## Lefter to the Editor

## Long noncoding RNA GIHCG is a potential diagnostic and prognostic biomarker and therapeutic target for renal cell carcinoma

Dear Editor,

We think that the paper by He et al<sup>1</sup>, published on European Review for Medical and Pharmacological Sciences and titled "Long noncoding RNA GIHCG is a potential diagnostic and prognostic biomarker and therapeutic target for renal cell carcinoma", is another important proof that circulating cell-free nucleic acids could serve as interesting non-invasive biomarkers for early diagnosis of several cancers. This is also the way forward to better personalize each therapy.

Renal cell carcinoma (RCC) is the most common subtype of kidney cancer. Approximately 90% of these tumors are classified as RCC and up to 80% as "clear cell" RCC. Most patients (> 75%) are diagnosed when the disease is already advanced or metastatic, mRCC, hence no more curable<sup>2-4</sup>. Recurrent and/or mRCC is associated with a poor 5-years survival, roughly 10%; however, in the last decade, a series of novel agents have been introduced in clinical practice and the outcomes are slowly improving<sup>5,6</sup>.

In particular, this article focuses attention on the expression level of GIHCG in the serum of RCC patients. This serum level is significantly unregulated in RCC patients compared with that in healthy controls. Therefore, the authors analyzed the clinical values of GIHCG in RCC. Long noncoding RNA is a kind of RNA molecule with a length transcript of more than 200 nt, which has the function to regulate the gene expression at epigenetic level but does not have the protein-encoding capacity<sup>7-9</sup>. More and more reports have demonstrated that lncRNAs play an important role in the development of a variety of carcinomas with a crucial role in cell proliferation, differentiation, apoptosis, and in all pathological processes. However, despite the high number of lncRNAs identified, to date, little is known about their role in cancer for vast majority of them; unlikely, only a small fraction of them have been characterized.

The paper explored the correlation between GIHCG expression level and clinicopathological traits in 46 RCC patients with a result that GIHCG is markedly increased in RCC tissues with advanced TNM stages. Furthermore, GIHCG expression is also significantly increased in RCC tissues with Fuhrman III and IV grades compared with that in Fuhrman I and II grades. The positive correlation between increased GIHCG expression and advanced TNM stages is confirmed by Pearson x²-tests. The confirmation of the association between GIHCG upregulated and an aggressive clinic-pathological traits and poor prognosis is given by Kaplan-Meier survival analysis. A crucial point of this study is the loss-of-function assays that show that deletion of GIHCG significantly represses cell proliferation and migration of RCC cells, highlighting the oncogenic roles of GIHCG.

Other reports have put in evidence the importance of IncRNAs for some clinical applications also in other cancer type. Nowadays, the role of IncRNAs as non-invasive biomarkers is beyond doubt. Surely the identification of all the dysregulated IncRNAs in RCC patient's serum on large-scale would help clinical choice especially in a period in which, given the many drugs registered, it becomes necessary to be able to predict, with good approximation, what is the best treatment for each patient<sup>10,11</sup>.

## **Conflict of interest**

The authors declare no conflicts of interest.

## References

- 1) HE ZH, QIN XH, ZHANG XL, YI JW, HAN JY. Long noncoding RNA GIHCG is a potential diagnostic and prognostic biomarker and therapeutic target for renal cell carcinoma. Eur Rev Med Pharmacol Sci 2018; 22: 46-54.
- 2) FACCHINI G, PERRI F, CARAGLIA M, PISANO C, STRIANO S, MARRA L, FIORE F, APREA P, PIGNATA S, IAFFAIOLI RV. New treatment approaches in renal cell carcinoma. Anticancer Drugs 2009; 20: 893-900.
- 3) Rossetti S, D'Aniello C, Iovane G, Scagliarini S, Laterza MM, De Vita F, Savastano C, Carteni G, Porricelli MA, Berretta M, Pisconti S, Facchini G, Cavaliere C. Sequential treatment with pazopanib and everolimus in metastatic renal cell carcinoma. Front Pharmacol 2017; 8: 484.
- 4) CECERE SC, ROSSETTI S, CAVALIERE C, DELLA PEPA C, DI NAPOLI M, CRISPO A, IOVANE G, PISCITELLI R, SORRENTINO D, CILIBERTO G, MAI-OLINO P, MUTO P, PERDONÀ S, BERRETTA M, PIGNATA S, FACCHINI G, D'ANIELLO C. Corrigendum: pazopanib in metastatic renal cancer: a "real-world" experience at National Cancer Institute "Fondazione G. Pascale". Front Pharmacol 2016; 7: 468. eCollection 2016.
- 5) D'ANIELLO C, VITALE MG, FARNESI A, CALVETTI L, LATERZA MM, CAVALIERE C, DELLA PEPA C, CONTEDUCA V, CRISPO A, DE VITA F, GRILLONE F, RICEVUTO E, DE TURSI M, DE VIVO R, DI NAPOLI M, CECERE SC, IOVANE G, AMORE A, PISCITELLI R, QUARTO G, PISCONTI S, CILIBERTO G, MAIOLINO P, MUTO P, PERDONÀ S, BERRETTA M, NAGLIERI E, GALLI L, CARTENÌ G, DE GIORGI U, PIGNATA S, FACCHINI G, ROSSETTI S. Axitinib after sunitinib in metastatic renal cancer: preliminary results from italian "real-world" SAX study. Front Pharmacol 2016; 7: 331.
- 6) CECERE SC, ROSSETTI S, CAVALIERE C, DELLA PEPA C, DI NAPOLI M, CRISPO A, IOVANE G, PISCITELLI R, SORRENTINO D, CILIBERTO G, MAIOLINO P, MUTO P, PERDONÀ S, BERRETTA M, PIGNATA S, FACCHINI G, D'ANIELLO C. Pazopanib in metastatic renal cancer: a "real-world" experience at National Cancer Institute "Fondazione G. Pascale". Front Pharmacol 2016; 7:287.
- 7) QIU MJ, TIAN H, PANG C, YANG ZJ, LI CQ, XU L. The curative effects of LPN combined LCA in treating with middle and advanced renal cancer. Eur Rev Med Pharmacol Sci 2016; 20: 584-588.
- 8) Chen J, Gu Y, Shen W. MicroRNA-21 functions as an oncogene and promotes cell proliferation and invasion via TIMP3 in renal cancer. Eur Rev Med Pharmacol Sci 2017; 21: 4566-4576.
- 9) Morgia G, Russo GI. Do exist the "perfect" biomarker in metastatic renal cancer? WCRJ 2014; 1: e415.
- 10) Fratino L. Metastatic renal cancer prognostic and predictive biomarkers. WCRJ 2014; 1: e343.
- 11) D'Aniello C, Cavaliere C, Licchetta A, Gnoni A, Pisconti S, Facchini G. Metastatic renal cancer: prognostic and predictive biomarkers review. WCRJ 2014; 1: e289.

C. D'Aniello<sup>1</sup>, S. Pisconti<sup>2</sup>, S. Facchini<sup>3</sup>, C. Imbimbo<sup>3</sup>, C. Cavaliere<sup>4</sup>

<sup>1</sup>Division of Medical Oncology, A.O.R.N. dei Colli – "Ospedali Monaldi-Cotugno-CTO", Naples, Italy <sup>2</sup>Department of Onco-Hematology Medical Oncology, S.G. Moscati Hospital of Taranto, Taranto, Italy <sup>3</sup>Urology Department, University of Naples, Federico II, Naples, Italy <sup>4</sup>Division of Medical Oncology, ASL NA 3 SUD, PO Nuovo Gragnano, Naples, Italy