REPORT

Report on participation of the ICMR International Fellow (ICMR-IF) in Training/Research abroad.

1. Name and designation of ICMR- IF : **Dr. Pallavi Shukla**
   Scientist C

2. Address: **Department of Molecular Endocrinology,**
   Indian Council of Medical Research-
   National Institute for Research in Reproductive Health (ICMR-NIRRH),
   Mumbai

3. Frontline area of research in which training/research was carried out : **Molecular Genetics, Genomics and cell biology**

4. Name & address of Professor and host institute **Dr. Keshav Singh,Professor of Genetics, Pathology and Environmental Health at Department of Genetics, School of Medicine, University of Alabama Birmingham, Alabama, USA**

5. Duration of fellowship : **1 year (31st Jan 2020-31st Jan 2021)**

6. Highlights of work conducted:

   i) Technique/expertise acquired : **CRISPR/CAS9 technique**
   SRB assay for cell proliferation study
   Cell Migration Assay
   Cell Invasion Assay
   mtDNA copy number analysis
   TCGA/CPTCA data analysis
   Subcellular fractionation (for nuclear And mitochondrial separation)

   ii) Research results, including any papers, prepared/submitted for publication

Title of the study: **Analysis of Abundance of Nuclear Mitochondrial DNA Segment (NUMT) and Role of *Yme1L1* Gene in Endometrial Cancer**

Yme1L1 is described to be the first numtogenesis suppressor protein. Yme1L1 (YME1 Like 1 ATPase) is a gene that encodes a protein which is the human ortholog of yeast mitochondrial AAA metalloprotease, Yme1p. It is localized in the mitochondria and plays an important role in mitochondrial protein metabolism. Further it also regulates mitochondrial structure and maintain normal cristae morphology. It's role in ensuring cell proliferation, proper assembly of respiratory complexes, mitophagy and apoptosis has also been recognized. Singh and group describe that loss of Yme1l1 leads to migration of mitochondrial DNA segments to nuclear DNA, process known as Numtogenesis. Increased abundance of nuclear mitochondrial DNA segments (NUMTs) may cause genomic instability and may play a role in cancer development. Yme1l1 is known to be involved in mitochondrial pathologies but its role in cancer is sparsely studied. Moreover, its role in racial disparity has not been reported. The research study was taken to study the role of Yme1L1 in endometrial cancer. The role of Yme1L1 in cancer is has not been elucidated yet.

Material Methods: We analyzed Clinical Proteomic Tumor Analysis Consortium (CPTAC) databases (https://proteomics.cancer.gov/programs/cptac) to study the expression of YME1L1 protein in endometrial cancer. The functional role of Yme1L1 was analysed in AN3CA cell line (endometrial cancer Type II) using CRISPR/CAS9 knockout followed by functional genomics techniques.

We identified many novel findings.

CPTAC data analysis

CPTAC data analysis showed that Yme1L1 protein expression is increased in uterine corpus endometrial carcinoma (UCEC) samples compared to normal samples (Fig. 1a). Yme1L1 protein expression is increased in all stages of UCEC samples compared to normal samples (Fig. 1b). Yme1L1 protein expression is significantly increased in all grades 1 of UCEC Samples compared to normal samples (Fig. 1c). Grade 3 is significantly increased as compared to grade 2 UCEC samples ($p<1E-12$). Yme1L1 expression is increased significantly in endometrial carcinoma, serous carcinoma UCEC samples and others compared to normal samples (Fig. 1d).