Form 3

Report for Joint/usage program for Endocrine/Metabolism

Date: April 19, 2016

To:

Director of Institute for Molecular and Cellular Regulation

1. Program No. 15004
2. Research title: Role of Y-family polymerases in repair of DNA interstand crosslinks

3. Objective of the research:
4. We aim to elucidate functions of multiple DNA polymerases including Y-family polymerases during DNA interstrand repair process.

5. Period

   April 1, 2015 – March 31, 2016
6. Project organization

Name of Applicant: Grant Stewart

Position: Group leader

Institution/department: School of Cancer Sciences, College of Medical and Dental Sciences, University of Birmingham

Name of Co-applicant:

Position:

Institution/department:

Name of Researcher in IMCR Takayuki Yamashita

Position: Professor

7. Research plans:

We plan to study how and which Y-family polymerases function, collaborating with other polymerases and enzymes involved in DNA metabolism, during multi-stage interstrand crosslink repair. For this purpose, we will use transformants expressing various Y-family polymerases, provided by Dr. Yamashita.

8. Research results:

Y-family polymerases and Fanconi anemia proteins co-operate in repair of DNA interstrand crosslinks. During our reserach described above, we identified a previously uncharacterized chromatin factor BOD1L as a component to maintain genome stability. Loss of BODL1 confers cellular sensitivity to replication stress and uncontrolled resection of damaged replication forks, due to a failure to stabilize RAD51 at these forks. Blocking DNA2-dependent resection or sown regulation of DNA helicases, BLM and FBH1, suppresses both catastrophic fork processing and the accumulation of chromosomal damage in BOD1L-deficient cells. These data indicate that BOD1L is a critical regulator to restrain nucleolytic degradation of damaged replication forks.

9. Publications and/or Presentations made through this collaboration

(Please summarize the report in 2 pages)