# CURRICULUM VITAE

**Nissar Ul Ashraf, PhD**
**Assistant Professor**
**Department of Biochemistry**
**Govt. Degree College Sopore**
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**About me:** *Teacher, Researcher, working to become leader and grow leaders in scientific field, and make world a better place.*

## EDUCATION

Ph.D Biological Sciences, Academy of scientific and Innovative Research (AcSIR), New Delhi, India

M.Sc. Biochemistry, University of Kashmir, Srinagar, India-190006

B.Sc. with Chemistry and Biology, University of Kashmir, Srinagar, India-190006

## RESEARCH EXPERIENCE:

2019-Current Assistant Professor, Biochemistry, **HED, J&K, India** (working on various projects related to NAFLD pathogenesis and treatment)

2017-2019:National Postdoc Fellow working on: Understanding the role of epigenetic mechanisms in pathogenesis of NAFLD. Epigenetics and Chromatin Biology Lab, Department of Biotechnology, **University of Kashmir, Srinagar, Hazratbal-190006**

2016-2017 Postdoc Fellow, Cell and Molecular and Cell Biology of Lipids, 315 Heritage Medical Research Centre, **University of Alberta, 11207-87 Ave, Edmonton, AB, Canada, T6G2S2**

2012- 2016 Senior Research Fellow at PK-PD (Pharmacokinetics-Pharmacodynamics) Toxicology Division, **Indian Institute of Integrative Medicine (CSIR), Jammu, India-180001**

2010- 2012 Junior Research Fellow at PK-PD Toxicology Division, **Indian Institute of Integrative Medicine (CSIR), Jammu, India-180001**

2008-2010 Project Assistant Level II at PK-PD Toxicology Division, **Indian Institute of Integrative Medicine (CSIR), Jammu, India-180001**

**RESEARCH AREAS:**

Molecular and cell biology of NAFLD pathogenesis.

**TEACHING AREAS:**

Biochemistry, Molecular Biology, Cell Biology, Metabolism, Immunology, Enzymology, Biotechnology, Public health, Biochemical and Biophysical techniques,

**SKILLS**

**Molecular Biology and Biochemistry**

Animal Cell culture, Flow Cytometry, Microscopy, SiRNA transfection, DNA/RNA extraction, Fatty acid oxidation and triglyceride turnover assays (radioactivity based), Lipase assay. PCR, RT-qPCR, Protein isolation/extraction, Western blot, Dot Blot, immunopreciptation, ChIP, MeDIP, drug treatment, blood biochemistry, ELISA, Immunocytochemistry, Zymography, Adeno-Virus transduction, Live cell imaging including intracellular $Ca^{2+}$ imaging, mitochondrial membrane potential studies using Jc-1 dye, MDC staining, Lysotracker staining, ROS measurement (confocal microscopy), Licensed user of radioactivity experiments,

**Animal handling and care**

- Mice/rat handling and dissection. Retro orbital injections, cutaneous injections, Blood collection from tail vein, Gas anaesthesia, cardiac puncture.
- Developed mouse model for NAFLD using C57BL/6J mice.
- Studied Pre-fibrogenic Events in Wistar Rat.

**Computer Proficiency:**

- Microsoft Office (Word, Excel, PowerPoint), Adobe Photoshop, EndNote, ChemBioDraw

**Statistical Software:**

- GraphPad Prism, Instat.

**National Examinations Qualified:**

- Qualified CSIR-UGC NET JRF examination (June 2009)
- Qualified ICAR (Indian Council of Agricultural research) NET examination (January 2009)

**National Awards/Fellowships:**

- DS Kothari Postdoctoral Fellowship, UGC, Govt. of India (2018-2019)
- Professor Noor Ul Islam award, Indian Academy of Biomedical science-2018
- National Postdoctoral Fellowship DST-SERB, Govt of India (2016)
- Senior Research Fellowship, Joint CSIR-UGC, Govt. of India (2012 to 2016)
- Junior Research Fellowship, Joint CSIR-UGC, Govt. of India (2010 to 2012)
- Best Paper award,CSIR-IIIM Jammu, 2014. (on annual day function, 2014)
- **Other Achievements:**

1. Qualified JK Public Services Commission examination with **First Rank** for selection as Assistant Professor at Higher Education Department, Govt. of J&K.
2. Qualified PhD Entrance examinations (Both written and Viva-Voce) at CSIR-IIIM, IISER Mohali and NBRC, Haryana, India
3. Qualified Entrance test for Pursuing Masers in Biochemistry at University of Kashmir
4. Qualified JK BOPEE Common Entrance Test for BUMS.

## ➢ Research Projects:

1. Understanding the role of epigenetic mechanisms in non alcoholic fatty liver disease (NAFLD)
   **Funding Agency**: DST –SERB, Govt. of India
   **Current Status**: Completed

## ➢ Advisory Board Member:

1. American Journal of Physiology, Biochemistry and Pharmacology

## ➢ Reviewed Papers for:

1. American Journal of Physiology, Biochemistry and Pharmacology
2. PLoS One
3. BBA: Molecular and Cell Biology of Lipids

## ➢ Talks Delivered Abroad/Within Country:

1. Molecular Mediators of hepatic Steatosis and Liver Injury; Disease Pathogenesis Series; `15 May, 2013, **Council of Scientific and Industrial Research-Indian Institute of Integrative Medicine (CSIR-IIIM), Jammu-180001**
2. Palmitate induced CD36 and SREBP1 upregulation is associated with intracellular $Ca^{2+}$ mediated ER Stress and CYP2E1-induced oxidative stress in *invitro* models of NAFLD/NASH: **5th International conference on Translational Cancer Research, New Delhi, February 6-9, 2014**
3. Cellular and Molecular Mechanism of lipotoxicity in Non alcoholic fatty liver disease: Retreat Meeting, 30-31 May, 2016, Group on Molecular and Cellular Biology of Lipids, **University of Alberta, 11207-87 Ave, Edmonton, AB, Canada, T6G2S2.**
4. Role of Human Carboxylesterase CES1 in Hepatic Triacylglycerol Metabolism: Molecular and Cellular Biology group Research progress meeting, 17 Jan, 2107 **University of Alberta, 11207-87 Ave, Edmonton, AB, Canada, T6G2S2.**
5. Autophagy induction reduces lipotoxicity and lipid accumulation in cellular model of Non Alcoholic Fatty Liver Disease (NAFLD) : 7th Annual conference of Indian Academy of Biomedical Sciences themed: Biochemical innovations: **Translating cellular cues into novel therapeutics, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, India: April 20-22, 2018**
6. Activation of mTORC1-G9a-H3K9me2 axis suppress autophagy in palmitate treated hepatoma cells: First Annual Research Meeting "**Recent Trends in Cell and Molecular Biology" 19- 20 March 2019. Department of Biotechnology, University of Kashmir.**

**Doctoral Thesis**
**Council of Scientific & Industrial Research**
**Indian Institute of Integrative Medicine, Canal Road Jammu-180001**
**Academy of Scientific and Innovative Research (AcSIR)**

My doctoral project was based on deciphering the biochemical and molecular basis of lipid and subsequent lipotoxicity in various *in vitro* and *in vivo* model(s) of metabolic disease (C57BL/6J mice). My data suggest that lipid burden dysregulates cellular metabolism, causes oxidative stress and disturbs intracellular $Ca^{2+}$ balance that terminates in endoplasmic reticulum (ER) stress, CYP2E1 induction, blockade of autophagy, lipid accumulation and lipoapoptosis. ER stress and oxidative stress form a vicious cycle in the pathogenesis of metabolic disease. ER stress associated with CYP2E1 and mitochondrial dysfunction play important role in the lipotoxic conditions. Metabolic and toxic manifestations including altered blood biochemistry, ER stress and CYP2E1 induction were evident in C57BL/6J mice fed with a diet rich in cholesterol and saturated fatty acids (2%-cholesterol/12% SFA-HC/HF) for 16 weeks. Histopathological analysis of livers of HC/HF fed mice showed micro and macro-vesicular steatosis, hepatocyte ballooning, infiltration of neutrophils and prominence of Kupffer cells. (***Nissar et al, Toxicology Research 2015***).

Stimulation of autophagy in human hepatoma by inhibiting ER stress using chemical chaperone(s) such as 4-phenyl butyric acid (4PBA) or mTORC1 inhibitor rapamycin/everolimus alleviated the suppression of autophagic turn over, decreased lipid accumulation and hence reduced lipotoxicity. Thus therapeutic intervention(s) using chemical chaperone which stabilise misfolded proteins such as 4PBA or other autophagy inducers could provide a promising strategy for treating lipotoxic conditions (***Nissar et al Journal of Lipid Research, 2017*).**

Apart from this, I was an important team member of project titled: "*Understanding ER stress and MAPK signalling in photodamage and skin carcinogenesis"*. In this case, we demonstrated that oxidative stress mediated Ca(2+) release manifests endoplasmic reticulum stress leading to unfolded protein response (***Farrukh MR, Nissar UA et al, 2014***); and activation of MAPK pathway (*Farrukh MR, Nissar UA et al, 2015)*. In a different study, we evaluated the effect of N-acetyl cysteine (NAC), an organosulfur compound from *Allium* plants, on experimentally induced hepatic prefibrogenic events in Wistar rat (***Nissar AU et al 2013***).

**Current Status: Work Published (***J of Lip Res 2017., Tox Res 2015., Free Radical Res 2015.* **)**

**Postdoctoral Fellowship**
**University of Alberta**
**315 Heritage Medical Research Centre**
**11207 - 87 Ave**
**Specific Aims:** Investigating the role of membrane-associated lipases in lipid metabolism
**Source of Funding:** Canadian Institute of Health Research (CIHR)

**Description of Research Done:**
**Title:**Human carboxylesterase 1 (CES1) reduces triacylglycerol turnover and fatty acid oxidation in McArdle-RH7777 cells
**Abstract:**
Mouse orthologue of human carboxylesterase1 (CES1) known as Ces1d/Ces3/TGH has been shown to play important role in the pathogenesis of non alcoholic fatty liver disease (NAFLD). However the direct effect of human CES1 on triglyceride (TG) turnover and fatty acid oxidation (FAO) is yet to be elucidated. In this study we studied the effect of CES1 on TG turnover and FAO. McArdle cells stably transfected with human CES1 (hTGH 35-5) showed decreased TG turnover and FAO as compared to cells stably transfected with empty vector (Pci Neo) in a pulse chase experimental setup. Gene expression analysis of FAO genes showed no significant difference between the two cell lines suggesting that difference in FAO is not due the difference in expression of genes. Blockade of ATGL functioning by Atglistatin reduced the FAO but had no effect on TG turnover. However blocking the lysosomal functioning by $NH_4Cl$ reduced both FAO and TG turnover. The reduction in TG turnover was more drastic in hTGH 35-5 as compared to Pci Neo cells. Combination of Atglistatin and $NH_4Cl$ reduced TG turnover as well as FAO in both the cells. Again the effect on TG turnover was more in hTGH35-5 cells suggesting that lysosomal function or autophagy is going on at slower rate in hTGH35-5 as compared to Pci Neo. Decreased pAMPK and LC3II levels in hTGH 35-5 also suggest decreased autophagy. In Conclusion, our results suggest that CES1 decreased TG turn over and FAO in McArdle cells and this could be due to decreased autophagy.

**Current Status: Manuscript under Preparation**

**National Postdoc Fellowship:**

**Chromatin and Epigenetics Lab**

**Department of Biotechnology, University of Kashmir**

Understanding the role of epigenetic mechanisms in Non alcoholic fatty liver disease

**Type and Funding:** National Postdoctoral Fellowship (NPDF)/DST SERB

**Specific Aims:**

To study histone modifications and its correlation with lipotoxicity in cellular models of NAFLD

Title of the MS: **Inhibition of mTORc1-G9a-H3K9me2 axis restores autophagy in fatty acid-induced lipotoxicity**

**Abstract:** Non alcoholic fatty liver disease (NAFLD) represents a spectrum of clinicopathological conditions ranging from simple fatty liver to steatohepatitis, fibrosis, cirrhosis and hepatocellular carcinoma in abscence of significant alcohol consumption. Defective autophagy and lipotoxicity are the hallmarks of NAFLD. However, the precise mechanism(s) for the defective autophagy in lipotoxic conditions is not fully known. In the present study, we found that exposure of human hepatoma cells (HepG2) to palmitate block autophagic flux and leads to lipid accumulation and cell death via mTORC1-G9a-H3K9me2 axis.HepG2 cells treated with palmitate showed mTORC1 activation as evident from increased phosphorylation of its substrate P70S6Kinase, which wasassociated with suppressed autophagy. Western blot analysis showed increased accumulation of SQSTM1/P62 and LC3II, decreased expression of Beclin1 and Atg7 in palmitate treated HepG2 cells. The decrease in autophagy was associated with increased levels of histone methyltransferase G9a in palmitate treated cells. Chromatin immunopreciptation (ChIP) analysis showed increased levels of repressive H3K9me2 mark at the promoter regions of Beclin1 and Atg7 in palmitate treated cells as compared to untreated control cells. Inhibition of mTORC1 by rapamycin in palmitate treated cells decreased the G9a levels and restored the expression of Atg7 and Beclin1, which was associated with increased autophagic flux as evident from decreased level of autophagic cargo SQSTM1/P62. Taken together, these findings reveal a novel axis between mTORC1-G9a-H3K9me2 in the regulation ofautophagic process and that inhibition of G9a could be a promising therapeutic target for treating lipotoxic conditions such as NAFLD.

**Current Status: Manuscript Communicated**

- **PUBLICATIONS :**

1. **Nissar U Ashraf** and Mohammad Altaf. Epigenetics: an emerging field in the pathogenesis of Non alcoholic fatty liver disease. **Mutation Research: Reviews in Mutation research (2018), 778: 1-12**
2. **Nissar Ul Ashraf,** Love Sharma, Malik A Mudasir, Lone A Nazir, Sheikh A Umar, Parduman R Sharma, Ram A Vishwakarma, Sheikh A Tasduq. Chemical chaperone 4-phenyl butyric acid (4PBA) reduces hepatocellular lipid accumulation and cell death through induction of autophagy. **Journal of Lipid Research Sep (2017), 58(9): 1855-1868**
3. **Nissar Ul Ashraf,** Love Sharma, Sheikh A Tasduq. Palmitic acid induced lipotoxicity is associated with altered lipid metabolism, enhanced CYP 450 2E1 and intracellular calcium mediated ER stress in human hepatoma cells .**Toxicology Research 4 (2015): 1344-1358**.
4. **Nissar Ul Ashraf,** Sheikh A Tasduq. Endoplasmic reticulum stress and Oxidative stress in the pathogenesis of Non-alcoholic fatty liver disease. **Free radical research (2015): 1-14.**
5. **Nissar Ul Ashraf**, Farrukh MR, Kaiser PJ, Rafiq RA, Afnan Q, Bhushan S, Adil HS, Subhash BC, Tasduq SA. Effect of N-acetyl cysteine (NAC), an organosulfur compound from Allium plants, on experimentally induced hepatic prefibrogenic events in Wistar rat.**Phytomedicine. 2013 Jul 15;20(10):828-33.**
6. Mufti Rana Farrukh, **Nissar Ul Ashraf**, Kaiser J Peerzada, Quadri Afnan, Praduman R Sharma, Shashi Bhushan, Sheikh A Tasduq. Glycyrrhizic acid (GA) inhibits Reactive Oxygen species mediated photodamage by blocking ER stress and MAPK pathway in UV-B irradiated human skin fibroblasts. **Journal of Photochemistry and Photobiology B: Biology 148 (2015): 351-357.**
7. Pathania, A. S., Guru, S. K., **Nissar Ul Ashraf,** Riyaz-Ul-Hassan, S., Ali, A., Tasduq, S. A., ... & Bhushan, S. A novel stereo bioactive metabolite isolated from an endophytic fungus induces caspase dependent apoptosis and STAT-3 inhibition in Human leukemia cells. **European journal of Pharmacology 765 (2015): 75-85**.
8. Farrukh MR, **Nissar Ul Ashraf**, Afnan Q, Rafiq RA, Sharma L, Amin S, Kaiser P, Sharma PR, Tasduq SA. Oxidative stress mediated Ca(2+) release manifests endoplasmic reticulum stress leading to unfolded protein response in UV-B irradiated human skin cells.**J Dermatol Sci. 2014 Jul;75(1):24-35.**
9. R. Farrukh, M.A.Zargar, A.Akhtar, S.A.Tasduq, S. Surjeet, **Nissar Ul Ashraf**, S. Rakshanda, A. Masood, S.A. Ganie and A. Shajrul. Antibacterial and antifungal activity of **Thymus serpyllum**: **Botany Research International 5 (2012): 36-39**

**10.** Afnan Q, Adil MD, **Nissar Ul Ashraf**, Rafiq AR, Amir HF, Kaiser P, Gupta VK, Vishwakarma R, Tasduq SA. Glycyrrhizic acid (GA), a triterpenoid saponin glycoside alleviates ultraviolet-B irradiation-induced photoaging in human dermal fibroblasts. **Phytomedicine. 2012 May 15;19(7):658-64.**

- **Manuscript under Preparation/Communication:**

**11.** **Nissar Ul Ashraf** et al. Human carboxylesterase 1 (CES1) reduces triacylglycerol turnover and fatty acid oxidation in McArdle-RH7777 cells (**Manuscript under preparation**).

**12.** **Nissar Ul Ashraf**el al. Inhibition of mTORc1-G9a-H3K9me2 axis restores autophagy in fatty acid-induced lipotoxicity(**Manuscript Communicated**)

**13.** **Nissar Ul Ashraf:** Crosstalk between Epigenetic mechanisms and Autophagy: Implications for Non alcoholic fatty liver Disease pathogenesis and treatment (**Manuscript Communicated**)

**Public Awareness articles/opinion piecesin local Dailies (Newspaper):**

1. An Emerging Public health concern (NAFLD): Greater Kashmir,
2. Soft Drinks: Sweet path to metabolic Disease, Rising Kashmir.
3. Management of Non alcoholic fatty liver Disease, Rising Kashmir

**ABSTRACTS PRESENTED IN CONFERENCES/SYMPOSIA**

**1)** Attended International conference on Genomic instability and cancer-2007, held at University of Kashmir, Srinagar, from July 22-26, 2007

**2)** **Nissar et al**, Potential chemoprevention of N- Nitrosodiethylamine induced pre neoplastic events by Acteoside in Wistar rat: XXIX Annual conference of the society of Toxicology held at the Food and Drug Toxicology Research centre, National Institute of Nutrition, Indian Council of Medical research, Hyderabad, November 4-7, 2009 (**Poster Presentation**)

**3)** **Nissar et al**,Palmitate induced CD36 and SREBP1 upregulation is associated with intracellular $Ca^{2+}$ mediated ER Stress and CYP2E1-induced oxidative stress in *invitro* models of NAFLD/NASH: 5$^{th}$ International conference on Translational Cancer Research, New Delhi, February 6-9, 2014 (**Oral Presentation**)

**4)** Attended 101$^{st}$ Indian Science Congress (Theme: Innovations in Science and Technology for Inclusive Development) held at University of Jammu, Jammu from 3-7$^{th}$ February 2014.

**5)** **Nissar et al,** Chemical Chaperone 4-phenyl butyric acid (4PBA) reduces hepatocellular lipid accumulation and lipotoxicity through induction of Autophagy: 25$^{th}$ Annual

Scientific meeting of Indian National Association for study of Liver, New Delhi, August 3-6, 2017 (**Award Winner).**

6) **Nissar et al,**Inhibition of Endoplasmic reticulum stress by 4 phenyl butyric acid reduced lipotoxicity and lipid accumulation through induction of autophagy in human hepatoma cells. 4th International Conference on Recent advances in Engineering sciences, Chandigarh , India; 26th Nov, 2107 (**Oral Presentation**)

7) **Nissar et al,**Palmitate induced lipotoxicity is associated with intracellular Ca2+ mediated ER stress and CYP2E1 oxidative stress in human liver cells; International Conference on Recent advances in Science, Agriculture, Engineering and Management; Bathinda, Panjab, India; 20th Nov, 2107 (**Oral Presentation**)

8. **Nissar et al,** Chemical chaperone 4-phenyl butyric acid (4PBA) reduces hepatocellular lipid accumulation and lipotoxicity through induction of autophagy; EMBO conference themed: Autophagy: Cellular mechanism(s) and significance in health and disease: 11th to 13th December, 2107, Institute of Life Sciences, Bhubaneswar, Orissa, India (**Poster Presentation**)

9. **Nissar Ul Ashraf,**Autophagy induction reduces lipotoxicity and lipid accumulation in cellular model of Non Alcoholic Fatty Liver Disease (NAFLD) : 7th Annual conference of Indian Academy of Biomedical Sciences themed: Biochemical innovations: Translating cellular cues into novel therapeutics, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, India: April 20-22, 2018 (**Award Winner**).

10. **Nissar Ul Ashraf,**Activation of mTORC1-G9a-H3K9me2 axis suppress autophagy in palmitate treated hepatoma cells: First Annual Research Meeting "Recent Trends in Cell and Molecular Biology" 19- 20 March 2019. Department of Biotechnology, University of Kashmir. **(Oral Presentation: Award winner)**

## Training Courses attended

1. Radiation Safety Course, University of Alberta, Canada, June 2016
   **(Course Grade: 90.63%)**
2. WHMIS University Personnel, University of Alberta, Canada, June 2016
   **(Course Grade: 95%)**
3. Concepts in Biosafety, University of Alberta, Canada, June 2016,
   **(Course Grade: 85%)**
4. Laboratory Safety Training, University of Alberta, Canada, June 2016,
   **(Course Grade: 92%)**
5. Animal Handling Training, University of Alberta, Canada, June 2016,
   **(Course Grade: Satisfactory)**
6. Hands on training in Drug discovery and Bioinformatics, University of Kashmir, March, 2019
7. Three weeks Induction Training Programme for newly appointed Assistant Professors of Higher Education Department, Govt. of J&K (27, May 2019-19, June 2019) at Govt. College of Education(IASE) Cluster University Srinagar.

- **Personal Details:**

**Name:** Nissar Ul Ashraf

**Name of Father:** Mohammad Ashraf Ahanger

**Permanent Address:** Mohalla Jalal Sahib, Down Town, Baramulla

Jammu & Kashmir-193101

**Correspondence Address:** Department of Biochemistry, Govt. Degree College, Sopore

**Languages:** Fluent in English, Hindi, Urdu and Kashmiri