CURRICULUM VITAE

Munindra Ruwali, PhD

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Academics

B. Sc. (First Class) Zoology, Botany, Chemistry (2000-2003): Lucknow Christian College, University of Lucknow, Lucknow, India, securing 65.7 % in aggregate.
M. Sc. (First Class) Biotechnology (2003-2005): Faculty of Science, Jamia Hamdard, New Delhi, India, securing 73.5 % in aggregate.
Ph. D. (Biotechnology) (2005-2011): Developmental Toxicology Division, Indian Institute of Toxicology Research (IITR), Lucknow-226001, India and Gautam Budh Technical University, formerly, Uttar Pradesh Technical University (UPTU), Lucknow, India.
Title of thesis: 'Association of genetic polymorphisms in ethanol and nicotine metabolizing cytochrome P450s and glutathione S-transferases with head and neck cancer'

Brief Chronology of Employment

January, 2011-December, 2012: Post-doctoral fellow, Molecular and Systems Toxicology, Department of Pharmaceutical Sciences, University of Basel, Basel, Switzerland.
August, 2007-August, 2010: Senior Research Fellow, Developmental Toxicology Division, IITR (Council of Scientific & Industrial Research), Govt. of India, India.
August, 2005-August, 2007: Junior Research Fellow, Developmental Toxicology Division, IITR (Council of Scientific & Industrial Research), Govt. of India, India.

Honours & Awards

- Recruited as a Marie Curie fellow of the International Fellowship Programme on Integrative Kidney Physiology and Pathophysiology (IKPP): A Swiss post-doctoral programme co-funded by the 7th framework programme (FP7) of the European Commission.
- Qualified All India CSIR-UGC (NET-JRF) examination conducted by Council of Scientific & Industrial Research (CSIR) and University Grant Commission (UGC), New Delhi, Govt. of India (2004).
- Qualified All India Graduate Aptitude Test in Engineering (GATE) examination conducted by Indian Institute of Technology (IIT) Delhi, Govt. of India (2004).

Technical Expertise

- **Molecular Biology:** Isolation of RNA and DNA, Real-Time PCR and PCR, Restriction Fragment Length Polymorphism (RFLP), Electrophoresis (Agarose and PAGE), Reporter gene assays.
- **Biochemistry:** Protein Estimation, Enzyme Assays for different Drug Metabolizing Enzymes, Western Blotting, ELISA.
- **Cell Biology:** *In vitro* cell culture.
- **Bioinformatics:** Familiar with using various bioinformatics software and primary molecular biological tools particularly for molecular epidemiological studies.
- **Animal Experimentations**: Successfully completed the Course in Laboratory Animal Science held at FMI, Basel, Switzerland (7th to 11th March 2011) for persons conducting animal experiments on mice/rats/rabbits, duly accredited by Federation of European Laboratory Animal Science Associations (FELASA).

Research Experience

Postdoctoral research: Molecular and Systems Toxicology, Department of Pharmaceutical Sciences, University of Basel, Basel, Switzerland (January, 2011-December, 2012).
(Research Adviser: Prof. Dr. Alex Odermatt)
Project title: "Investigation of susceptibility to nutritional challenges upon renal mass reduction: impact on cell defense, hormonal regulation and inflammation". The work involved a wide range of molecular biology, biochemistry and cell biology methods like optimization of mammalian cell culture conditions, application of reporter gene assays to measure nuclear receptor function and oxidative stress, gene expression studies using real-time RT-PCR and several enzyme activity assays. Besides, the application of high-content imaging using a Cellomics ArrayScan instrument was also done.
Western-style diet, consisting of high levels of fructose and saturated fat, is a major risk factor for the development of Chronic Kidney Disease (CKD). The multifaceted mechanisms responsible for dietary induced kidney pathologies are not fully characterized. However, prolonged oxidative stress, inflammation and activation of the Renin Angiotensin Aldosterone System (RAAS) are strongly linked with CKD, which may additionally be potentiated by loss of renal mass. Our studies focused specifically on the Nrf2/NFκB pathways, which are master regulators of cell defense and the inflammatory responses, respectively. For the in vitro studies, we used human renal proximal tubular cells (HK-2) in order to study possible molecular mechanisms contributing to fructose-induced renal damage progression. Results from NFκB nuclear translocation and reporter gene activity suggest that fructose may lead to the activation of an inflammatory response while Nrf2 system was not changed. Furthermore, rat liver H4IIE cells, stably transfected with an ATF6 sensitive luciferase reporter, with an NF-kappaB responding luciferase reporter, or with an Nrf2-responsive luciferase reporter, were employed to further study effects of fatty acids on redox pathways. Saturated fatty acids like palmitic acid resulted in an increased oxidative stress and inflammation. For the in vivo studies, we assessed the impact of reduced renal mass in the form of uninephrectomy (UNX), on the hepatic Nrf2 and RAAS in male Sprague-Dawley rats. In collaboration with the University of Fribourg, Fribourg, Switzerland, sham-operated and uninephrectomized rats were analyzed at 1, 2, 4, 8 or 12 weeks following surgical intervention. UNX resulted in a two-fold increase in the expression of renin while Nrf2 system was not changed. This may have implications in the development of hepatic fibrosis as several reports have pointed to the elevated renin levels in cases of hepatic fibrosis.

Doctoral research: Developmental Toxicology Division, Indian Institute of Toxicology Research (IITR), Lucknow-226001, India and Gautam Budh Technical University, formerly, Uttar Pradesh Technical University (UPTU), Lucknow, India (August, 2005-August, 2010).
Research Superviser: Dr. Devendra Parmar
Head & neck squamous cell carcinoma (HNSCC) is one of the most common non-cutaneous malignancies worldwide and has a particularly high incidence in South East Asian countries and is one of the leading cancers among males in India. Epidemiological studies have shown that 90% of all cancers are related to environmental factors with tobacco smoke, alcohol and diet being the main attributable exposures. Besides exposure to environmental factors, sequence variations in genes coding for phase I and phase II enzymes, such as members of the cytochrome P450 (CYP) and glutathione S-transferase (GST) families may potentially alter individual susceptibility to environment induced cancer like HNSCC. The study aimed to investigate the association of polymorphism in phase I (*CYP2E1, CYP2A6*) and phase II (GSTs) enzymes, with head and neck squamous cell carcinoma (HNSCC), and response in cases receiving radio-chemotherapy in ethnic North Indian population.
Association of the functionally important polymorphisms of phase I *CYP2E1* and *CYP2A6* with HNSCC risk: A significant increase in HNSCC risk was observed in cases with variant genotypes of *CYP2E1*5B* (*RsaI*) or *CYP2E1*6* (*DraI*). Haplotype analysis revealed that haplotype T-A was associated with a greater than 10-fold increase in risk for HNSCC. A several fold increase in HNSCC risk in cases carrying a combination of variant genotypes of *CYP2E1* with the null genotype of *GSTM1* or *XRCC1* variant genotypes was also observed. Alcohol or tobacco use (both smoking and chewing) were also found to interact with variant genotypes of *CYP2E1* in significantly enhancing HNSCC risk. This increase in risk associated with an interaction of *CYP2E1* genotypes with *GSTM1* or *XRCC1* or with tobacco and alcohol use demonstrates the importance of gene–gene and gene–environment interactions in the development of HNSCC. However, in contrast to that observed for *CYP2E1*, multivariate logistic regression analysis revealed statistically significant decrease in risk to HNSCC in cases with variant genotypes (*CYP2A6*1B* and *CYP2A6*4C*) of *CYP2A6*. The risk associated with these variant genotypes was found to be further decreased in cases carrying a combination of variant genotypes of *CYP2A6* and *GSTP1*. A similar decrease

in risk was observed in cases with variant genotypes of *CYP2A6* or *GSTP1* and who were regular tobacco users (cigarette smokers or tobacco chewers). Interestingly, only 27% of the cases carrying the variant forms of *CYP2A6* (**1A/*4C + *1B/*4C + *4C/*4C*) responded to the treatment for HNSCC when compared to those with wild-type genotype (69%). However with *GSTP1*, cases with homozygous mutant genotype (*Val/Val*) showed a superior treatment response (75%) when compared to cases with wild-type genotype (25%). Further, cases carrying a combination of variant genotype of *CYP2A6* and wild-type genotype of *GSTP1* exhibited a very poor treatment response demonstrating that polymorphisms in *CYP2A6* and *GSTP1* not only modified the risk to HNSCC but also played a major role in determining the chemotherapeutic response.

Association of the functionally important polymorphisms of GSTs with HNSCC risk: Statistical analysis showed an increase in risk to HNSCC in the patients with null genotype of *GSTM1* or *GSTT1*. Our data further showed that combination of deletion genotypes of GST (*GSTM1* and *GSTT1*) confer an even higher risk of HNSCC. Interestingly, *GSTP1* wild type genotype in combination with *GSTM1* null or *GSTT1* null genotype increased susceptibility for HNSCC. Likewise, a much greater risk for HNSCC was observed in the patients carrying a genotype combination of *GSTM1* null, *GSTT1* null and *GSTP1* (*Ile/Ile*). Our data have further provided evidence that tobacco use (smoking and chewing) and alcohol consumption are the important risk factors for HNSCC in cases with null genotypes of *GSTM1* or *GSTT1*. The study, thus, provides evidence that GST polymorphism modifies the susceptibility to HNSCC and has further demonstrated importance of gene-environment interaction in modulating the risk to HNSCC.

Post Graduate Training and Experience

- Summer Project entitled "***Serum Protein Electrophoresis for Diagnosis of Multiple Myeloma***" at All India Institute of Medical Sciences (AIIMS), New Delhi, India.
- Dissertation project entitled "***Herbs with anti-Salmonella activity: Screening and biochemical evaluation***" at Molecular Biology Lab, Department of Biotechnology, Hamdard University, New Delhi, India.

Mentoring Experience

During PhD, successfully mentored 12 students of M. Sc. and M. Tech courses for their thesis. It includes helping them in designing and planning various projects, method standardizations, data analysis & guidance in interpretation and thesis writing.

Publications

1. **Ruwali M.**, Khan A.J., Shah P.P., Singh A.P., Pant M.C., Parmar D. Cytochrome P450 2E1 and head and neck cancer: interaction with genetic and environmental risk factors. Env. Mol. Mut. 50 (2009) 473-482.
2. **Ruwali M.**, Pant M.C., Shah P.P., Mishra B.N., Parmar D. Polymorphism in cytochrome P450 2A6 and glutathione S-transferase P1 modifies head and neck cancer risk and treatment outcome. Mutat. Res. 669 (2009) 36–41.
3. **Ruwali M.**, Parmar D. Association of functionally important polymorphisms in cytochrome P450s with squamous cell carcinoma of head and neck. Indian J. Exp. Biol. 48 (2010) 651-665.
4. **Ruwali M**., Singh M., Pant M.C., Parmar D. Polymorphism in glutathione S-transferases: susceptibility and treatment outcome for head and neck cancer. Xenobiotica. 41 (2011) 1122-30.
5. Khan A.J., **Ruwali M.**, Choudhuri G., Mathur N., Husain Q., Parmar D. Polymorphism in Cytochrome P450 2E1 and interaction with other genetic risk factors and susceptibility to alcoholic liver cirrhosis. Mutat. Res. 664 (2009) 55-63.
6. Yadav S.S., **Ruwali M.**, Shah P.P., Mathur N., Singh R.L., Pant M.C., Parmar D. Association of poor metabolizers of cytochrome P450 2C19 with Head and Neck cancer and poor treatment response. Mutat. Res. 644 (2008) 31-37.
7. Yadav S.S., **Ruwali M.**, Pant M.C., Shukla P., Singh R.L., Parmar D. Interaction of drug metabolizing cytochrome P450 2D6 poor metabolizers with cytochrome P450 2C9 and 2C19 genotypes modify the susceptibility to Head & Neck cancer and treatment response. Mutat. Res. 684 (2010) 49-55.
8. Singh A.P., Shah P.P., **Ruwali M.**, Mathur N., Pant M.C., Parmar D. Polymorphism in cytochrome P4501A1 is significantly associated with head and neck cancer risk. Cancer Invest. 27 (2009) 869-76.

9. Singh A.P., Pant M.C., **Ruwali M.**, Shah P.P., Prasad R., Mathur N., Parmar D. Polymorphism in cytochrome P450 1A2 and their interaction with risk factors in determining risk of squamous cell lung carcinoma in men. Cancer Biomark. 8 (2010) 351-9.
10. Singh M., Shah P.P., Singh A.P., **Ruwali M**., Mathur N., Pant M.C., Parmar D. Association of genetic polymorphisms in glutathione S-transferases and susceptibility to head and neck cancer. Mutat Res. 638 (2008) 184-194.

Presentations

1. **Ruwali M**., Lister A., Odermatt A. Effects of fructose on cell defense capacity, inflammation and xenobiotic toxicity in renal proximal tubular cells. Presented at the Annual Research Meeting, Department of Pharmaceutical Sciences, University of Basel, Basel, Switzerland on February 14, 2012.
2. **Ruwali M.**, Khan A.J., Pant M.C., Parmar D. Genetic Polymorphisms in CYP2E1 and XRCC1 as Risk Factors for the Development of Head and Neck cancer. Presented at 77th Annual Meeting of the Society of Biological Chemists (India) held at IIT-Madras, Chennai, India, from December 18 – 20, 2008.
3. **Ruwali M**., Shah P.P., Singh A.P., Khan A. J., Pant M. C., Mishra B. N., Parmar D. Genetic Polymorphisms of Xenobiotic Metabolizing Enzymes as Risk Factors for the Development of Head and Neck cancer. Presented at 40th Annual conference of Indian Pharmacological Society (IPS) held at Mohali, India, November 1st -3rd. 2007.
4. **Ruwali M**., Shah P.P., Singh A.P., Singh M. , Khan A. J., Pant M. C., Mishra B. N., Parmar D. Polymorphism in cytochrome P450 2E1 and Glutathione-S- Transferases (GSTs) and susceptibility to head and neck squamous cell carcinoma (HNSCC). Presented at International Symposium on Genomic Instability and Cancer, Srinagar (July 22-26, 2007).
5. **Ruwali M**., Shah P.P., Singh A.P. , Singh M. , Khan A.J. , Pant M.C., Parmar D. Association of functionally important polymorphisms of Cytochrome 450 2E1 and Glutathione S- transferases (GSTs) with susceptibility to oral cancer. Presented at 39th Annual conference of Indian Pharmacological Society (IPS) held at Jaipur, India, December 21st Dec-23rd Dec. 2006.
6. Yadav S.S., Shah P.P., **Ruwali M**., Pant M.C., Parmar D. Association of functionally important polymorphisms of Cytochrome 450 2C19 (CYP2C19) with susceptibility to Oral cancer. Presented at 39th Annual conference of Indian pharmacological society (IPS) held at Jaipur, India, December 21st Dec-23rd Dec. 2006.
7. Yadav S.S., Shah P.P., **Ruwali M**., Pant M.C., Parmar D. Functionally important polymorphism in drug metabolizing cytochrome P450s with susceptibility to head and neck cancer (HNSCC) and treatment response. Presented at Functionally important polymorphism in drug metabolizing cytochrome P450s with susceptibility to head and neck cancer (HNSCC) and treatment response (July 22-26, 2007).
8. Yadav S.S., Shah P.P., **Ruwali M**., Pant M.C., Parmar D. Functionally important polymorphisms in drug metabolizing cytochrome P450s with susceptibility to Head and Neck Cancer (HNSCC) and association with treatment response. Presented at 40th Annual conference of Indian Pharmacological Society (IPS) held at Mohali, India, November 1st -3rd. 2007.
9. Khan A.J., **Ruwali M.**, Choudhuri G., Parmar D. Genetic polymorphisms in Cytochrome P450 2E1 and Glutathione S-transferases and susceptibility to alcoholic liver cirrhosis. Presented at 77th Annual Meeting of the Society of Biological Chemists (India) held at IIT-Madras, Chennai, India, from December 18 – 20, 2008.
10. Pant M.C., Parmar D., Shukla P., Gupta D., Bisht S.S., Gupta S., Gupta R., Yadav S.S., Dhawan A., Verma J., **Ruwali M.**, Singh S., Bhatt M.L., Srivastava K., Mishra D., Verma V.P., Divyesh, Paul S., Singh S. CYP2D6 polymorphism in head and neck carcinoma patients and its correlation with treatment response. Presented at 2nd International Conference on Innovative Approaches in Head & Neck Oncology held at Barcelona, Spain, 26-28 February, 2009 and published in supplement of the official journal of ESTRO: Radiotherapy and Oncology.
11. Dhawan A., **Ruwali M**., Maurya S.S., Khan A.J., Pant M.C., Singh S., Gupta D., Shukla P., Bisht S.S., Verma J., Parmar D. Association of genetic polymorphisms in drug metabolizing enzymes and susceptibility to head and neck squamous cell carcinoma and treatment response. Presented at National Oncology Update-2010 (5^{th} Meeting of Armed Forces Oncology Group), Organized by Oncology Centre, Command Hospital (Central Command), Lucknow, India, from 24^{th}-25^{th} July, 2010. **The presentation was awarded the first prize.**

12. Maurya S.S., **Ruwali M**., Pant M.C., Parmar D. Functionally important polymorphisms in carcinogen metabolizing enzymes and susceptibility to head and neck cancer (HNSCC). Presented at XXXVI Annual Conference of Environmental Mutagen Society of India (EMSI) held at VIT University, Vellore, India (February 4-6, 2011).
13. Lister A., **Ruwali M.**, Odermatt A. Investigation of susceptibility to nutritional challenges upon renal mass reduction: impact on cell defense, hormonal regulation and inflammation. Presented at NCCR Kidney.CH – 2nd Site Visit of SNF and Review Panel held at University of Zurich, Zurich, Switzerland from June 11 – 12, 2012.

Workshop/Symposia/Training

1. Attended the Indo-French Pharmacogenomics Symposium for young scientists organized by Indo-French Centre for the Promotion of Advanced Research held at Amrita Institute of Medical Sciences and Research Centre & Hotel Le Meridien Kochi, Kerala, India, 11th and 12th December 2007.
2. Completed the Training Programme on Technology Led Entrepreneurship of HRDG, CSIR conducted by the Faculty of Indian Institute of Management (IIM), Bangalore from June 2-27, 2008 at Indian Institute of Chemical Technology (IICT), Hyderabad.
3. Attended the International Symposium on Prognostic and Predictive Factors in Cancer Management: Clinical Applications at Chhatrapati Shahuji Maharaj Medical University, Lucknow, December 15-16, 2008.
4. Participated in the deliberations on genetic basis of breast cancer at the 14th Annual National Conference of Breast Cancer Foundation of India organized by the Department of Radiotherapy, CSM Medical University, Lucknow from 7-8th March, 2010.
5. Attended the 44th Annual Meeting of the Swiss Society of Nephrology (SGN-SSN) Congress, Dec 7, 2012, Zurich, Switzerland.
6. Completed the e-Learning Course in "Basic Principles in Nephrology" from Sep 12-Dec 12, 2012 as part of Kidney.CH education programme at University of Bern, Bern, Switzerland.

Personal Details

Date of Birth : December 11, 1981
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Residence : S/O Late Mr. Hari Shankar Ruwali,
49, Ashutosh Nagar, Krishna Nagar, Lucknow, UP-226023 (India).

Dr. Munindra Ruwali