

## Review of: "Non-canonical scaffold-type ligase complex mediates protein UFMylation"

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The manuscript explores the minimal requirements for UFMylation and mechanistic insights into the ligase machinery through establishment a robust in vitro reconstitution system using purified active components of the UFM1 enzymatic pathway. The study is well designed and manuscript is well written. The results from the study provide important insights into the mechanism of UFMylation modification process. The concerns I have are the following:

- 1. The authors concluded that polyUFM1 chains are formed via K69, I am not sure whether K69 works for all polyUFM1 chains or it is specifically for the substrate ASC1 used in the assay.
- 2. Whether or not the results from in vitro reconstitution system can be validated in cells by co-expression of the factors used in reconstitution system.

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