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Association of the expression level of lncRNAs GAS5, HAND2-AS1, LINC00152, and LINC00339 and tumor size and the lymphogenous metastasis in clear cell renal cell carcinoma

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INTRODUCTION & AIM

The frequency of clear cell renal cell carcinoma (ccRCC) metastasis reaches 25-30% which makes it urgent to search for prognostic biomarkers. Long non-coding RNAs (lncRNAs) regulate biological processes and may serve as prognostic markers. The **aim** of our study was to compare the expression of lncRNAs GAS5, HAND2-AS1, LINC00152 and LINC00339 in tumors and normal kidney tissue and analyze the association of its changes with clinicopathological parameters of ccRCC.

METHOD

We used archival RNA samples (RIN>7) from 70 primary tumors with a confirmed diagnosis of ccRCC and 70 adjacent normal kidney tissues. Expression analysis was performed by RT-qPCR. B2M and ACTB were used as reference. Statistical analysis was performed using a multivariate ANOVA test ($p \leq 0.05$).

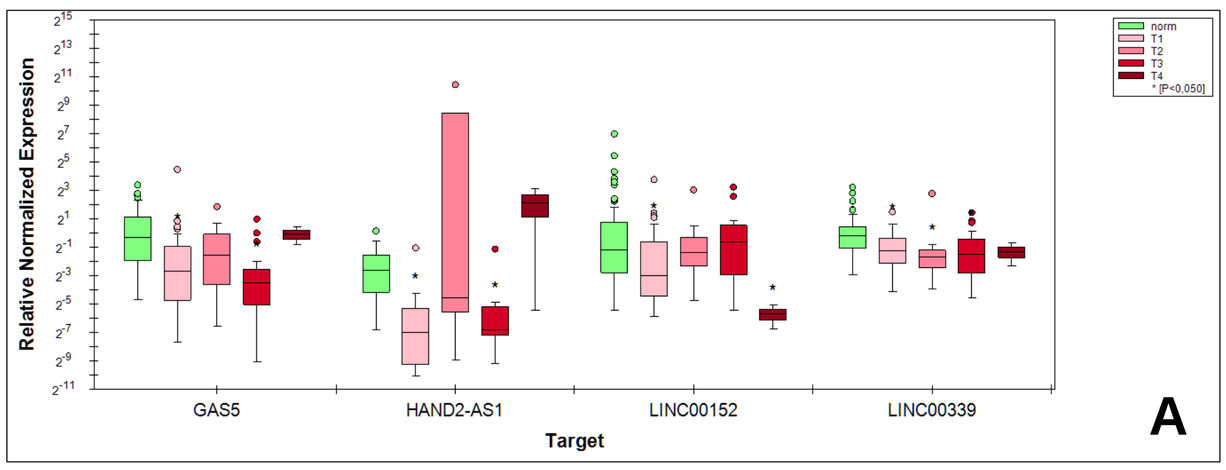

Fig. 1. Comparison of expression levels of lncRNAs GAS5, HAND2-AS1, LINC00152 and LINC00339 in tumors with different T (A) and N (B) criteria according TNM classification and normal kidney tissues.

RESULTS & DISCUSSION

An expression decrease of GAS5 by 5.25, HAND2-AS1 by 5.92, LINC00152 by 2.04, and LINC00339 by 2.34 times was revealed in the tumor tissues. The expression of LINC00152 did not change at T1, T2 and T3 (the TNM classification) and decreased by 33.43 times when the tumor grows beyond Gerota's fascia (T4). LINC00152 expression was lower in T4 tumors compared to tumors of a smaller size: T1/T4 - 10.86 times, T2/T4 - 22.76 times, T3/T4 - 27.11 times. LINC00152 expression decreased 4.71 times in cases with multiple lesions of regional lymph nodes (normal/N2), incl. compared with tumors with no metastases in the lymph nodes (N0/N2) or one affected lymph node (N1/N2) by 4.36 and 7.26 times, respectively. HAND2-AS1 had a lower level of expression in tumors with multiple lesions of regional lymph nodes: normal/N2 – 15.02 times, N0/N2 – 5.84 times, N1/N2 – 4.04 times.

lncRNA	GAS5		HAND2-AS1		LINC00152		LINC00339	
	Fold Change	p	Fold Change	p	Fold Change	p	Fold Change	p
N0	-5,61	0,000000	-3,71	0,189591	-1,99	0,048172	-2,63	0,000001
N1	-2,60	0,188419	-5,12	0,085948	-2,14	0,068964	-1,50	0,511150
N2	1,71	0,598437	-15,02	0,014201	-4,71	0,032266	-2,01	0,304683

Table 1. Expression alterations in tumors with different N criteria according TNM classification vs. normal kidney tissues.

CONCLUSION

The significant decrease in the expression of HAND2-AS1 and LINC00152 when more than one regional lymph node is affected (N2 according to the TNM classification) in ccRCC allows to propose them as prognostic markers of lymphogenous metastasis in the absence of the ability to evaluate regional lymph nodes (Nx).

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