



P2.027: FBXO5-mediated KEAP1 Degradation Inhibits Ferroptosis and Promotes NSCLC Radioresistance

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INTRODUCTION

- Radioresistance is the main cause of radiotherapy failure in non-small cell lung cancer (NSCLC).
- F-box only protein 5 (FBXO5), also known as Emi1, acts as a specific component of the ubiquitin ligase complex.
- FBXO5 has been reported as a potential prognosis predictor of NSCLC, but the mechanism remained unclear.

DISCUSSION AND CONCLUSION

- High expression of FBXO5 is associated with radioresistance of NSCLC by promoting the ubiquitination degradation of KEAP1 and inhibiting radiation- or erastin-induced ferroptosis.
- Our work indicates that FBXO5 may serve as a biomarker for predicting radiosensitivity in NSCLC and represents a potential therapeutic target.

METHODS

- We demonstrated bioinformatic analysis on a variety of RNA-seq databases including the data from Cancer Genome Atlas (TCGA), Gene Expression Omnibus (GEO).
- Then we constructed stable cell lines of A549 using lentivirus and colony formation assays were performed.
- The underlying mechanisms were evaluated using in vitro experiments, including IP-MS, immunoprecipitation, western blot analysis, quantitative polymerase chain reaction, flow cytometry, malondialdehyde assays and GSH/GSSG assays.

RESULTS

Figure1. High-expressed FBXO5 is a negative prognosis predictor in NSCLC
Figure2. FBXO5 Promotes NSCLC Radioresistance in vitro

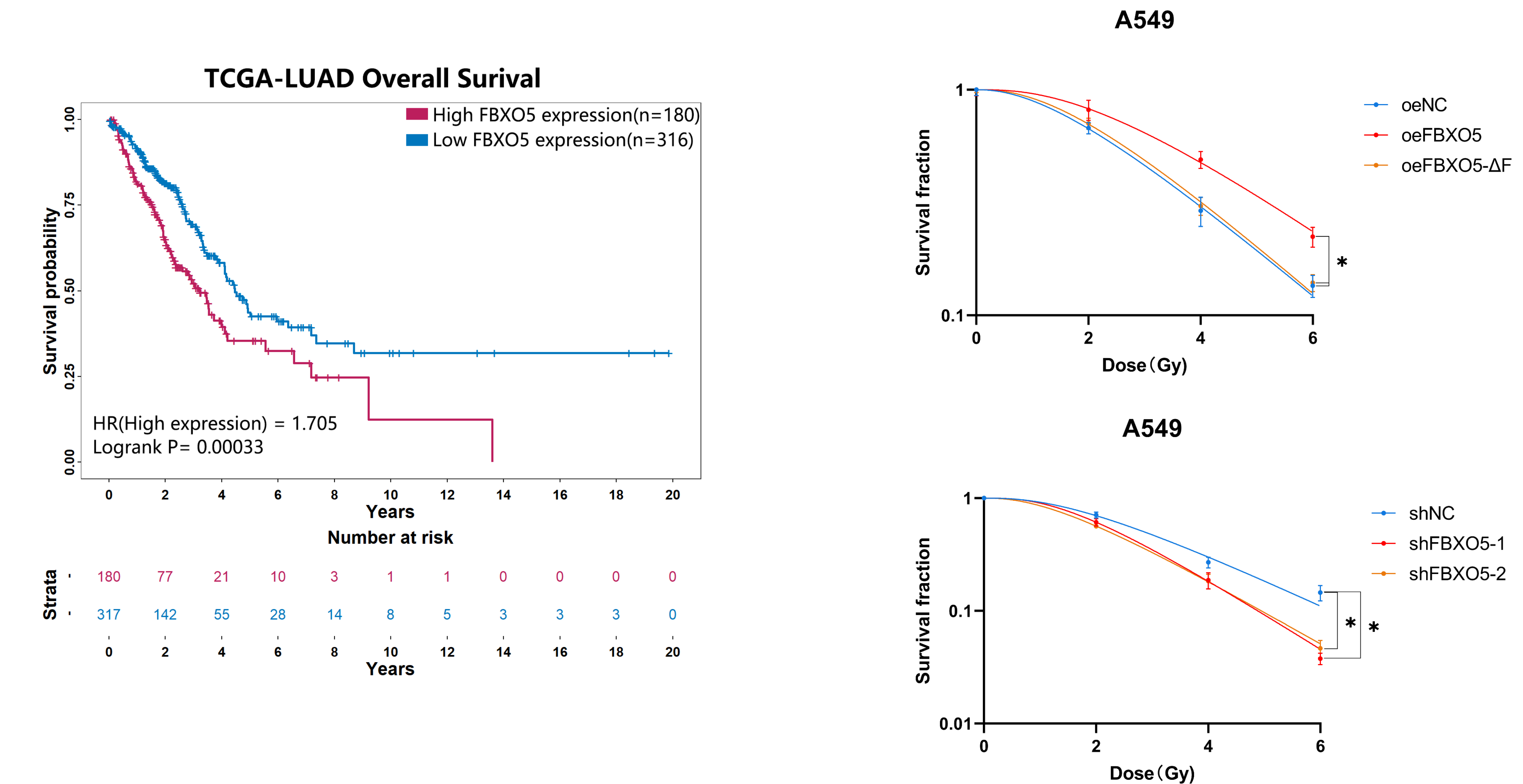


Figure3. IP-MS indicates FBXO5 promoting the ubiquitination degradation of KEAP1

IP-MS					
Proteins	PSMs	Unique Peptides	Proteins	PSMs	Unique Peptides
FBXO5	63	23	FBXO5	35	17
ETF1	47	21	SKP1	27	12
SKP1	36	11	ETF1	23	17
RUVBL2	31	20	RPL5	22	11
SASS6	30	24	KEAP1	18	15
EEA1	28	26	MTHFD1	16	15
MYBBP1A	20	19	CCT8	16	16
KEAP1	20	10	RUVBL1	15	11
IPO5	20	16	EIF3A	15	13
HSP90AA1	20	11	ZC3H14	14	8

A549

PC9

Figure4. High expression of FBXO5 is associated with radioresistance of NSCLC by promoting the ubiquitination degradation of KEAP1 and inhibiting radiation induced ferroptosis

