

## **A Identification of a highly recurrent C18ORF8-NEDD4L gene fusion in esophageal squamous cell carcinoma**

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**BACKGROUND:** One patient with local advanced esophageal squamous cell carcinoma (ESCC) had a poor response to neoadjuvant chemoradiotherapy in a phase III double-blind randomized clinical trial (NCT01216527) was further included in a transcriptome sequencing program. Interestingly, a gene fusion of autophagy-related gene C18orf8 with E3 ubiquitin-protein ligase NEDD4L (C18ORF8-NEDD4L) was detected. **HYPOTHESIS:** C18ORF8-NEDD4L is a novel genomic fusion in ESCC patients. It may be associated with chemoradiotherapy response. **METHODS:** Polymerase chain reaction (PCR), rapid-amplification of cDNA ends approach and Sanger Sequencing techniques were used to identify the fusion transcripts, the full length C18ORF8-NEDD4L and fusion sites. Eight ESCC cell lines were screened for C18ORF8-NEDD4L fusion, and applied to test the functional impacts of C18ORF8-NEDD4L in vitro. Additionally, the frequency of C18ORF8-NEDD4L was detected in 205 fresh ESCC samples. **RESULTS:** The genomic breakpoint was identified at the end of exon4 of C18orf8 and intron 9 of NEDD4L in patient tumor and further proved by PCR and Sanger sequencing, which provided the solid evidences for existence of gene fusion. In addition, the fusion gene harbors 4 different transcripts with full-length identified. The C18ORF8-NEDD4L was also detected in two ESCC cell lines, KYSE180 and KYSE520. Moreover, the ectopic expression of C18ORF8-NEDD4L in ESCC cell lines was correlated with increased resistance to radiation and chemotherapy. Furthermore, C18ORF8-NEDD4L fusion was found in 24 (11.7%) out of 205 ESCC patient samples, suggesting high level of recurrence.