HECTD3

The E3 ubiquitin ligase HECTD3 is a homologue of the E6 protein carboxyl terminus, which plays a crucial role in biological processes and tumorigenesis. However, the functional characterisation of HECTD3 in glioblastoma is still elusive.

Determination of the functional role of HECTD3 in glioblastoma was made by a combination of HECTD3 molecular pattern analysis from human glioblastoma databases and subcutaneous and in situ injections of tumours in mice models.

This study reports that the DOC domain of HECTD3 interacts with the DNA binding domain of PARP1, and HECTD3 mediated the K63-linked polyubiquitination of PARP1 and stabilised the latter expression. Moreover, the Cysteine (Cys) 823 (ubiquitin-binding site) mutation of HECTD3 significantly reduced PARP1 polyubiquitination and HECTD3 was involved in the recruitment of ubiquitin-related molecules to PARP1 ubiquitin-binding sites (Lysines 209 and 221, respectively). Lastly, activation of EGFR-mediated signalling pathways by HECTD3 regulates PARP1 polyubiquitination.

These results unveil the potential role of HECTD3 in glioblastoma and strongly preconise further investigation and consider HECTD3 as a promising therapeutic marker for glioblastoma treatment [1].

1)
Zhang G, Tan R, Wan S, Yang R, Hu X, Zhao E, Ding X, Zhang J, Li B, Liang P, Cui H. HECTD3 regulates the tumourigenesis of glioblastoma by polyubiquitinating PARP1 and activating EGFR signalling pathway. Br J Cancer. 2022 Sep 10. doi: 10.1038/s41416-022-01970-9. Epub ahead of print. PMID: 36088509.