REPORT

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

1. Name and designation of ICMR- IF : Dr Adarsh Wamanrao Barwad
   Additional Professor of Pathology

2. Address :1048, Dept of Pathology,
   All India Institute of Medical Science,
   New Delhi 110029

3. Frontline area of research in which training/research was carried out:
   Molecular Technique (RNA Sequencing) in Renal Transplant Pathology

4. Name & address of Professor and host institute :
   Prof. Parmjeet S. Randhawa
   Division of Transplantation Pathology,
   The Thomas E Starzl Transplantation Institute,
   University of Pittsburgh,
   E737 UPMC-Montefiore Hospital,
   3459 Fifth Ave, Pittsburgh, PA 15213, USA.

5. Duration of fellowship with exact date : March 27th 2023 to Sept 26th 2023

6. Highlights of work conducted : As Below

i) Technique/expertise acquired :

RNA Sequencing, Data analysis and Bioinformatics

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

Methods: RNAseq based Banff Human Organ Transplant (BHOT) gene expression (GE) analysis. was used to probe the molecular signature of TCMR-MVI in comparison with C4d+, DSA+ antibody mediated rejection (ABMR), stable renal function (STA), and TCMR without MVI. Transcriptome analysis utilized CLC genomic workbench and R-studio software.

Results: No gene set was specific for any diagnostic category, and all were expressed at low levels in STA biopsies. BHOT gene set scores could differentiate ABMR from TCMR and TCMR-MVI, but not TCMR from TCMR-MVI. TCMR-MVI under-expressed several genes associated with ABMR including DSATs, ENDAT, Immunoglobulin genes, ADAMDEC1, PECAM1 and NK cell transcripts (MYBL1, GNLY), but overexpressed C3, NKBBIZ and LTF. On the other hand, there was no significant difference in the expression of these genes in TCMR-

MVI vs TCMR. This indicates that the GE profile of TCMR MVI aligns more closely with TCMR than ABMR. The limitations of classifying biopsies using the binary ABMR-TCMR algorithm, and the occurrence of common pathogenesis mechanisms amongst different rejection phenotype was highlighted by the frequent presence of molecular mixed rejection.

Conclusions: T-cell mediated mechanisms play a significant role in the pathogenesis of MVI. GE was broadly between rejection phenotypes, but molecular scores varied substantially between biopsies with the same Banff grade. It was not always possible to achieve precise molecular score-based diagnostic categorization of individual patients.

- Manuscript is prepared for submission to Indexed Journal.
- Abstract of the study will be submitted to upcoming Annual Meeting of UCSAP 2023.

iii) Proposed utilization of the experience in India:

The experience gained during the fellowship will be further utilized for conducting large sample study on Indian patients in the form of extramural research grant and same will be translated for routine clinical practice as a diagnostic test which is still not available in the country

Signature of ICMR-IF

ICMR Sanction No. I N DO/F RC/452(Y -53\ 12022-23{ H&H RD Dated: 19.10.2022