課題番号（Project number） 56

Proteomic pursuit of the causes for premature aging, Werner and Rothmund Thomson syndromes

［1］組織（Research group）：

代表者（Principal Investigator）：

Vilhelm Bohr
(National Institute on Aging, NIH)

対応者（Host researcher at IDAC）：

Akira Yasui
(IDAC, Tohoku University)

研究費（Expenditure report of research funds）：

consumable goods 300,000 Yen

［2］研究経過（Research setup）

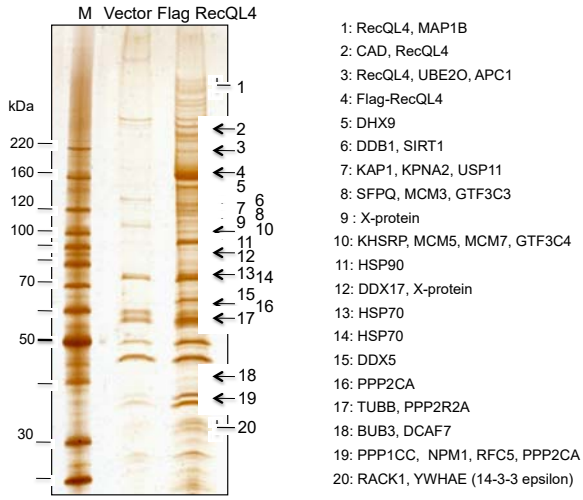
RecQ helicases consist of a highly conserved family of proteins that play significant roles in DNA metabolic processes including DNA replication, DNA repair, and DNA recombination. The two yeast species, S. *scerevisiae* and *S. pombe* each express only a single RecQ helicase (Sgs1 and Rqh1, respectively), whereas five RecQ homologs are expressed in mammalian cells: RECQ1, BLM, WRN, RECQL4, and RECQ5. BLM, WRN, and RECQL4 are linked to autosomal recessive disorders characterized by genomic instability and cancer predisposition. Bloom syndrome and Werner syndrome are associated with defects in BLM and WRN, respectively, whereas RECQL4 deficiency is associated with three rare autosomal recessive diseases: Rothmund-Thomson syndrome (RTS), Baller-Gerold syndrome, and RAPADILINO syndrome. BLM and WRN play important roles in DNA repair and replication and have also been implicated in telomere maintenance. Although WRN and BLM have been fairly well characterized, RECQL4 has only recently been intensively investigated. Recent reports suggest that RECQL4 plays at the crossroads of genomic instability and aging processes, the mechanisms of which remain elusive.

In order to understand the function of RECQL4 in aging process, we undertook a proteome analysis of RECQL4.

［3］成果（Research outcomes）

（3－1）研究成果（Results）

We have established a HEK293 cell line, which expresses the FLAG-tagged RECQL4 gene in a Tet-inducible manner. Using this cell-line we immune-precipitated RECQL4 protein complex with antibody against FLAG and separated the precipitants by gel electrophoresis (Fig. 1).



（3－2）波及効果と発展性など（Future perspectives）

There are still many interacting proteins to be determined. We are characterizing the functions of the interaction by analyzing whether they affect RecQ4L functions in terms of helicase and strand annealing activity. We are testing the binding affinities. Such studies will help us identify the DNA metabolic pathways in which RecQL4 participates.

［4］成果資料（List of Papers）

1. Sykora P, Kanno S, Akbari M, Kulikowicz T, Baptiste BA, Leandro G, Lu H, Tian J, May A, Becker KA, Croteau DL, Wilson DM III, Sobol RW, Yasui A and Bohr VA. DNA polymerase beta participates in mitochondrial DNA repair. *Mol Cell Biol*. 2017, doi: 10.1128/MCB.00237-17.