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## Overexpression of HIV-1 reverse transcriptase increases tumorigenic and metastatic activity of Malignant cells

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HIV-1 infection is often accompanied by oncological complications attributed to immune suppression, and angiogenic and/or directly oncogenic properties of HIV Tat, Nef and p17. Here, we studied oncogenicity of HIV-1 reverse transcriptase (RT). Panel of murine adenocarcinoma 4T1luc2 (Perkin Elmer, USA) subclones stably expressing consensus HIV-1 FSU_A RT or its variants with primary mutations of resistance to nucleoside (RT_An) or non-nucleoside inhibitors (RT_Ann) common in the territory of former USSR[1], was generated by lentiviral transduction of 4T1luc2 cells. Parental 4T1luc2; 4T1luc2RT (multiplicity of infection/MOI 1, 5, 20); 4T1luc2RT_An, and 4T1luc2RT_Ann subclones (MOI10) were subcutaneously implanted into BALB/c mice. Tumor growth was monitored by morphologic measurements and bioluminescence imaging (BLI; Perkin Elmer). After three weeks, mice were sacrificed, tumors and organs were excised, subjected to ex vivo BLI, then dehydrated, paraffin-embedded and sectioned. Number of metastatic cells was assessed by BLI and in parallel, quantified on haematoxylin-eosin-stained slides by computer-assisted morphometry (NIS-Elements software, Nikon, Japan). Splenocytes were isolated, stimulated with RT-derived peptides, and IFN-γ/IL-2 secretion was assessed by Fluorospot (Mabtech, Sweden). Within 10 days, all subclones formed palpable tumors. 4T1luc2RT-tumors grew faster than those formed by 4T1luc2, or 4T1luc2RT_An, or 4T1luc2RT_Ann cells ($p<0,05$). 4T1luc2RT tumor-bearing mice had more metastasis in lungs and liver than mice implanted with 4T1luc2 cells. Drug-resistance mutations decreased metastatic activity of 4T1luc2RT_An and 4T1luc2RT_Ann subclones below that of parental 4T1luc2 cells ($p<0,05$). Expression of RTs induced no immune response. Thus, expression of nonmutated RT increases tumorigenic and metastatic activity of malignant cells. Supported by RFBR#17_54_30002, and 17_04_00583.

### Speaker Biography

Elizaveta Starodubova has completed her PhD in the Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, and continued her postdoctoral studies there and at the Department of Microbiology, Tumor and Cell Biology (MTC), Karolinska Institutet, Stockholm. She performs her studies in the field of antigen processing and design of prototype DNA-vaccines against viral infections and cancer.

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