-2008). Project amount Rs. 60.00 lakhs
- Co-PI for the DST Project entitled: “Study of diseases and metabolism in human and plant Systems” (2009-2012). Project amount for the procurement of 800 MHz

FT NMR spectrometer etc., Project amount Rs. 11.00 crore.

- PI for the ICMR project entitled: “Comparative Metabolomic and treatment followup study of Saliva by Nuclear Magnetic Resonance in Periodontitis”, (2015-2017). Project amount Rs 14.00 lakhs.
- PI for the DST project entitled: Glycoprotein acetyls (GlycA), cholesterol esters and metabolic profiling in serum of Gall Bladder cancer patients by NMR spectroscopy, (2018-2021). Project amount Rs 36.37 lakhs.

## **RESEARCH EXPERIENCE**

### ***Have worked in the following areas of research:***

- Structure determination of bioactive molecules from natural source by NMR methods.
- NMR studies on diversified organic molecules.
- In vivo  $^{31}\text{P}$  NMR studies on filarial worms (*Acanthocheilonema viteae* and *Brugia malayi*) and their long-term *in vivo* exposure to drugs.
- NMR studies on intracranial cystic mass lesions.
- Methodology for detailed NMR analysis and dynamics in expanded porphyrins.
- Metabolomics in medicinally important plants and human diseases.

## **AREA OF PRESENT WORK**

### **Metabolomics in human diseases and in medicinally important plants by NMR spectroscopy.**

**Metabolomics** using NMR spectroscopy is now a well-established technique for obtaining information regarding the metabolic profile of body fluids, tissue extracts and tissues. “Metabolomics/Metabonomics: is a quantitative measurement of time related multi-parametric metabolic responses of multicellular systems to pathophysiology, exogenous or endogenous stimuli or genetic modification”. Its potential of joining genomics, transcriptomics and proteomics, provides extensive information about a living system, which can be further utilized in drug development, diagnostics and health screening. Under pathological conditions some of these genes and proteins either get up-regulated or down-

regulated resulting in the derangement in concentrations of various metabolites or altered metabolic pathways result in new molecular entity suitable for diagnostic evaluation. Similarly, plant metabolomics is more complex and NMR spectroscopy is a commonly applied technique in plant metabolomics and has been used to analyze a range of chemically diverse metabolites including catechins, aliphatic compounds, aromatic compounds, organic acids, phenolics, fatty acids, steroids, sugars and bioactive molecules from the plant extracts. Our group is involved in metabolic profiling of body fluids obtained from patients suffering from, parasitic, meningitis, urosepsis and in spinal cord injury (SCI) with follow-up treatment in order to identify significant metabolic confounders correlating the disease state. Moreover, native tissue based HR-MAS NMR metabolomics in oral, gall bladder and breast cancer for rapid differentiation of malignant and non-malignant tissues. In plant metabolomics, our group is involved in identifying bioactive secondary metabolic entities in medicinally and economically important plants.

### **Research Publications (Peer Reviewed):**

1. Anup Paul, Surendra Kumar, Anubhav Raj, A. A. Sonkar, Sudha Jain, Atin Singhai and **Raja Roy** (2018). Alteration in lipid composition differentiates breast cancer tissues: A  $^1\text{H}$  HRMAS NMR metabolomic study. ***Metabolomics***, DOI: 10.1007/s11306-018-1411-3.
2. Tusha Tripathi, Anil Bhatiaa, Suruchi Singh, Kunwar Sarvendra, Abdul Rahman Khan, Om P. Sidhu and **Raja Roy** (2018). Metabolite Profiling of *Commiphora wightii* (Guggul) with Respect to Seasons. ***Nat.Prod.Comm.*** **10**, 1345-1348.
3. G. Nagesh Babu, Manjeet Gupta, Vimal K. Paliwal, Suruchi Singh, Tanushri Chatterji and **Raja Roy** (2018) Serum metabolomics study in a group of Parkinson's disease patients from northern India. ***Clinica Chimica Acta.*** **480**, 214.
4. Alka Singh, Rajeshwar Nath Srivastava, Ashok Agrahari, Suruchi Singh, Saloni Raj, Tanushri Chatterji, Abbas Ali Mahdi, Ravindra Kumar Garg and **Raja Roy** (2018). Proton NMR based serum metabolic profile correlates with the neurological recovery in treated acute spinal cord injury (ASCI) subjects: A pilot study. ***Clinica Chimica Acta.*** **480**, 150.
5. Anil Bhatia, Tusha Tripathi, Suruchi Singh, Hema Bisht, Hari M. Behl, **Raja Roy** and Om P. Sidhu (2018). Comprehensive metabolite profiling in

distinct chemotypes of *Commiphora wightii*. **Natural Product Research**. DOI: 10.1080/14786419.2018.1431629.

6. Abdul-Hamid Emwas, Edoardo Saccenti, Xin Gao, Ryan T. McKay, Vitor A. P. Martins dos Santos, **Raja Roy** and David S. Wishart (2018). Recommended strategies for spectral processing and post-processing of 1D <sup>1</sup>H-NMR data of biofluids with a particular focus on urine. **Metabolomics**. DOI: 10.1007/s11306-018-1321-4.
7. Rohit Khanna, Kapila Kumar and **Raja Roy** (2018). A case study of primary malignancy of buccal mucosa using proton HR-MAS NMR spectroscopy on tissue specimens. **Journal of Oral Biology and Craniofacial Research**. **8**, 68.
8. Neeraj Rastogi, Nidhi Tyagi, Ovender Singh, B. S. Hemanth Kumar, Udai P. Singh, Kaushik Ghosh and **Raja Roy** (2017). Mn(II) based T1 and T2 potential MRI contrast agent appended with tryptamine: Recognition moiety for A $\beta$ -plaques. **Journal. Inorg. Biochem**. **177**, 76.
9. Manvendra Pratap Singh, Mona Saxena, C.S. Saimbi, Jamal M Arif and **Raja Roy** (2017), Metabolic profiling by <sup>1</sup>H NMR spectroscopy of saliva shows clear distinction between control and diseased case of periodontitis. **Metabolomics**. DOI: 10.1007/s11306-017-1245-4 (in press).
10. Tanushri Chatterji, Suruchi Singh, Manodeep Sen, A.K. Singh, G.R. Agarwal, D.K. Singh, J.K. Srivastava, A Singh, R.N. Srivastava and **Raja Roy** (2017), Proton NMR metabolic profiling of CSF reveals distinct differentiation of meningitis from negative controls. **Clinica Chimica Acta**. **469**, 42.
11. Anil Bhatia, Baleshwar Meena, Sanjeev K. Shukla, Om P. Sidhu, Dalip K. Upreti, Anuradha Mishra, **Raja Roy** & Chandra Shekhar Nautiyal (2017). Determination of Pentacyclic Triterpenes from *Betula utilis* by High-Performance Liquid Chromatography and High Resolution Magic Angle Spinning Nuclear Magnetic Resonance Spectroscopy. **Analytical Letters**. **50**, 233.
12. Suruchi Singh and **Raja Roy** (2016), The Application of Absolute Quantitative <sup>1</sup>H NMR Spectroscopy in Drug Discovery and Development. **Expert Opinion On Drug Discovery**. **11**, 695.
13. Tanushri Chatterji, Suruchi Singh, Manodeep Sen, Ajai Kumar Singh, Pradeep Kumar Maurya, Nuzhat Husain, Janmejai Kumar Srivastava, Sudhir Kumar Mandal and **Raja Roy** (2016), Comprehensive <sup>1</sup>H NMR metabolic profiling of body fluids for differentiation of meningitis in adults. **Metabolomics**. **12**, 130.
14. Abdul-Hamid Emwas, **Raja Roy**, Ryan T. McKay, Danielle Ryan, Lorraine Brennan, Leonardo Tenori, Claudio Luchinat, Xin Gao, Ana Carolina Zeri, G. A. Nagana Gowda, Daniel Raftery, Christoph Steinbeck, Reza M Salek and David S. Wishart (2016). Recommendations and Standardization of

Biomarker Quantification Using NMR-based Metabolomics with Particular Focus on Urinary Analysis. **J.Proteome.Res.** **15**, 360.

15. Suruchi Singh, Tanushri Chatterji, Manodeep Sen, Ishwar Ram Dhayal, Swati Mishra, Nuzhat Husain, Apul Goel and **Raja Roy** (2016). Serum procalcitonin levels in combination with  $^1\text{H}$  NMR spectroscopy: A rapid indicator for differentiation of urosepsis. **Clinica Chimica Acta.** **453**, 205.
16. Anil Bhatia, S.K.Bharti, Tusha Tripathi, Anuradha Mishra, Om P. Sidhu, **Raja Roy** and C.S. Nautiyal (2015). Metabolic profiling of *Commiphora wightii* (Guggul) reveals a potential source for pharmaceuticals and nutraceuticals. **Phytochemistry.** **110**, 29.
17. Surender Kumar, Shailendra Kumar, **Raja Roy**, A.S.Rathore, M.M.Goel, Gaurav Agarwal and Sandeep Kumar (2015). High Resolution Magic Angle Proton Magnetic Resonance Spectroscopy (HRMAS) in Intact Sentinel Node Biopsy from Breast Cancer Patients: A New Diagnostic Tool!. **Journal of Surgery.** **10**, 227.
18. Vibhor V. Borkar, Ujjal Poddar, Niraj Kumari, Suruchi Singh, **Raja Roy** and Surender K. Yachha (2015). Duodenal Morphometry and Small Bowel Permeability in Children with Portal Hypertension. **J. Pediatr. Gastroent. and Nutrition.** **60**, 171.
19. Abdul-Hamid Emwas, Claudio Luchinat, Paola Turano, Leonardo Tenori, **Raja Roy**, Reza M. Salek, Danielle Ryan, Jasmeen S. Merzaban, Rima Kaddurah-Daouk, Ana Carolina Zeri, G. A. Nagana Gowda, Daniel Raftery, Yulan Wang, Lorraine Brennan and David S. Wishart (2015). Standardizing the experimental conditions for using urine in NMR-based metabolomic studies with a particular focus on diagnostic studies: a review. **Metabolomics.** **11**, 872.
20. S.K.Bharti and **Raja Roy** (2014). Metabolites Identification in NMR-based Metabolomics. **Current Metabolomics.** **2**, 163.
21. Suruchi Singh, Shatakshi Srivastava, **Raja Roy**, K. Gaurav, S. Kumar, Abhinav A Sonkar, M.M. Goel and R. Garg (2014). Metabolic profiling of cervical tubercular lymphadenitis tissues by proton HR-MAS NMR spectroscopy. **Metabolomics**, **10**, 975.
22. D.V.Singh, S.K.Bharti, Shikha Agarwal, **Raja Roy** and Krishna Mishra (2014). Study of interaction of human serum albumin with curcumin by NMR and docking. **J. Mol. Model.** **20**, 1.
23. P.Rana, M.Gupta, A.R.Khan, B.S.Hemant Kumar, **Raja Roy** and S.Khushu (2014), NMR based metabolomics reveals acute hippocampal

metabolic fluctuations during cranial irradiation in murine model. **Neurochem. Int.** **74**, 1.

24. R. Tyagi, P. Rana, M. Gupta, D. Bhatnagar, S. Srivastava, **Raja Roy** and S. Khushu (2014), <sup>1</sup>H NMR spectroscopic analysis detects metabolic disturbances in rat urine on acute exposure to heavy metal tungsten alloy based metals salt. **Chem. Biol. Interact.** **211**, 20.
25. Ajesh Goyal, U.C.Ghoshal, Imran Ahmad, **Raja Roy**, Deepakshi Srivastava, Samir Mohindra, V.A.Saraswat, C.L.Khetrapal (2013), Frequency and factors associated with increased small intestinal permeability in patients with portal hypertension. **Tropical Gastroenterology.** **34**, 136.
26. Shatakshi Srivastava, **Raja Roy**, Santosh Kumar, Hari Om Gupta, Devendra Singh, Jitendra Kumar Kushwaha, Abhijit Chandra, Abhinav Arun Sonkar (2013), Cholesterol and its esters as serum biomarkers in malignant Obstructive Jaundice: A single step <sup>1</sup>H NMR metabolomic approach. **Metabolomics.** **9**, 1181.
27. Deepak Gurbani, Santosh Kumar Bharti, Ashutosh Kumar, Alok K. Pandey, Godson R.E.E. Ana, Ambrish Verma, Altaf Husain Khan, Devendra K. Patel, M.K.R. Mudiam, Swatantra K. Jain, **Raja Roy** and Alok Dhawan (2013), Polycyclic aromatic hydrocarbons and their quinones modulate the metabolic profile and induce DNA damage in human alveolar and bronchiolar cells. **International Journal of Hygiene and Environmental Health.** **216**, 553.
28. Bacopa Monnieri Modulate Aluminium Induced Macromolecular Changes in Rat Brain: A Magnetization Contrast Brain Imaging Study”, Sandeep Tripathi, Sanjay Annarao, **Raja Roy** and Abbas Ali Mahdi. **Am. J of Neuroprotect. and Neuroregeneration.** (2013), **5**, 101.
29. Anil Bhatia, Santosh K. Bharti, Shri K. Tewari, Om P. Sidhu and **Raja Roy** (2013), Metabolic profiling for studying chemotype variations in *Withania somnifera* (L) Dunal fruits using GC-MS and NMR spectroscopy. **Phytochemistry.** **93**, 105.
30. Santosh Kumar Bharti, Anu Behari, Vinay Kumar Kapoor, Niraj Kumari, Narendra Krishnani and **Raja Roy** (2013), Magic Angle Spinning NMR Spectroscopic Metabolic Profiling of Gall Bladder Tissues for Differentiating Malignant from Benign Disease. **Metabolomics.** **9**, 101.
31. Neeraj Rastogi, Kalyan Mitra, Dinesh Kumar, and **Raja Roy** (2012), Metal Ions as Cofactors for Aggregation of Therapeutic Peptide Salmon Calcitonin. **Inorg. Chem.** **51**, 5642.

32. Shatakshi Srivastava, Hema Bisht, O.P. Sidhu, Ashish Srivastava, P.C. Singh, R.M. Pandey, S. K. Raj, **Raja Roy** and C.S. Nautiyal (2012), Changes in the metabolome and histopathology of *Amaranthus hypochondriacus* L. in response to *Ageratum enation virus* infection. **Phytochemistry**, **80**, 8.
33. Santosh Kumar Bharti and **Raja Roy** (2012), Quantitative <sup>1</sup>H NMR Spectroscopy **Trends in Analytical Chemistry**, **35**, 5.
34. Shatakshi Srivastava, A.A. Sonkar and **Raja Roy** (2012), Oral Squamous Cell Carcinoma: Insights with metabonomics. **Chemistry & Biology Interface**. **2**, 206.
35. Ritu Tyagi, Poonam Rana, Mamta Gupta, Ahmad Raza Khan, M. Memita Devi, Deepak Bhatnagar, **Raja Roy**, Rajendra P. Tripathi and Subash Khushu (2012), Urinary metabolomic phenotyping of nickel induced acute toxicity in rat: an NMR spectroscopy approach. **Metabolomics**. **8**, 940.
36. Santosh Kumar Bharti, Virendra Jaiswal, Ujjala Ghoshal, Uday Chand Ghoshal, Sanjay S. Baijal, **Raja Roy** and C.L. Khetrapal (2012), Metabolomic profiling of amoebic and pyogenic liver abscesses: An *in-vitro* NMR study. **Metabolomics**. **8**, 540.
37. S.K. Bharti, Anil Bhatia, S.K. Tewari, O.P. Sidhu and **Raja Roy** (2011), Application of HR-MAS NMR spectroscopy for studying chemotype variations of *Withania somnifera* (L.) Dunal. **Magn.Reson.Chem.** **49**, 659.
38. Preeti Singh, Madan Godbole, Geeta Rao, Sanjay Annarao, Kalyan Mitra, **Raja Roy**, Arvind Ingle, Gaurav Agarwal and Swasti Tiwari (2011), Inhibition of autophagy stimulate molecular iodine-induced apoptosis in hormone independent breast tumors. **Biochem.Biophys.Res.Comm.** **415**, 181.
39. O.P. Sidhu, Sanjay Annarao, Sandipan Chatterjee, Rakesh Tuli, **Raja Roy** and C.L. Khetrapal (2011), Metabolic alterations of *Withania somnifera* (L.) Dunal fruits at different developmental stages by NMR Spectroscopy. **Phytochem Analysis**. **22**, 492.
40. V.K Singh, V. Srivastava, V. Singh, N. Rastogi, **Raja Roy**, A.K. Shaw, A.K. Dwivedi, R. Srivastava, B.S. Srivastava (2011), Overexpression of Rv3097c in Mycobacterium bovis BCG abolished the efficacy of BCG vaccine to protect against Mycobacterium tuberculosis infection in mice. **Vaccine**. **29**, 4754.
41. Shatakshi Srivastava, **Raja Roy**, Vivek Gupta, Ashish Tiwari, A. N. Srivastava and A. A. Sonkar (2011), Proton HR-MAS MR Spectroscopy of Oral Squamous Cell Carcinoma Tissues: An *ex-vivo* study to Identify Malignancy Induced Metabolic Fingerprints. **Metabolomics**. **7**, 278.

42. A. Mishra, S. Hutait, S.Bhuomik, N.Rastogi, **Raja Roy** and S.Batra (2011), Utility of Allylic Azides for the Synthesis of Fused Triazoles and Tetrazoles via Intramolecular Cycloaddition. **Synthesis**. **16**, 2731.
43. Sunil Kumar, U. C. Ghoshal, Kamaiah Jayalakshmi, **Raja Roy**, Asha Misra and C. L. Khetrapal (2010), Abnormal Small Intestinal Permeability in Patients with Idiopathic Malabsorption in Tropics (Tropical Sprue) Does not Change Even After Successful Treatment. **Dig. Dis. Sci**. **56**, 161.
44. Sandipan Chatterjee, Shatakshi Srivastava, Om Prakash Sidhu, Rajender Singh Sangwan, **Raja Roy**, C.L.Khetrapal and Rakesh Tuli (2010), Comprehensive metabolic fingerprinting of *Withania somnifera* leaf and root extracts. **Phytochem**. **71**, 1085.
45. O.P. Sidhu, Sanjay Annarao, Uday Pathre, S. K. Snehi, S. K. Raj, **Raja Roy**, Rakesh Tuli and C.L.Khetrapal (2010), Metabolic and histopathological alterations of *Jatropha mosaic begomovirus* infected *Jatropha curcas* L. by HR-MAS NMR spectroscopy and Magnetic Resonance Imaging. **Planta**, **232**, 85.
46. A.K.Verma, Preeti Khamaria, Jyoti Gupta, D.P.Singh, B.S.Joshi, **Raja Roy**, A.K.Mishra and Ram Pratap. (2010) Bio-transformation of FXR antagonist CDRI 80/574. **ARKIVOC** i. 1.
47. Shatakshi Srivastava, **Raja Roy**, Sudhir Singh, Praveen Kumar, Diwakar Dalela, S.N.Shankwar, Apul Gupta and A.A. Sonkar (2010), Taurine -a possible fingerprint biomarker in Non-Muscle Invasive Bladder Cancer: A pilot study by <sup>1</sup>H NMR Spectroscopy. **Cancer Biomarkers**. **6**, 11.
48. Pratima Tripathi, Lakshmi Bala, Rajan Saxena, S.K.Yachha, **Raja Roy** and C.L.Khetrapal (2009), <sup>1</sup>H NMR spectroscopic study of Blood Serum for the Assessment of Liver function in liver transplant patients. **J Gastrointestin Liver Dis**. **18**, 329.
49. K. Jayalakshmi, U.C. Ghoshal, S. Kumar, A. Misra, **Raja Roy** and C. L. Khetrapal (2009), Assessment of Small Intestinal Permeability using <sup>1</sup>H-NMR Spectroscopy. **J Gastrointestin Liver Dis**. **18**, 27.
50. Lakshmi Bala, P. Tripathi, G. Bhatt, K. Das, **Raja Roy**, G. Choudhuri and C. L. Khetrapal (2009), <sup>1</sup>H and <sup>31</sup>P NMR studies indicate reduced bile constituents in patients with biliary obstruction and infection. **NMR in Biomed**. **22**, 220.
51. V Lakshmi, R Kumar, K Pandey, BS Joshi, **Raja Roy**, KP Madhusudanan, P Tiwari, AK Srivastava (2009). Structure and activities of a steroidal saponin from *Chlorophytum nimonii* (Grah) Dalz. **Nat. Prod. Res**. **23**, 963.
52. Divya Misra, Vivek Gupta, Abhinav A Sonkar, Usha Bajpai and **Raja Roy** (2008), Proton HR-MAS NMR Spectroscopic Characterization of

Metabolites in Various Human Organ Tissues: Pancreas, Brain and Liver from Trauma Cases. **J. Physiol. Chem. & Phys. & Med. NMR.** **40**, 67.

53. RP Parti, R. Shrivastava, S Srivastava, AR Subramanian, **Raja Roy**, BS Srivastava, and R Srivastava.(2008), A transposon insertion mutant of Mycobacterium fortuitum attenuated in virulence and persistence in a murine infection model that is complemented by Rv3291c of Mycobacterium tuberculosis. **Microb Pathog.** **45**, 370
54. Santosh K Bharti, Neeraj Sinha, Bhawani S Joshi, Sudhir K Mandal, **Raja Roy** and C L Khetrapal (2008), Improved Quantification from <sup>1</sup>H-NMR Spectra Using Reduced Repetition Times. **Metabolomics.** **4**, 367.
55. Abhijeet Deb Roy, K. Jayalakshmi, Somnath Dasgupta, **Raja Roy** and B. Mukhopadhyay (2008), Real time HR-MAS NMR: Application in reaction optimization, mechanism elucidation and kinetic analysis for heterogeneous reagent catalyzed small molecule chemistry. **Magn.Reson.Chem.** **46**, 1119.
56. Abbas A. Mahdi, Sanjay Annarao, Sandeep Tripathi, Akbar Nawab, Farzana Mahdi, Mahdi Hasan, **Raja Roy** and C.L. Khetrapal (2008), Correlation of Age-Related Metabonomic Changes in <sup>1</sup>H NMR Serum and Urine Profiles of Rats with Cognitive Function. **The Open Magnetic Resonance Journal.** **1**, 12
57. Sanjay Annarao, O.P. Sidhu , **Raja Roy**, Rakesh Tuli and C.L. Khetrapal (2008), Lipid profiling of developing *Jatropha curcas* L. seeds using <sup>1</sup>H-NMR Spectroscopy. **Bioresource technol.** **99**, 9032
58. Sandeep Tripathi, Somashekar B. S, Abbas Ali Mahdi, Ashish Gupta, Farzana Mahdi, Mahdi Hasan, **Raja Roy** and C. L. Khetrapal (2008), Aluminum Mediated Metabolic Changes in Rat Serum and Urine: A Proton Nuclear Magnetic Resonance Study. **J.Biochem. Molecular Toxicology.** **22**, 119.
59. Laxmi Bala, A Sharma, R.K. Yellapa, **Raja Roy**, Gour Choudhuri and C.L. Khetrapal. (2008), <sup>1</sup>H NMR spectroscopy of ascitic fluid: discrimination between malignant and benign ascites and comparison of the results with conventional methods. **NMR in Biomed.** **21**, 606.
60. Arunachalam Subramanian, Bhawani Shankar Joshi, Abhijeet Deb Roy, **Raja Roy**, Vivek Gupta and Ramandeep S. Dang (2008), NMR Spectroscopic Identification of Cholesterol Esters, Plasmalogen and Phenolic Glycolipids as Finger-Print Markers of Human Intracranial Tuberculomas. **NMR in Biomed.** **21**, 272.
61. Ruchika Chakrabarty, Jyoti Rao, Aparna Anand, Abhijeet Deb Roy, **Raja Roy**, G. Shankar, P.R. Dua and Anil K. Saxena (2007), Rational design, synthesis and evaluation of (6aR\*,11bS\*)-1-(4-fluorophenyl)-4-{7-[4-(4-fluorophenyl)-4-oxobutyl]1,2,3,4,6,6a,7,11b,12,12a(RS)-

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Presently having an RG score of 42.46 i.e. 97.6% percentile in the official website of Research Gate.

#### Patents:

1. Novel spermicidal and antifungal agents.

Anil Kumar Dwivedi, Vishnulal Sharma, Niharika Kumaria, Kiran Kumar, Gopal Gupta, Jagdamba Prasad Maikhuri Janak Dulari Dhar, Pradeep Kumar, Abdul Haq Ansari, Praveen Kumar Shukla, Manish Kumar, **Raja Roy**, Kunnath Padmanabhan Madhusudhanan, Ram Chandra Gupta. **Indian Patent No. 245815**, 2001.

2. Isolation of tigogenin pentaglycoside from Chlorophytum nimonii.

Lakshmi Vijay, Kartikay Pandey, **Raja Roy**, Bhawani Shankar Joshi, Padmanabhan Madhusudanan Kunnath, Ramesh Chandra, Arvind Kumar Srivastava, Deepak Raina, Anil Kumar Rastogi. **US Patent No. 7160866**, 2009.

## **Future Vision for Centre of Biomedical Research (CBMR)**

**Raja Roy**

### **An Inter-Institutional Phenome Research Centre and Facility at CBMR Lucknow for diagnostics and precision medicine: From Bench to Bedside**

**Phenome Laboratory for Interdisciplinary research and training in Biomedical Sciences is being proposed for translation research. It will involve interdisciplinary experts from the CBMR, SGPGIMS, KGMU and RMLIMS, Lucknow.**

India is second to China with a population of 1.26 billion people which accounts for 17.5% of the world population. India is projected to be the world's most populous country, with a growth rate of 1.41%, by 2025, surpassing China. This vast population is a major challenge to the limited health care system challenged by the lack of early diagnosis and screening of chronic and infectious diseases, especially in the rural areas. Improved public health and primary health care systems are essential for the implementation of a manageable approach to this challenging problem. Chronic and infectious diseases also lead to a serious loss of national productivity and revenue. Chronic diseases depend on the genetic disposition of the individuals. Numerous genomic studies have been conducted in the last 15 years to seek insights into India's demographic and cultural diversity. These studies paint a complex and conflicting picture. Such a genetic variation of the Indian population will lead to a large variation of chronic diseases based on the location and region. The major chronic diseases inflicting the Indian population are cardiovascular, respiratory diseases, mental disorders, diabetes, and cancer. There are high incidences tobacco related cancers. "Tobacco use accounts for 40% of all cancers." The estimate of the actual number of diabetics in India is around 40 million. This means that India actually has the highest number of diabetics of any one country in the entire world. In addition, that there are a large number of people prediabetic condition. IGT (Impaired Glucose Tolerance) which is a prediabetic condition or hyperglycemia is a mounting problem in India.

The infectious diseases include tuberculosis, malaria, filariasis, visceral leishmaniasis, leprosy, HIV infection, and childhood cluster of vaccine-preventable diseases are given priority for control through centrally managed vertical programs.

Present day science and technology is now advancing traditional diagnostic methods and taking down to the molecular level. What we discover about the causes of disease can be used to improve healthcare. This is revolutionary! It is a great opportunity and the right time for the Center of Biomedical Research (CBMR), Lucknow to take a lead in this area of biomedical research and provide the leadership to India as this Centre is conducting research on diagnostics and disease monitoring using Magnetic Resonance technology since its creation (2002) at SGPGIMS campus Lucknow.

### **Phenome & Phenome Research**

Scientists have been studying the human genome for many years, seeking to understand the building blocks of DNA on which the human body is based. But it is the interaction of these genes with the environment which makes an actual organism with particular characteristics. This study of the nexus of genes and the environment is called phenomics, and it represents the next step to expanding the bounds of our knowledge of human health. A phenome describes a person's internal chemistry, including all of the molecules that are a result of a person's genetics and lifestyle. Phenomics is the systematic measurement and analysis of qualitative and quantitative traits, including clinical, biochemical, and imaging methods, for the refinement and characterization of a phenotype. Research tells us that phenomes change all of the time, often in response to environmental influences. These kinds of influences are wide-ranging. A person's environment includes everything from the chemicals in their home and food in their diet to how much they exercise, stress levels, medication, vaccinations and more. By better understanding phenomes, we will be able to unlock the mysteries of the human condition. The systemic study of phenomics can be done on a large scale utilizing high-throughput proton NMR spectroscopy and Mass spectrometric analytical armamentarium which are robust and reliable techniques for metabonomic applications with high reproducibility. Metabolic phenotyping based on the exploratory biochemical analysis of biological fluids, tissues and tissue extracts involves systematic profiling of multiple metabolite concentrations and their fluctuations in response to genetic modulations, lifestyle, the environment, drugs, diet and other stimuli in order to characterize the beneficial and adverse effects of these kinds of interactions and to evaluate the biochemical mechanisms involved in such changes. It can help us understand how our environment makes us more or less susceptible to heart disease, cancer, gastrointestinal diseases, infections and other health conditions. Metabolic phenotyping has already found application in many disease studies and also in complex interacting systems such as between humans, their nutrition and their symbiotic gut microflora. The possibility of predicting post-dose drug effects from baseline metabolic profiles has been demonstrated (pharmaco-metabolomics) as a potential effector for personalized medicine.

Metabolic phenotyping generally uses biofluids or cell, and intact tissues as primary sources of metabolic fingerprint data. Urine and serum are the most commonly studied biofluids, and are easily obtained and prepared while intact tissues are being obtained either through biopsy or during surgical procedure.

These metabolic profiling technologies use mainly NMR spectroscopy and chromatography-mass spectrometry (MS). The multivariate spectroscopic data produced are typically analyzed using chemometric techniques to identify significant metabolic combinations that can be used for sample classification and global biomarker discovery.

The study of phenome through metabolic phenotyping will enable the government and medical authorities to address global public health in ways not foreseen. The environment has a greater effect on a person's tendency to specific diseases and conditions. As we learn more about the relationship between genetics and environment through metabolic profiling, scientists and clinicians will be able to transform our understanding of physical characteristics and disease, enabling significant advances in medical treatments. Understanding the huge potential to transform lives through the study of phenomes, we plan to establish a collaborative networking between KGMU, RMLIMS and SGPGIMS Lucknow to create the new Phenome Research Laboratory in Northern India. Based inside the campus of a super speciality hospital (Sanjay Gandhi Post Graduate Institute of Medical Sciences), the Phenome Laboratory would be the first large-scale national phenomics facility where all the three units i.e. Molecular Synthesis and Drug Discovery and Translation Cell Biology unit at the Centre will be actively involved. One of the major challenges

that the study of phenomes would face is the need to generate and manage large data sets. The generation of large amounts of high-quality data at relatively low cost would be the basic necessity. To ensure this result, the Phenome Laboratory will use high-throughput analytical methods to dramatically increase the scale of sampling. This would be a central facility which will collaborate with various other clinical research institutions around the country for expanding the area of research.

By sampling at an unprecedented scale, researchers will have large data sets to analyze, putting them in a better position to discover new 'biomarkers' faster. These biomarkers hold the key to why one individual or population may be more susceptible to a disease than another or why treatments are effective in one individual and not in another. As research on phenomics continues, these biomarkers will enable clinical researchers to develop better, safer treatments, including those that can be specifically selected to match an individual's personal phenome. This has the potential to revolutionize the way in which we treat a wide variety of diseases. To assure scientific integrity and get the most value out of the data collected, the laboratory will develop and maintain rigid quality control methods and procedures to test and track samples. A stringent level of quality control will guarantee precision and harmonize phenomics methodologies, allowing this powerful resource to be easily and accurately shared with medical and scientific communities in all parts of this country. In addition, this quality control will enable us to serve as a national data collection for organizations around the country.

**In brief the aim of the phenome research is.....**

- ❖ To discover new disease biomarkers, this will enable the real-time diagnostics, disease severity staging and therapeutic efficacy monitoring in order to improve clinical decision-making enhancement of disease classification.
- ❖ To generate a huge scalable and translatable data of global phenotype (patients & healthy controls) by integrating the conventional clinical diagnostic information, chemical pathology with advanced omics-based biomarker discover.

**Expected Outcome of the research:**

- ❖ Transform our understanding of people's biochemical characteristics and the causes of disease, which could result in faster diagnosis and more effective treatments;
- ❖ Develop and set high standards of quality control and procedures to help harmonize methodologies globally;
- ❖ Detailed understanding would leverage to potential new drug targets for the discovery of new and safer drugs;
- ❖ Serve as an national data collection centre for other scientists and clinicians in government, academia and industry in order to accelerate the translation of biomedical discoveries into better health care; and
- ❖ Train a new generation of students, scientists and clinicians on applying their knowledge of spectroscopic analysis and analytical methodologies to solve health problems.

**Justification for setting up Phenome Research Laboratory at CBMR:** Over the years, the Centre (formerly known as Centre of Biomedical Magnetic Resonance), in which I was involved since its inception has established the state-of-the art bio-magnetic resonance unit and metabolomics was one of the major research activities. Presently >40% faculty members of the Centre are actively working in this area in collaboration with three major premier Medical Institutions at Lucknow i.e. KGMU, RMLIMS, and SGPGIMS. Additional privilege, CBMR is in SGPGIMS campus and very nearer to KGMU and RMLIMS. Therefore, setting up of Phenome Research Laboratory at CBMR will be most adequate in order to perform metabolic phenotyping on human serum, urine and real time (tissue) specimens, particularly of critically ill patients. Moreover, major clinical groups from these Institutions are also committed and actively involved for creating such type of Laboratory at CBMR. This research laboratory will focus in understanding the phenotypic variations (involving large sample size) in healthy and diseased human subjects using two complimentary analytical methods viz. NMR and chromatographic MS technology for understanding individual metabolism and for future usage in precision medicine and therapy in Cancer and other diseases.

## **Initial Research Programmes**

**1. Surgical Patient Phenotyping:** Operating theatres are mostly free of chemical diagnostic information, as the timescale for surgical decision making is very short. Clinical risk scores have variable sensitivity and specificity. So, more robust prognostic biomarkers are needed to improve the quality of surgical care through early detection of surgical disease and operative risk prediction and reduction.

Oral Cancer is a major cause of mortality and morbidity with approximately 6 million deaths each year worldwide. Squamous Cell Carcinoma of head and neck (HNSCC) is fifth most common cancer in the world. It is commonly prevalent in males and is more prevalent in developing countries as compared to the developed ones. The incidence rate varies in men from 1 to 10 cases per hundred thousand populations in many countries. Surgery followed by radiotherapy and or chemotherapy is the only clinical intervention for the prognosis of the disease. The prognosis of oral cancer is very poor as recurrence rates are very high. Even aggressive combinations of surgery, radiotherapy and chemotherapy, could not much improve the five-year survival rates. This poor survival rate is probably due to the development of multiple primary tumors and advanced extent of disease at the time of diagnosis or due to tumor cell invasions in the normal tissues. In our earlier study we had already demonstrated that HR-MAS NMR is capable of differentiating malignant tissue specimens with an accuracy of more than 98%. We need to further explore the potential of real time tissue NMR spectroscopic analysis during surgery along with five year follow up of these patients for more precise surgical excision for better prognosis of the disease.

Breast cancer comprises of 10.4% of all cancer incidences among women, making it the fifth most common cause of death worldwide. There are numerous aspects of breast cancer like different stages (spread), number of lymph nodes involved, tumour size, perineural and lympho-vascular invasion (aggressiveness), genetic makeup and survival greatly depends on these factors. These factors are determined by histopathological examination. Currently histopathology is the gold standard for diagnosing and determining prognostic factors in cancer breast. But histopathological examination is routinely hampered by human errors, lengthy and careful tissue processing and long wait for report. Therefore, in order to efficiently assess the alterations in metabolic profile of breast cancer with malignant perineural invasion, malignant thrombi in vessel, malignant infiltration of skin and malignant lymph node, an extensive study will be performed on different tissue

specimens of breast cancer patients using real time HR MAS NMR spectroscopy during surgery for improved prognosis after surgery leading to low recurrence rate along with five year followup of the patients. Our earlier investigation has demonstrated diagnostic accuracy of more than 98% on Intact Sentinel Node Biopsy from Breast Cancer Patients on seventeen subjects and for large cohort of subjects for lipidomics using HR-MAS NMR spectroscopy.

**A team of Surgeons from KGMU and basic scientists will be involved for NMR tissue based phenomics for better patient management in the above mentioned cancer patients.**

Target is to provide sensitive, specific and efficient vehicles for delivering novel real-time diagnostics to aid 'on table' decision-making in surgery. Rapid metabolic phenotyping approaches, which use **high resolution magic angle spinning (HR-MAS) NMR** and mass spectrometry/imaging of tissue biopsy and biofluid samples, have proven useful for generation of diagnostic biomarker information about some diseases in human beings.

At CBMR in collaboration with SGPGIMS, KGMU, initially we like to focus on rapid metabolic phenotyping approaches for the surgical cases of oral- and breast cancers.

**2. Cancer Patients:** Although early detection of cancer, adjuvant systemic therapy and chemotherapy have improved cancer survival, treatment decisions are made on the basis of prognostic parameters that do not identify all at-risk patients. A new paradigm for patient stratification based on modelling multi-level patient phenotypes will beneficially influence patient outcomes by improving optimisation of therapeutic strategies. To improve detection and staging of cancer and enhance clinical decision-making with respect to treatment and prognosis using integrated metabolic spectroscopy in conjunction with routine clinical/histopathologic data is another target at CBMR in collaboration with SGPGIMS, KGMU and RMLIMS.

**3. Critical Care Phenotyping (Sepsis and Pneumonia):** Critical care is associated with high mortality, long-term disability and imposes a heavy economic burden on each national health system. Sepsis and ventilator-associated pneumonia (VAP) are the most common infections diagnosed in the intensive care unit (ICU) and in spite of advances in diagnostic techniques and management these remain the common cause of hospital morbidity and mortality.

The number of deaths from Sepsis each year has almost doubled since 1980, with more patients developing the condition. The disease state of sepsis knows no limits in terms of whom it can affect. From the new-born to the elderly, the incidence of sepsis is increasing and will continue to increase due to several causes including but not limited to antibiotic resistant bacteria to an increasing number of chronic disease states including diabetes, heart failure, and cancer. India currently tackles ~8 lacs cases of Sepsis every year of which overall mortality rate in ICU patients is ~12% and in the severe stage Sepsis patients it is ~60%, with the elderly having the highest death rate.

Ventilator-associated pneumonia (VAP) refers to bacterial pneumonia developed in patients who have been mechanically ventilated for duration of more than 48 h. The incidence of early-onset VAP (within 96 h) was found to be 27% while the late-onset type (>96 h) was 73%. Late-onset VAP had poor prognosis in terms of mortality (66%) as compared to the early-onset type (20%).

Lack of gold standard for diagnosis is the major culprit of poor outcome of sepsis and VAP. Biomarkers are needed for risk stratification, early diagnosis of complications and interventional optimisation. The purpose is to improve outcomes by studying the entirety of the patient's journey through a period of severe illness or surgery from point of presentation to distant recovery.

#### ***4. Global Phenotyping on healthy subjects vs professional Yoga subjects and meditators:***

Since yoga and yogic kriya is our ancient Science, and the personnel who are performing yoga as a routine practice will definitely show a significant degree of metabolic variations in their body fluids viz. urine and serum when compared with normal healthy subjects (That is my strong belief!). Phenotyping investigation of serum and urine metabolites associated with different tens of thousands healthy blood donors groups will be undertaken from the one of the established blood bank and with the professional yoga subjects, in order to determine the serum and urine metabolic differences of all healthy donors groups with different metabolite concentration. The subjects will also be evaluated using fMRI obtaining the holistic and comprehensive information. Initially, chemometric multivariate unsupervised (PCA) will be applied to examine the intrinsic variation in the serum of all healthy blood donors' groups and professional yoga subjects and meditators. This interdisciplinary study intends to explore latent disease if any in healthy blood donor's serum and urine by NMR spectroscopy, chromatographic Mass spectrometric analysis and fMRI when compared with professional Yoga subjects and meditators, this research may provide a sound modern scientific explanation of our ancient science. This work may have a great societal impact throughout the globe.

This investigation will allow examining the influence of the habitual diet on metabolic phenotype, to determine which metabolites exert the greatest influence and also develop additional test criteria along with the existing test protocol for safer blood transfusion in patients of any. Our study indicates that metabolic profiling is a powerful tool to identify metabolites differences and may be useful in clinical studies exploring disease pathogenesis.

In order to discriminate among all healthy blood donors, use of serum and urine will be of advantage as well as the data can be used as healthy controls against other diseases.

#### ***5. Phenotyping of other infectious and parasitic diseases (meningitis, hydatid cyst etc.):***

**Meningitis** is one of the most devastating infectious diseases in developing as well as in underdeveloped countries. Despite the availability of several therapies, the most common forms of meningitis in adults, viz., bacterial meningitis (BM), tuberculous meningitis (TBM) and cryptococcal meningitis continue to be potentially fatal illnesses that can lead to death or permanent neurological sequelae in the patient if not diagnosed at an early stage. The cornerstone of management of meningitis depends on the rapid diagnosis and prompt treatment. The gold-standard culture method is usually insensitive if antibiotic treatment has already started, and it often takes a period of 6–8 weeks to confirm the tubercle bacilli. Timely treatment is usually based on clinical symptoms and a baseline test of the cerebrospinal fluid (CSF). Therefore, rapid differentiation of meningitis is the need of the hour for timely treatment of the patient for proper management.

**Cystic Echinococcosis** is a worldwide disease caused by larval stages of the parasite *Echinococcus granulosus*. Echinococcosis (also known as hydatid disease) is an important public health problem in many parts of the world, especially in rural areas where sheep and cattle are raised. *Echinococcus* tapeworms are parasitic organisms with a two-stage life cycle- Dog (definitive host) and sheep/cattle or human (Intermediate host). When infection occurs in humans, cycle comes to a dead end. Hydatid disease is endemic mainly in the Mediterranean countries, the middle East, the Baltic areas, South America, India & North China. Prevalence :1% to 7% with annual incidences of up to 32 cases per 100000 in hospital? based studies in endemic

areas. Females are more at risk than males, with an increase in prevalence with age. The liver and lungs are the most common sites for cyst formation in humans, although any organ can be involved. Preoperative surgical planning to determine and recognizes complications, such as rupture, infections and therefore to assess resectability. Recurrence may develop due to: Peritoneal soiling during emptying of a fertile cyst or from further re-infestation of the patient. Residual vesicles, even if the cyst was carefully emptied or after incomplete resection. In India, a single study performed earlier along with one of our co-investigators has evaluated  $^1\text{H}$  NMR metabolomics as a diagnostic tool for the rapid determination of the cases of Fertility Assessment of Hydatid cyst using aspirated cystic fluid. However, till date no study has explored urinary biomarkers for differentiating-- Intra-abdominal Hydatid cyst by metabolomics as well as to assess its fertility. It is therefore proposed to perform urine and serum-based phenotyping for differentiation of staging of hydatid cyst which will help in framing strategies for non-surgical / surgical management.

### **Translational Cell Biology Unit**

It has been designed to translate the biological discoveries towards better patient healthcare and this unit recently came in existence in 2017 at ours Centre. By bridging between basic and clinical science, we intend to develop and validate effective targets towards innovative healthcare solutions. We aim to discover novel target proteins and their associated functional mechanisms towards development of new markers for early detection and treatment of life-threatening diseases like cancer, cardiovascular complications, infectious, tropical diseases etc. and their role in correlating the biomarkers identified through phenome research. It is extremely important towards the identification of novel targets for better healthcare as the phenotype of these disease are everchanging and the current market available drugs sometimes show resistance for eg. TDR (Total Drug Resistance) in Tuberculosis, less performance, side effects exhibiting the need of development of new markers for next generation effective entities without side effects.

Presently, one faculty is working and his recent discovery towards identification of novel marker G protein beta 5 in different chemotherapeutics induced cardiac complications is in line of the mandate of this unit of CBMR. This work using different mouse models have clearly identified one common mediator which different chemo drugs employ to initiate cardiac damages. The future aim is to collect surgical cancer tissue specimens from Indian patients with or without varied chemotherapeutic treatment (alone or combination), we aim to solidify our previous findings towards development of G protein beta 5 as clinical marker for identifying and lowering the future risk of cardiac complications in cancer patients.

### **Molecular Synthesis and Drug Discovery Unit**

This Centre has this unit since 2013 and the faculties are presently involved in method development in organic synthesis and drug discovery on neurological disorders. Since CSIR-CDRI, Lucknow is already involved in drug research since last 70 years, there is no need to duplicate similar research at our Centre as we do not possess appropriate infrastructure for performing research on drug discovery and an enormous amount of fund will be required to execute such type of research programme. This total team of faculty will be channelized for synthesizing disease specific MRI contrast agent that respond to physiology and metabolism, including targeted  $\text{Gd}^{3+}$ -

based agents that respond to binding events *in vivo*, paramagnetic CEST (Chemical Exchange Saturation transfer) agents that offer multi-color imaging of metabolic events in different diseases and theranostics which will be extremely helpful in-patient care where a non-invasive diagnostic dilemma exists even at this modern age. For eg. differential diagnosis of meningitis, category of aggressiveness in tumors in cancer along with its chemotherapeutic monitoring. Moreover, the biomarkers identified through the outcome of the phenome research in different diseases, new molecular entities will be synthesized by this Unit as chemo sensors which could be further utilized in the remote areas of State for diagnostic evaluation of different diseases.