Form 3

Report for Joint/usage program for Endocrine/Metabolism

Date: April 24, 2016

To:

Director of Institute for Molecular and Cellular Regulation

1. Program No. 15003
2. Research title: Role of Fanconi anemia (FA)/Breast cancer (BRCA) pathway in oncogene-induced replication stress responses

3. Objective of the research: The FA/BRCA pathway plays an important role in maintenance of genomic integrity and tumor suppression. The objective of the present research is to clarify the role of FA/BRCA pathway in oncogene-induced genomic instability.

4. Period April 1, 2015 — March 31, 2016

5. Project organization

Name of Applicant: Toshiyasu Taniguchi
Position: Member
Institution/department: Divisions of Human Biology and Public Health Sciences, Fred Hutchinson Cancer Research Center

Name of Co-applicant:
Position:
Institution/department:

Name of Researcher in IMCR Takayuki Yamashita
Position: Professor

6. Research plans:

   Dr. Yamashita established experimental systems in which inducible expression of cyclin E or c-myc causes aberrant replication and subsequent DNA damage. Taking advantage of these systems, we will first study the behavior of the FA/BRCA pathway by biochemical and immunofluorescence analyses. Second, we will study the effects of deficiency of the FA/BRCA pathway on oncogene-induced replication and DNA damage.

7. Research results:

We found that overexpression of oncogenes such as c-myc and cyclin E induced monoubiquitination and increased chromatin binding of FANCD2, suggesting that the F/BRCA pathway is activated in response to oncogene-induced replication stress. We are currently studying effects of RNAi-mediated depletion of FA proteins on replication fork dynamics and genomic instability in c-myc and cyclin E-expressing cells.

8. Publications and/or Presentations made through this collaboration

(Please summarize the report in 2 pages)