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Cancer-upregulated gene-2 (*CUG2*) increases the protein stability of enhancer of zeste homolog (EZH2) by negatively regulating the beta-TrCP-mediated degradation

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Enhancer of zeste homolog-2 (EZH2) is a component of the polycomb repressive complex-2 (PRC2), which mediates the gene silencing through trimethylation of histone H3 on lysine 27 (H3K27). Several studies reported that EZH2 overexpression is commonly found in diverse malignancies including prostate and breast cancer. Beta-TrCP is a substrate-recognition subunit of $SCF^{beta\text{-}TrCP}$ ubiquitin ligase and it is reported that EZH2 is another interactor of beta-TrCP as a substrate of SCF complex. On the other hand, our recent study found that cancer-upregulated gene 2 (*CUG2*), which was originally identified as a putative proto-oncogene and is frequently overexpressed in various tumors, interacts with and stabilizes the protein level of EZH2. In this study, we show that EZH2 protein is destabilized by beta-TrCP overexpression and recovered by *CUG2* co-expression. Moreover, we found that *CUG2* binds to beta-TrCP and the protein level of beta-TrCP is decreased in CUG2-overexpressed cells, suggesting that *CUG2* may increase EZH2 protein stability through negative regulation of beta-TrCP-mediated EZH2 degradation. Previously, it is reported that both of *CUG2* and EZH2 possess putative nuclear localization signal (NLS) and are predominantly located in the nucleus. In this study, we also demonstrate that *CUG2* may mediate the nuclear translocation of beta-TrCP, proposing that *CUG2* may regulate the activity of $SCF^{beta\text{-}TrCP}$ ubiquitin ligase in the nucleus. These findings suggest that *CUG2* may negatively regulate the beta-TrCP-mediated EZH2 protein turnover in the nucleus and be involved in EZH2-induced tumorigenesis.

Biography

Yeongmi Cheon has obtained her Master's degree at Chungnam National University, South Korea. Presently she is pursuing PhD in Molecular Biotechnology at Department of Bioscience and Biotechnology, Chungnam Graduate School.

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