

## COMMENTARY TO HABILITATION THESIS<sup>1</sup>

Renal cancer represents 3-4% of all cancers and remains one of the most lethal urological malignancies. The incidence of renal cell carcinoma in the Czech Republic has been traditionally one of the highest worldwide. Oncological treatment outcomes are largely dependent on early diagnosis, correct prognosis and the ability to predict the treatment response in case of systemic treatment. Despite intensive research and progress, the situation in all of the above mentioned topics is unsatisfactory: There are currently no reliable biomarkers available for routine practice for early detection, prognosis, treatment response or follow-up of renal cancer, there is still a significant proportion of advanced tumours (locally advanced or metastatic) at the time of diagnosis and the correct selection of patients for the particular type of systemic treatment or its combination with surgical treatment remains a challenge. We therefore rely on the detection of the disease by imaging examinations (very often incidentally) and we also use imaging practically uniformly when monitoring patients after surgical or systemic treatment. Selection of treatment of metastatic renal cancer is based on histological and clinical factors combined into risk nomograms with little space for individualization of treatment, which is often influenced only by the general clinical condition and comorbidities, not by the characteristics of the tumour. Non-coding RNAs whose levels can be determined in tissues and body fluids and which are able to differentiate tumour tissue from non-tumour tissue and tumour patients from or healthy individuals represent a significant shift forwards. Presented papers confirm the diagnostic and prognostic value of many subgroups of these RNAs (especially miRNAs, piRNAs and long non-coding RNAs). A detailed analysis of the tumour tissue may thus reveal biomarkers of potentially aggressive renal carcinomas, recurrent tumours or tumours poorly responsive to treatment with tyrosine kinase or immune checkpoint inhibitors. The determination of circulating non-coding RNA levels as a minimally invasive method of diagnosis fits into the attractive concept of so-called liquid biopsy of cancer. The results are encouraging. The use of urine as a completely non-invasive source of biomarkers is also attractive. Here, the data is still premature and insufficient. Last but not least, in vitro and in vivo tests reveal the therapeutic potential of

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<sup>1</sup> The commentary must correspond to standard expectations in the field and must include a brief characteristic of the investigated matter, objectives of the work, employed methodologies, obtained results and, in case of co-authored works, a passage characterising the applicant's contribution in terms of both quality and content.

many of the RNAs described, which, in combination with novel therapies for metastatic renal cancer, could lead to prolonged overall and cancer-specific survival in this group of patients.

**[1] FEDORKO, Michal,** Igor KISS a Dalibor PACÍK. Uroonkologická problematika senia. Nádory ledvin. In: MATĚJOVSKÁ KUBEŠOVÁ, Hana a Igor KISS. *Geriatrická onkologie*. 1. vyd. Praha: Mladá fronta, 2015. s. 120-124. Edice postgraduální medicíny. ISBN 978-80-204-3738-9.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	60%	80%	

**[2] FEDORKO, Michal.** Diagnostické možnosti časného zjištění nádorů ledvin, role nádorových markerů při stanovení dalšího postupu. *Urologické listy*. 2011, **9**(4), 7–11. ISSN: 1214-2085.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	100%	100%	

**[3] FEDORKO, Michal,** Dalibor PACÍK, Gabriel VARGA, Roman WASSERBAUER, Motasem GHAZAL a Mohamed Ismail Abdo NUSSIR. MikroRNA v patogenezi renálního karcinomu a jejich využití pro stanovení diagnózy a prognózy RCC. *Urologické listy*. 2015, **13**(1), 27–31. ISSN: 1214-2085.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	80%	80%	

**[4] FEDORKO, M,** D PACIK, R WASSERBAUER, J JURACEK, G VARGA, M GHAZAL a MI NUSSIR. MicroRNAs in the pathogenesis of renal cell carcinoma and their diagnostic and prognostic utility as cancer biomarkers. *INTERNATIONAL JOURNAL OF BIOLOGICAL MARKERS* [online]. 2016, **31**(1), E26–E37. ISSN 0393-6155.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	70%	90%	

**[5] FEDORKO, M,** M STANIK, R ILIEV, M REDOVA-LOJOVA, T MACHACKOVA, M SVOBODA, D PACIK, J DOLEZEL a O SLABY. Combination of MiR-378 and MiR-210 Serum Levels Enables Sensitive Detection of Renal Cell Carcinoma. *INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES* [online]. 2015, **16**(10), 23382–23389. ISSN 1422-0067.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
10%	20%	25%	10%

**[6] FEDORKO, M,** J JURACEK, M STANIK, M SVOBODA, A POPRACH, T BUCHLER, D PACIKL, J DOLEZEL a O SLABY. Detection of let-7 miRNAs in urine supernatant as potential diagnostic approach in non-metastatic clear-cell renal cell carcinoma. *BIOCHEMIA MEDICA* [online]. 2017, **27**(2), 411–417. ISSN 1330-0962.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20%	10%	40%	20%

**[7] MACHACKOVA, T,** H MLCOCHOVA, M STANIK, J DOLEZEL, **M FEDORKO,** D PACIK, A POPRACH, M SVOBODA a O SLABY. MiR-429 is linked to metastasis and poor prognosis in renal cell carcinoma by affecting epithelial-mesenchymal transition. *TUMOR BIOLOGY* [online]. 2016, **37**(11), 14653–14658. ISSN 1010-4283.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
5%	10%	10%	10%

**[8] ILIEV, R, M FEDORKO \*(corresponding author)\*,** T MACHACKOVA, H MLCOCHOVA, M SVOBODA, D PACIK, J DOLEZEL, M STANIK a O SLABY. Expression Levels of PIWI-interacting RNA, piR-823, Are Deregulated in Tumor Tissue, Blood Serum and Urine of Patients with Renal Cell Carcinoma. *ANTICANCER RESEARCH* [online]. 2016, **36**(12), 6419–6423. ISSN 0250-7005.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
10%	20%	15%	10%

**[9] ILIEV, R,** M STANIK, **M FEDORKO,** A POPRACH, P VYCHYTILOVA-FALTEJSKOVA, K SLABA, M SVOBODA, P FABIAN, D PACIK, J DOLEZEL a O SLABY. Decreased expression levels of PIWIL1, PIWIL2, and PIWIL4 are associated with worse survival in renal cell carcinoma patients. *ONCOTARGETS AND THERAPY* [online]. 2016, **9**. ISSN 1178-6930.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
10%	10%	10%	10%

**[10] FEDORKO, M.,** J. BOHOŠOVÁ, A. POPRACH a D. PACÍK. Long non-coding rnas and renal cell carcinoma. *Klinicka Onkologie* [online]. 2020, **33**(5), 340–349.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	90%	80%	