Project number　56

Analysis of RecQL4 proteome leading to premature aging in Rothmund Thomson syndromes

［1］Research group

Principal Investigator (PI)：
Vilhem A. Bohr
(National Institute on Aging, NIH, USA)

Host researcher at IDAC：
Akira Yasui, Shinichiro Kanno
(IDAC Tohoku University)

Expenditure report of research funds：
Consumables 100,000 YEN

［2］Research setup

Rothmund-Thomson syndrome (RTS) is a rare condition that affects many parts of the body, especially the skin. The gene defect in two-thirds of cases is due to mutations in a gene called RECQL4, which harbors a helicase domain with a similarity to that of *E. coli* RecQ. In NCBI database there are hundreds of candidates of RecQL4 interaction registered (2022 March10). Therefore, interaction under special cellular conditions may be useful to understand its cellular function.

［3］Research outcomes

（3－1）Results

In order to obtain stress response of RecQL4 in human cells, we immunoprecipitated Flag-tagged RecQL4 in the 293 cells treated with H_2O_2 or Arsenite and compared the precipitants with control (Fig.1). All the interacting proteins have been identified by mass spectrometry (not shown). This response of RecQL4 to Arsenite seems to be a major response of this protein and may contribute to the cell survival against Arsenite killing effect of cell.

There is a quite significant difference between the interactions of RecQL4 in the presence of H_2O_2 or Arsenite.

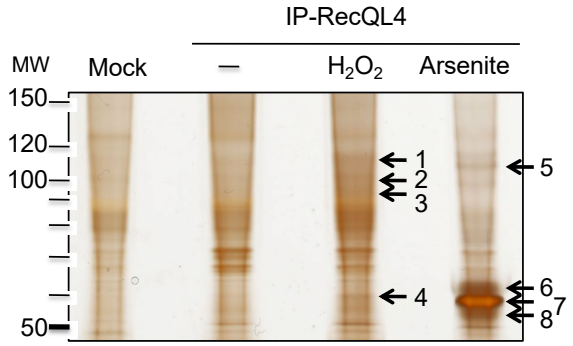

Fig.1 Analysis of interacting proteins of RecQL4 expressed in 293 cell after treatment with H_2O_2 or Arsenite.

We are interested in the cellular responses of RecQL4 to Arsenite. Here in Fig. 2 large foci induced by Arsenite were observed in the nucleus of U2OS cell. These foci contain interacting proteins identified in Fig. 1.

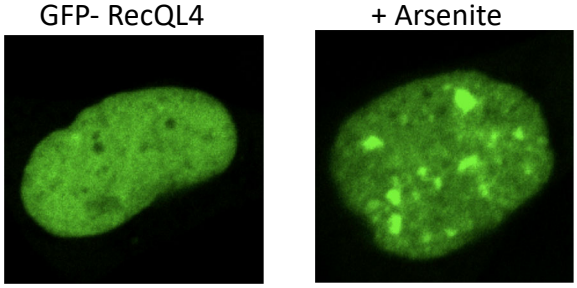

Fig. 2 Foci formation of GFP-tagged RecQL4 in the nucleus of U2OS cell by treating cells with Arsenite.

（3－2）Future perspectives

Many of RecQ homologues are involved in a list of premature aging syndrome, from Werner Syndrome (WS) to RTS. Arsenite response of RecQL4 may be here firstly reported. While it has been reported that RecQL4 plays important roles in DNA damage response and repair, its oxidative response, especially against chemically induced oxidative stress, may be important and should be analyzed more intensively.

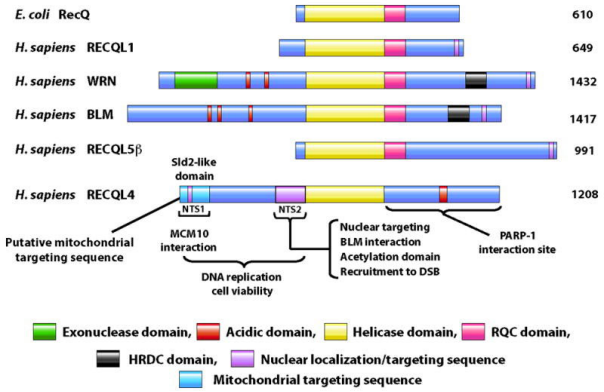

Fig. 3 Comparison of RecQ homologues

［4］List of research achievements

None.