Reviewer’s report

Title: Fanconi anemia with sun-sensitivity caused by a Xeroderma pigmentosum-associated missense mutation in XPF

Version: 0 Date: 17 Jul 2017

Reviewer: Minoru Takata

Reviewer’s report:

This paper describes identification of two XPF/FANCQ/ERCC1 mutations by whole exome sequencing in a ~50 y.o. patient having phenotypes compatible with FA (malformations, hypocellular marrow, microcephaly etc but without any malignancy) and perhaps mild XPF (sunlight sensitivity). The patient derived cells showed MMC sensitivity that was corrected by introduction of WT XPF. The authors explain that the clinical manifestations in FA-Q patient could be highly variable, and that could depend on how much proportion of mutant protein can escape from misfolding (in Discussion)

These analyses clearly demonstrated that the patient has FA caused by XPF mutations (FA-Q). Figure 2F is highly informative. I have only a few comments.

1. The cells express small amount of XPF protein with correct size and a small amount of this protein seems to be localized to chromatin as well (Fig 1I). This observation is at odds with the previous report that XPF mutation invariably leads to cytoplasmic localization due to misfolding (Ahmad et al. pLOSGenetics 2010). It would be interesting to compare cells (3104 cells and XPF cells preferably having the same mutation as 3104) in terms of XPF protein localization in parallel. This is just a suggestion.

Minor comments:

1. XP42RO in Figure 2C. This is not explained in the Legend

2. The sentence in line 296-300 was difficult to follow. Is this because of any kind of miss editing? Perhaps "were" in line 298 should be "where"?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes
Are the conclusions drawn adequately supported by the data shown? 
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review? 
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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