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Letter to the Editor

Expression of AKR1C3, β-Catenin and LEF1 in Esophageal Squamous Cell Carcinoma and the Relationship with Radiation Resistance

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Dear Editor-in-Chief

AKR1C3 is C3, a member of aldo-keto reductase (AKR) family 1, which is a redox enzyme. AKR1C3 expression in tissues with prostate cancer increases significantly, which is positively correlated with the clinical staging of prostate cancer (1).

In this study, to detect the AKR1C3 expression in esophageal cancer and verify whether it is related to radiation resistance, 61 patients were selected who were treated in Tangshan People's Hospital, Tangshan China from January 2010 to December 2016 as the study subjects.

This study was approved by the Ethics Committee of Tangshan People's Hospital. Patients who participated in this research, signed the informed consent.

All of the patients received radiotherapy. The results of experiments showed that there was no difference in the AKR1C3 expression in cytoplasm between the two groups, but high expression of AKR1C3 in nucleus may enhance radiation resistance in patients with esophageal cancer (Table 1).

Table 1: Relationship between Short-term Efficacy of Radiotherapy and AKR1C3 Expression in Nucleus, β-catenin Expression, LEF1 Expression

Group	***n***	***AKR1C3 Expression in Nucleus***				
		P25	P50	P75	Z	*P*
Effective Group	30	1.750	2.500	4.500	-2.014	0.044
Ineffective Group	31	1.000	8.000	9.000		
				β-catenin Expression		
		P25	P50	P75	Z	*P*
Effective Group	30	1.00	2.000	4.500	-2.198	0.028
Ineffective Group	31	1.000	8.000	9.000		
				LEF1 Expression		
		P25	P50	P75	Z	*P*
Effective Group	30	1.000	2.000	3.250	-2.751	0.006
Ineffective Group	31	2.000	4.000	6.000		

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The results of this study are consistent with the previous reports on the relationship between AKR1C3 expression and radiation resistance in esophageal cancer (2). β-catenin gene, known as serial catenin (cadherin-related protein), is an iconic gene in the Wnt/β-catenin signaling pathway, which is essential for the establishment and maintenance of epithelial layer. β-catenin is closely related to the occurrence and development of various types of breast cancer (3).

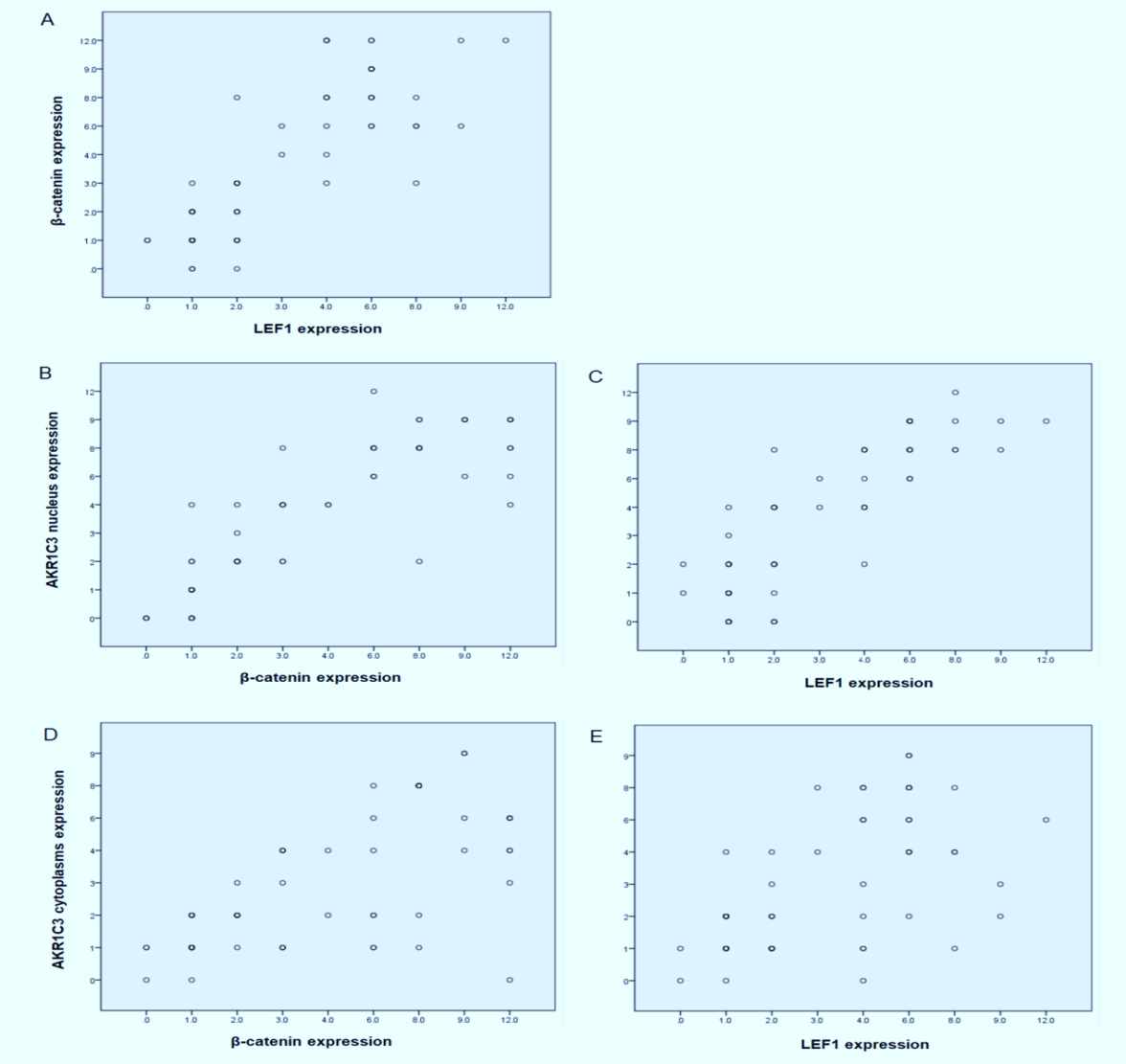

Fig. 1: Scatter Diagram of Correlation between AKR1C3, β-catenin and LEF1 expression in ESCC. A: Correlation between β-catenin and LEF1 protein expression. There was a monotonic relationship between β-catenin expression and LEF1 expression, rs=0.808, *P*<0.001. B: Correlation between AKR1C3 nuclear expression and β-catenin expression. There was a monotonic relationship between AKR1C3 expression in nucleus and β-catenin expression, rs=0.876, *P*<0.001. C: Correlation between AKR1C3 nuclear expression and LEF1 expression. There was a monotonic relationship between AKR1C3 expression in nucleus and LEF1 expression, rs=0.841, *P*<0.001. D: Correlation between AKR1C3 cytoplasmic expression and β- Correlation of catenin expression. There was a monotonic relationship between AKR1C3 expression in cytoplasm and β-catenin expression, rs=0.665, *P*<0.001. E: Correlation between AKR1C3 cytoplasmic expression and LEF1 expression. There was a monotonic relationship between AKR1C3 expression in cytoplasm and LEF1 expression, rs=0.593, *P*<0.001

LEF1 gene, known as lymphocyte binding enhancing factor, is one of the key genes in the Wnt pathway. LEF1 is highly expressed in many tumor cells, which can promote the invasion of breast cancer cells, and it is associated with the growth, proliferation and invasion of cells (4). This study detected the expression of β-catenin and LEF1 protein and found that β-catenin protein was mainly expressed in cytoplasm and nucleus, and LEF1 protein was mainly expressed in nucleus. And high expression of β-catenin and LEF1 protein was associated with radiation resistance in patients with esophageal cancer (Table 1). The results are consistent with previous reports on the high expression of β-catenin and LEF1 genes in radiation-resistant cell lines of esophageal cancer (5).

At present, the mechanism of AKR1C3 enhancing radiation resistance of esophageal cancer tumor cells is still not clear. It may be related to its activation or involvement in the activation of some radiation resistance related signaling pathway. This study detected the expression of AKR1C3, β-catenin and LEF1 protein in tissues and cells of ESCC and found that AKR1C3 expression in cytoplasm and nucleus was positively correlated with the expression of β-catenin and LEF1 (Fig. 1). According to the correlation coefficient, the nucleoprotein expression of AKR1C3 has stronger relationship with the expression quantity of β-catenin and LEF1. Thus, AKR1C3 nuclear aggregation may be involved in triggering activation Wnt/β-catenin signaling pathway.

The results further showed that β-catenin and LEF1 are important components of Wnt/β-catenin signaling pathway, with a positive correlation between them. Wnt/β-catenin pathway is a known signal transduction pathway associated with tumor radiation resistance that is already known After Wnt/β-catenin signaling pathway is activated, β-catenin transfers from cytoplasm to nucleus, and joined TCF/LEF1 family, which can recruit coactivators β-catenin into the enhancing elements of genes they target (6).

Conflict of interest

The authors declare that there is no conflict of interest.

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