sunitinib resistance, but the picture remains unclear. On the other hand, few prognostic factors have been validated as predictive biomarkers of sunitinib response. Thus, it is urgent to elucidate the underlying mechanisms of sunitinib resistance and discover reliable biomarkers that can predict sunitinib response in RCC patients.

Methods: Exosomes can be secreted from multiple types of cells and participate in intercellular communication by transmitting intracellular cargoes, such as proteins and nucleic acids. Increasingly, some studies have suggested that exosomes from stromal cells could potentially affect therapeutic response though transfer of proteins and miRNAs. However, whether exosomes derived from resistant cancer cells can confer drug resistance to sensitive cells needs to be illustrated. Moreover, components embedded in circulating exosomes may serve as easily accessible biomarkers for the evaluation of drug response in patients. Long non-coding RNA (lncRNA) is a heterogeneous class of transcripts with a minimum length of 200 bases and without protein-coding potential. lncRNAs are involved in multilevel regulation of gene expression, including transcriptional regulation by recruiting chromatin-modifying complexes and post-transcriptional regulation by interacting with miRNAs, mRNAs or proteins. Emerging evidence supports the notion that lncRNAs modulate numerous hallmarks of cancer, including proliferation, apoptosis, metastasis and metabolism. However, the roles of lncRNAs in sunitinib resistance are poorly understood. In this study, we identify an upregulated lncRNA (lncARSR) in sunitinib-resistant RCC cells. We then investigate the contributions of lncARSR to sunitinib resistance and its therapeutic implications for sunitinib-resistant RCC patients.

Results: Herein we identified an lncRNA, named lncARSR (lncRNA Activated in RCC with Sunitinib Resistance), that correlated with clinically poor sunitinib response. lncARSR promoted sunitinib resistance via competitively binding miR-34/miR-449 to facilitate AXL and c-MET expression in RCC cells. Furthermore, bioactive lncARSR could be incorporated into exosomes and transmitted to sensitive cells, thus disseminating sunitinib resistance. Treatment of sunitinib-resistant RCC with locked nucleic acids (LNA) targeting lncARSR or an AXL/c-MET inhibitor restored sunitinib response.

Conclusions: lncARSR may serve as a predictor and a potential therapeutic target for sunitinib resistance.

Keywords: Sunitinib; renal cancer; receptor tyrosine kinase (RTK); long non-coding RNA (lncRNA)

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AB072. A feed forward loop between lncARSR and YAP activity promotes expansion of renal tumor-initiating cells

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Background: Renal cell carcinoma (RCC) is the most common kidney cancer in adults prognosis. Increasing appreciation of cell heterogeneity and a challenging disease with poor within clear cell renal cell carcinoma (ccRCC) has focused attention on a distinct subpopulation of cells called tumour initiating cells (T-ICs) or cancer stem cells (CSCs) in ccRCC. T-ICs exhibit extended self-renewal potential and tumour initiating ability. Tumours that harbour an abundant T-IC population or have high expression of stemness-related genes may signal a poor clinical outcome in RCC patients. Therefore, identification of the underlying mechanisms governing renal T-ICs propagation may lead to the discovery of promising therapeutic strategies for RCC patients.

Methods: Long non-coding RNA (lncRNA) is a subgroup of transcripts with more than 200 nt and limited coding potential. lncRNAs modulate biological process via diverse mechanisms, including mobilizing transcriptional co-regulators or chromatin-modifying complex at transcription level, and interacting with RNAs and protein complex or modifying signal proteins at post-transcription level. Several lncRNAs have been reported to regulate the self-renewal of T-ICs especially liver T-ICs. Nevertheless, the role of

lncRNA in the regulation of renal T-ICs remains unknown. lncARSR (lncRNA Activated in RCC with Sunitinib Resistance, ENST00000424980) was a newly identified lncRNA to promote the sunitinib resistance of RCC in our previous study. Accumulating evidence indicated that T-ICs surviving from drug therapy and giving rise to tumour regrowth might be a major culprit for therapeutic resistance. Indeed, the expression signature of stem cell or targets of Nanog, Oct4, Sox2 and c-Myc (NOSM) in human ESCs were significantly enriched in our mRNA profile of sunitinib-resistant RCC cells (GSE69535), prompting us to explore the role of lncARSR in renal T-ICs.

Results: In this study, we first find that lncARSR is highly expressed in primary renal T-ICs and predicts poor prognosis. Next, by using loss-of-function analysis in T-ICs and gain-of-function analysis in RCC cells, we demonstrate that lncARSR promotes the self-renewal capacity, tumorigenicity and metastasis of renal T-ICs. Further mechanism study reveals that lncARSR interacts with Yes-associated protein (YAP) to block its phosphorylation by LATS1, facilitating YAP nuclear translocation. Interestingly, we find that YAP in turn promotes the transcription of lncARSR, forming a feed-forward loop. Clinical investigation also confirms the correlation between lncARSR and YAP, and demonstrates the value of combining lncARSR and YAP to improve the prognostic accuracy for RCC patients.

Conclusions: Altogether, we discover that lncARSR promotes the expansion of renal T-ICs via interacting with YAP.

Keywords: Tumour initiating cells (T-ICs); renal cell carcinoma (RCC); Yes-associated protein; lncRNA

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AB073. Clinicopathologic characteristics, therapy and outcomes of primary ureteral small cell carcinoma: a case series and systematic review of the literature

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Background: To review the experience of diagnosis and treatment of primary small cell carcinoma (SCC) in our institution and discuss the clinicopathologic characteristics, treatments and outcomes of patients with primary ureteral SCC.

Methods: Patients diagnosed with ureteral SCC in our institution from January, 2007 to December, 2016 were reviewed. In addition, we performed a systematic literature review in October 2016 on case reports and case series of ureteral SCC. The clinicopathologic characteristics, treatments and outcomes of this rare disease were analyzed.

Results: A total of 32 patients were included in our analysis (4 cases from our institution and 28 cases from the literature). Most patients (71.0%) were male with an average age of 66.6 years (range, 48–80 years). The most common symptoms were hematuria (n=14, 48.3%) and flank pain (n=14, 48.3%). All patients received surgery, with 12 (37.5%) patients underwent multimodality therapy. Regional or distant recurrence occurred in 11 patients, among which only 1 patient presented bladder recurrence. The overall median survival for the patients was 17 months, with a 1- and 3-year survival rates 51.9% and 30.3%, respectively. In a univariate analysis, female (P=0.009), pure SCC (P=0.03), advanced T stage (P=0.04) were associated with worse overall survival.

Conclusions: Ureteral SCCs are extremely rare neoplasms with aggressive natural history and poor prognosis. T stage, tumor components and gender may be important factors influencing prognosis. A multimodality treatment is recommended for the management. However, further studies are needed to improve the treatment strategy.

