SUMMARY

Current doctoral thesis is dealing with biological behavior, morphology and cytogenetical features of rare urogenital tumors with a particular emphasis on renal tumors. Dr. Kvetoslava Michalova (birth name Peckova) was focused on this topic during her postgradual study at Charles University in Prague, Medical Faculty in Pilsen, in years 2014-2017. In her publication activity, the author focused on rare tumors of urogenital tract. The 20 publications published over a span of three years are presented in a form of a commentary. Seven of them are first-author papers and these are briefly introduced below.

The first paper entitled “Renal cell carcinoma with leiomyomatous stroma-further immunohistochemical and molecular genetic characteristics of unusual entity“ dealt with the relationship between renal cell carcinoma (RCC) with leiomyomatous stroma (LS) and clear cell RCC with reactive LS. It led to the conclusion, that only genetic analysis of *VHL* gene mutation, *VHL* hypermatylation and chromosome 3p loss of heterozygosity can be used as a distinguishing tool. The „real“ RCC with LS lack the above described genetic abnormalities which is in contrary to the clear cell RCC, which is characterized by them. The distinction between these two entities is of clinical importance, as the „real“ RCC with LS seems to be an indolent tumor as no aggressive cases have been described to date whereas clear cell RCC may have unfavourable outcome.

In the second study termed „Aggressive and nonaggressive translocation t(6;11) renal cell carcinoma: comparative study of 6 cases and review of the literature“ we compared nonaggressive tumors with one aggressive case. We based our conclusions on clinico-pathological data, morphological features, IHC, molecular genetics and literature review. Eventually, the conclusion was that aggressive tumors, in contrary to the nonaggressive cases, occur in older population, have grossly visible necroses, usually lack morphology typical for nonaggressive tumors and in addition to translocation of *TFEB* gene, they are also *TFEB* amplified.

The third study entitled „Mucinous spindle and tubular renal cell carcinoma: analysis of chromosomal aberration pattern of low-grade, high-grade, and overlapping morphologic variant with papillary renal cell carcinoma“ was aimed to map the spectrum of chromosomal aberations occuring in different morphological variants of this rare antity. This study has shown that both low-grade and high-grade variant are cytogeletically relatively unifrom (multiple chromosomal losses). However, some cases resembling papillary RCC exhibited gains of chromosomes 7 and 17 and we consequently rediagnosed them as papillary RCC. Chromosomal analysis is thus essential in atypical cases, especially in those morphologically close to the papillary RCC. If polysomy 7 and 17 is found, such cases should not be classified as mucinous spindle and tubular RCC, but as papillary RCC.

Eighteen cases of chromophobe renal cell carcinoma (CRCC) with neuroendocrine (NE) features were selected to the fourth study named “Chromophobe renal cell carcinoma with neuroendocrine and neuroendocrine-like features. Morphologic, immunohistochemical, ultrastructural, and array comparative genomic hybridization analysis of 18 cases and review of the literature”. The cases were divided into 2 groups based on their positivity/negativity with NE markers: 4 cases of CRCC with “true” NE differentiation and 14 cases of CRCC with features mimicking NE differentiation. It is evident, that the majority of CRCC with NE

features represent just architectural variant and not real NE differentiation. Both groups have different genetic background and also biological behavior, which makes their distinguishing clinically important.

The study entitled “Cystic and necrotic papillary renal cell carcinoma: prognosis, morphology, immunohistochemical, and molecular-genetic profile of 10 cases“ represents the fifth first-author paper. Because the presence of necrosis in RCC (especially in clear cell RCC) is generally considered as an adverse prognostic feature, the goal of this study was to demonstrate that type 1 papillary RCC can present as a large hemorrhagic/necrotic unicystic lesion and that such appearance in this particular setting does not affect clinical course. However, the aim of the current study is not to establish the new prognostic criteria for type 1 papillary RCC, but rather to select morphologically uniform subset of type 1 papillary RCC with unusual gross and microscpic features and draw attention to the fact that necrosis in these tumor types does probably not have any prognostic significance.

The sixth and seventh publications are dealing with tumors of the testis and since they both are related to the same subject, they are discussed together. Sixth publication termed „Primary Signet Ring Stromal Tumor of the Testis: A Study of 13 Cases Indicating Their Phenotypic and Genotypic Analogy to Pancreatic Solid Pseudopapillary Neoplasm“ and seventh entitled „Solid Pseudopapillary Tumor: A New Tumor Entity in the Testis? Reply“ address the analogy between primary signet ring stromal tumors of the testis (PSRSTT) and solid pseudopapillary tumor (SPT) of the pancreas. Briefly, the fact that certain testicular tumors have an analogue in the pancreas became evident with the acquisition of one testiculart tumor, which was histologically composed of component identical to SPT of the pancreas and of component identical to PSRSTT. As a result, both IHC testing and molecular analysis of the testicular case revealed the same features as would be expected in pancreatic SPN which allowed us to consider this tumor „pancreatic analogue solid pseudopapillary tumor of the testis“ (PA-SPT). Owing to the very pronounced signet ring cell component in the PA-SPT we came to the idea that there might also be a connection between PSRSTT and SPT of the pancreas. In the 6th publication we compared 13 cases of PSRSTT with one case PA-SPT and 19 cases of pancreatic SPT. Both the immunoprofile anf molecular genetics were identical in all analyzable cases which led us to the conclusion that PA-SPT and PSRSTT represent the morphological spectrum of the same entity and that both of them are related to the pancreatic SPT. This concept was further strengthened by the group of italian authors who in the form of letter to editor reacted to the first description of PA-SPT. They reported another 2 cases of testicular tumors in all aspects identical to our cases and supported thus our hypothesis that PA-SPT and PSRSTT represent dictinct entity analogic to the pancreatic SPT. Seventh publication represents our reply to this letter to the editor.