REPORT

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

1. **Name and Designation of ICMR-IF:**
   Dr. Ravindra M Samartha, *Assistant Professor*

2. **Address**:
   Department of Research, Bhopal Memorial Hospital & Research Centre (ICMR), (Dept. of Health Research, Ministry of Health & Family Welfare, Govt. of India), Raisen Bypass Road, Karond, Bhopal (MP)-462038, INDIA

3. **Frontline area of research in which Training /research was carried out:**
   Molecular & Cellular Biology: "Role of DNA damage signaling in genomic instability"

4. **Name & address of Professor and host Institute:**
   Dr. Yoshihisa Matsumoto, *Associate Professor & PI*
   Tokyo Institute of Technology, Research Laboratory for Nuclear Reactors, N 1-30; 2-12-1, Ookayama, Meguro-ku, Tokyo 152-8550 JAPAN.

5. **Duration of fellowship:**
   Six Months [October 8, 2014- April 7, 2015].

6. **Highlights of work conducted:** Worked on the research project "Role of DNA damage signaling in genomic instability". Conducted the purification of a phosphorylation-specific antibody and elucidated the dose- and time-response of the phosphorylation of XRCC4 protein by DNA-PK. Also, obtained an interesting result, indicating the importance of the phosphorylation in DNA double-strand break repair.

   i) **Technique/expertise acquired**:
   1) Cell culture,
   2) Transfection,
   3) Colony Formation Assay,
   4) Antibody Purification,
   5) ELISA,
   6) Western Blotting,
   7) Immunoprecitation,

   ii) **Research results, including any papers, Prepared/submitted for publication**:

Research Results:

XRCC4 is shown to be phosphorylated by DNA-PK *in vitro* and *in vivo* but the site(s) and the significance of phosphorylation in DNA double-strand break repair have remained to be clarified. We purified the antibody, which reacts specifically with DNA-PK-phosphorylated XRCC4. Specificity was verified by ELISA assay. Using this antibody, the phosphorylation status of XRCC4 in human cervical carcinoma HeLa cell was examined by Western blotting. Radiation-induced phosphorylation of XRCC4 could be detected immediately after irradiation and even after 1 Gy irradiation. This shows that the detection of XRCC4 phosphorylation by phosphorylation-specific antibody is highly sensitive. Furthermore, we established a cell line expressing XRCC4 lacking the phosphorylation site and showed that it is more radiosensitive than normal XRCC4-expressing cells. These results indicated XRCC4 phosphorylation by DNA-PK plays an essential role in DNA double-strand break repair and maintenance of genomic integrity.

Published papers:

Conference Paper: Ravindra Mahadeo Samartha, Mukesh Kumar Sharma, Shoji Imamichi, Mikoto Fukuchi, Yoshihisa Matsumoto (2015): XRCC4 phosphorylation as indicator of DNA-dependent protein kinase functionality in living cells. Pp.55. [Presented at "*17th Symposium on Sensitization of Cancer Treatment", during February 6-7, 2015 at Nara, Japan*].

Membership: International Cancer Treatment Sensitized Research Association (IASCT), 2015.

iii) Proposed utilization of experience In India:

The techniques and training acquired during fellowship will be utilized into the ongoing and future programmes of the parent Institute.

ICMR Sanction No.
No. INDO/FRC/452/Y-2/2014-15-IHD
Dated: 29/09/2015

Signature of ICMR-IF 15/9/15

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