

Zebrafish Ubc13 is required for Lys63-linked poly-ubiquitination and DNA damage tolerance.

Jie Li¹, Rui Wen², Parker L. Andersen², Yuping Liang¹, Wei Xiao¹, Zongbin Cui².
Institute of hydrology, ¹Chinese Academy of Science, China. ²Dept. Of Microbiology and Immunology, University of Saskatchewan, Canada.

Ubiquitination is an important post-translational protein modification that functions in diverse cellular processes of all eukaryotic organisms. Conventional Lys48-linked poly-ubiquitination leads to the degradation of specific proteins through 26S proteasomes, while lys63-linked poly-ubiquitination appears to regulate protein activities in a non-proteolytic manner. To date, Ubc13 is the only known ubiquitin conjugating enzyme capable of poly-ubiquitinating target proteins via Lys63-linked chains, and this activity absolutely requires a Ubc variant (Uev or Mms2) as a co-factor. However, Lys63-linked poly-ubiquitination and error-free DNA damage tolerance in zebrafish are yet to be defined. Here, we report molecular cloning and functional characterization of two *ubc13* zebrafish genes, *ubc13a* and *ubc13b*. Analysis of their genomic structure, nucleotide and protein sequence indicates that the two genes are highly conserved during evolution and derived from the whole genome duplication. Zebrafish Ubc13 proteins are able to physically interact with yeast or human Mms2 and both *ubc13* genes are able to functionally complement the yeast *ubc13* null mutant for spontaneous mutagenesis and sensitivity to DNA damaging agents. In addition, upon DNA damage, the expression of zebrafish *ubc13a* and *ubc13b* is induced during embryogenesis and zebrafish Ubc13 is associated with nuclear chromatin. These results suggest the involvement of Lys63-linked poly-ubiquitination in the DNA damage response in zebrafish.