**REPORT**

**Report of the Fellow who availed Fellowship/Training under Human Resource Development for Health Research**

1. Name and designation of Fellow :  Dr. Y. Suneetha, Assistant Professor

2. Address  : Department of Zoology

Sri Venkateswara University

Tirupati-517502

3. Type of Fellowship and period : ICMR, HRD, Short Term Fellowship

4. Duration of fellowship : 3 Months [March 2 – June 1, 2015]

5.         Frontline area of research in which :

           Training /research was carried out

*Genomics*: “To understand the beneficial effects of several cell protective and anti-cancer molecules, including MitoQ, SS31 and anti-aging agent, resveratrol against cell-priliferation and neurodegeration”

6.       Name & address of mentor and host institute :

Dr. P. Hemachandra Reddy,

Executive Director and Chief Scientific Officer of Garrison Institute on Aging

Professor of Cell Biology and Biochemistry, Neuroscience/Pharmacology and Neurology

Texas Tech University Health Sciences Center

3601 4th Street / MS / 9424 / 4A 124

Lubbock, Texas 79430

 7.         Highlights of work conducted             :

            i)          Technique/expertise acquired           :

(Give in about 150 words)

The purpose of my research training was to understand the beneficial effects of several cell protetive and anti-cancer molecules, including MitoQ, SS31 and anti-aging agent, resveratrol against cell-priliferation and neurodegeration. MitoQ and SS31 are mitochondria-targeted molecules, are known to protect cells from oxidative insults and mitochondrial toxicities. However, their anti-cancer properties are less known. As an initial process of my training, I used mouse neuroblastoma (N2a) and molecular biology and cell biology techniques, including: 1) real-time RT-PCR, 2) mitochondrial-dependent reduction of 3-(4,5-dimethyl-thiazol-2-yl)-2,5-diphenyl-tetrazolium bromide (MTT), 3) immunoblotting and 4) oxygen consumption ratio and studied anti-cancer and cell protective properties of MitoQ, SS31 and resveratrol. I measured mRNA expressions and protein levels of cell cycle genes - CDK4, CDK5, CDK6 and ANACP2 and mitochondrial dynamics genes Drp1 and Fis1 (fission), Mfn1, Mfn2, Opa1 (fusion) and CypD (matrix) in N2a cells treated and untreated with MitoQ, SS31 and resveratrol. Further, using Seahorse XF96 extracellular flux analyser, oxygen consumption ratio was measured in treated and untreated N2a cells.

ii)  Research results, including any papers,

prepared/submitted for publication :

(Give in about 300 words)

**Research Results:**

We have analyzed the

***i) protective effects of mitochondrial division inhibitor 1 (Mdivi1) and mitochondria-targeted molecules – MitoQ and SS31 in striatal neurons that stably express mutant Htt STHHDhQ111/Q111:***

The XFe96 extracellular flux analyzer analysis of spare respiratory capacity, particularly oxygen consumption ratio was significantly increased in STHDhQ111/Q111 neurons treated with Mdivi 1, MitoQ and SS31 relative to untreated STHDhQ111/Q111 neurons. The Cell viability was significantly increased in STHDhQ111/Q111 neurons treated with Mdivi 1 (P=0.039), MitoQ (P=0.0367) and SS31 (P=0.0438) relative to untreated STHDhQ111/Q111 neurons. The cell death assays revealed that both apoptotic and necrotic cell deaths were reduced in STHDhQ111/Q111 neurons treated with Mdivi 1, MitoQ and SS31 compared to untreated neurons.

***ii) partial deficiency of Drp1 inhibiting the Drp1- amyloid beta (Aβ) interactions:***

Decreased mRNA expressions and protein levels of Drp1 and Fis1 (fission) and CypD (matrix) genes, and increased levels of Mfn1, Mfn2 and Opa1 (fusion), Nrf1, Nrf2, PGC1α, TFAM (biogenesis) and synaptophysin, PSD95, synapsin 1, synaptobrevin 1, neurogranin, GAP43 and synaptopodin (synaptic) were found in 6-month-old Drp1+/-xAβPP mice relative to AβPP mice. Mitochondrial functional assays revealed that mitochondrial dysfunction is reduced in Drp1+/-xAβPP mice relative to AβPP mice, suggesting that reduced Drp1 enhances mitochondrial function in AD neurons.

***iii) Drp1-phosphorylated tau interactions in Alzheimer’s disease (AD) neurons:***

Measurement of phosphorylated tau studies revealed that soluble and phosphorylated tau levels were significantly reduced in Drp1+/-xTau mice relative to Tau mice, indicating that reduced Drp1 decreases soluble and phosphorylated tau production in AD progression.

***iv) impact of p53 mutations on p53-MDM2 interaction:***

Results showed that a large deviation in the total solvent accessible surface area, structure solvent energy and average gain in the complex formation properties of mutant p53-MDM2 complexes compared to the native ones. Neural network analysis showed that structural features are important for predicting the impact of mutants on p53-MDM2 interaction.

**Publications:**

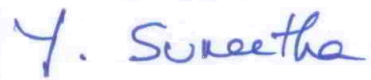
* **Y. Suneetha**, K. Naidu and P.H. Reddy (2015) A Systematic Approach to Analyze the Impact of p53 Mutations on p53-MDM2 Interaction Using Machine Learning. Abstract submitted to the Annual Meeting of Society for Neuroscience to be held at Chicago October 17-21, 2015.
* X. Yin, M. Manczak, R. Kandimalla, A.K. Pandey, C.S. Kuruva, **Y. Suneetha** and P.H. Reddy (2015) Mitochondrial Division Inhibitor 1 and Mitochondria-Targeted Molecules MitoQ and SS31 Protects Against Mutant Htt-induced Mitochondrial toxicities in Huntington’s Disease Neurons. Abstract submitted to the Annual Meeting of Society for Neuroscience to be held at Chicago October 17-21, 2015.
* M. Manczak, R. Kandimalla, A.K. Pandey, X. Yin, C.S. Kuruva, **Y. Suneetha**, D. Fry, C. Osborn and P.H. Reddy (2015) Reduced Dynamin-related Protein 1 Protects Against Amyloid Beta, Mitochondrial Toxicities and Synaptic Damage in Alzheimer’s Disease. Abstract submitted to the Annual Meeting of Society for Neuroscience to be held at Chicago October 17-21, 2015.
* R. Kandimalla, M. Manczak, A.K. Pandey, X. Yin, C.S. Kuruva, **Y. Suneetha**, D. Fry, C. Osborn and P.H. Reddy Reduced Dynamin-related Protein 1 Protects Against Phosphorylated Tau, Mitochondrial Dysfunction and Synaptic Damage in Alzheimer’s Disease. Abstract submitted to the Annual Meeting of Society for Neuroscience to be held at Chicago October 17-21, 2015.
* **Y. Suneetha**, C. Kumaraswamy Naidu (2015). Analyzing the impact of PTEN mutations conferring susceptibility to breast cancer: A bioinformatics approach. Abstract submitted to (ACM-BCB 2015) The 6th ACM conference on Bioinformatics, Computational Biology and Health Informatics to be held at Atlanta, GA, September 9-12, 2015.

**Membership:** Society for Neuroscience (SFN), 2015

iii)  Proposed utilization of the experience

in the Parent Institute. (Please specify the project developed whether originally proposed/ new project) :

The project developed is a **new project**. The techniques and training acquired during the fellowship will be utilized in the ongoing project entitled “**A novel approach to elucidate the *pten* expression and mutations in breast cancer**” and future programmes of the parent institute.



                                                                               Signature of the Fellow

**CLAIM SHEET**

(To be filled in by the Fellow)

 1.         Name, Designation and Address  : Dr.Y.Suneetha, Assistant Professor

Department of Zoology

Sri Venkateswara University

Tirupati-517502, Andhra Pradesh

2.         ICMR Sanction letter No. and date    : ICMR Lr. No. HRD Fellowship-II (3)/2014-15

dated 09.10.2014 & 6.11.2014

 3.         Broad area of research                  : Genomics

 4.         Chosen area of training                  : Cell protective and anti-cancer molecules,

 5.         Name, designation & address of : Dr.P.Hemachandra Reddy

Professor/Mentor of host institute        Executive Director and Chief Scientific Officer

Garrison Institute on Aging, Professor of Cell

Biology and Biochemistry, Neuroscience/

Pharmacology and Neurology

Texas Tech University Health Sciences Center

3601 4th Street / MS / 9424 / 4A 124

Lubbock, Texas 79430, USA

 6.         Duration of the training : 3 months   (02.03.2015 to 01.06.2015)

 7.         Details of expenditure on the training

 A         TRAVEL:

 i)                    Place of work in India                                  : Tirupati

ii)                  Port of embarkation with date of departure  : Chennai, 26th February 2015

 iii)                Port of disembarkation with date of arrival  : Dallas (USA) 27th February 2015

 iv)                Venue of training if in a city different from : Lubbock

iii) above

v)                  Air fare for onward travel to venue by shortest route : Provided by ICMR

vi)        Air fare for return travel                                             : Provided by ICMR

vii)       Total expenditure on Air travel (v + vi)                : Provided by ICMR

B.        Fellowship USD 3000 x 3 months                             : USD 9000

C.        Contingency                                                             : Rs. 30,000/-

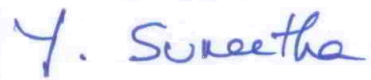
(VISA fee, SEVIS fee and Health insurance)

            iii) Taxi charges from place of duty to airport and back  :  Rs.10,000/-

D.        Total (A to C)                                                                     : Rs. USD 9000 + INR 40,000/-

**Certificate :**

 Certified that I have participated in the above training/research programme and the particulars furnished above are correct. I also certify that I have not received any financial assistance from any other source.



 Date: 15.06.2015                                                                                    Signature

Dr. Y. Suneetha

Assistant Professor

Department of Zoology

Sri Venkateswara University

Tirupati-517502

**Please attach the following documents:**

1. Original receipts for items claimed against contingency grant (Item. C).
2. Original receipt of Hotel/Guest house accommodation charges to be submitted by Senior Fellows.

**Details to be furnished by Fellow**

 1.         Total grant received                                        : USD 8500

 2.         Sanction Letter no. & date                            : HRD Fellowship-II (3)/2014-15

dated 09.10.2014 & 6.11.2014

 3.         Total expenditure incurred on training : USD 9000 + INR 40,000/-

            of the Fellow

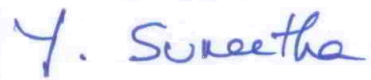
 4.         Amount to be released to the concerned Fellow  : USD 500 + INR 40,000/-

5.         Balance (if available) returned/being returned to DHR/ICMR: Not applicable

6.         Utilization certificate in the proforma enclosed : Yes

**Certificate:**

            Certified that Fellow has been paid grant as sanctioned by ICMR column 2 above for training abroad and as per guidelines of the DHR Fellow of HRD scheme.



  Date:   15.06.2015                                                              Signature

Dr.Y.Suneetha

Assistant Professor

Department of Zoology

Sri Venkateswara University

Tirupati-517502

**UTILIZATION CERTIFICATE**

1.         Title                                                                 : HRD Fellowship Sponsored by DHR

 2.         Address of the Institution                              : Sri Venkateswara University, Tirupati

3.         Name & designation of Fellow                  : Dr. Y. Suneetha

Assistant Professor

Department of Zoology

 4.         DHR/ICMR sanction letter no. & date         : HRD Fellowship-II (3)/2014-15

dated 09.10.2014 & 6.11.2014

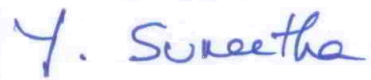
 5.         Amount that was available for expenditure    :

 6.         Actual expenditure                                         : USD 9000 + INR 40,000/-

 7.         Unspent balance if any                                   : NIL

 8.         Balance to be reimbursed to the Fellow     : USD 500 + INR 40,000/-

Certified that out of USD 9000 + INR 40,000/- of grant-in-aid sanctioned during the financial year 2014-15 in favour of Dr. Y. Suneetha, Assistant Professor, Department of Zoology, Sri Venkateswara University, Tirupati DHR Fellowship awardee under DHR/ICMR sanction letter No. HRD Fellowship-II (3)/2014-15 dated 09.10.2014. A sum of USD 8500 has been utilized for the purpose of research/training abroad in respect of Dr. Y. Suneetha, the fellow for which it was sanctioned and that the balance amount of USD 500 + INR 40,000/- due to the awardee may please be reimbursed.



Date:   15.06.2015                                                                      Signature of Fellow

**CONTINGENCY**

1. VISA Fee : Rs. 10,240=00
2. Health Insurance : Rs. 8,641=00
3. SEVIS Fee (USD 180) : Rs. 11,160=00

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Total Rs. 30,041=00

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