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Circulating tumor cells in renal cancer

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Klézl P. [1], Sonsky J. [1], Grill R. [1], Pospisilova E. [2], Kolostova K. [2], Bobek V. [2]

[1]University Hospital Kralovske Vinohrady, Dept. of Urology, Prague, Czech Republic, [2]University Hospital Kralovske Vinohrady, Dept. of Laboratory Diagnostics, Lab. Genetics, Prague, Czech Republic

Introduction & Objectives: Circulating tumor cells (CTCs) are being an undeniable part of a connection between primary tumors and secondary metastatic sites. The CTC-examination belongs to the group of liquid biopsy tests, which are provided in patients to get more detailed information on heterogeneity of tumor disease under minimally invasive procedures (e.g. blood withdrawal). The main target of the presented study was to monitor CTC- presence in patients with renal cancer undergoing surgery. As next, molecular character of CTCs was evaluated by gene expression analysis.

Materials & Methods: Patients (n=118) undergoing surgical renal resection because of tumor mass presence were included into the study. The main target of the study was to characterize level of tumor dissemination by testing CTC presence in peripheral blood. Peripheral blood (2x8ml, EDTA) was withdrawn in time points to follow up the dynamics of CTC-changes (before surgery, 4thday after surgery, 6 weeks after surgery, 6-12 months after surgery) to follow up the dynamics of CTC- changes. In total 374 blood samples were evaluated. To enrich CTCs a size-based separation protocol and tube MetaCell® was used. CTC presence is evaluated in two steps: first by single cell cytomorphology, second by molecular testing (qPCR analysis). Gene expression of following genes was tested: ACTB, EPCAM, MUC1, KRT6, KRT7KRT18, KRT19, VIM, CD24, CD44, CD68, CD45, PD-L1(CD274), VEFG, VEGFR (FLT1), HER2.

Results: CTCs were detected independently on the sampling point in up to 90% of the tested samples in patients undergoing renal resection. Gene expression analysis revealed elevated gene expression in CTCs for genes KRT18 (keratin 18), VIM (vimentin) if compared to the control white blood cell fraction. These genes could be then used in future analysis for CTC identification. As next, it was shown that the character of CTCs undergoes changes during follow-up period. From the therapeutic point of view the most interesting changes were seen in patients with CTCs expressing elevated VEGF (vascular endothelial growth factor) and/or PD-L1 (Programmed Death ligand 1, CD274). Both genes could be used for therapy indication: VEGF for anti-angiogenic therapy and PD-L1 for immunotherapy. Interestingly, elevated PD-L1 expression is associated with elevated expression of CD44 and FLT1 (VEFGR).

Conclusions: The obtained data show a significant potential of CTC-character testing for immunotherapy indication.