RSU conference "Knowlege for use in practice" April 1-3, 2019
http://conference2019.rsu.lv/

Expression of HIV reverse transcriptase in implanted murine adenocarcinoma cells increases burden of liver metastasis in BALB/c mice: a pilot study

Dzeina Mezale (1), Ekaterina Bayurova (2, 3) Ilze Strumfa (1), Andrejs Vanags (4), Ilze Fridrihsone (1), Stefan Petkov (5), Ilya Gordeychuk (2, 3, 5, 7) Juris Jansons (6), Maria Isaguliants (1, 2, 3)

(1) Department of Pathology, Riga Stradins University, Riga, Latvia; (2) Chumakov Federal Scientific Center for Research and Development of Immune-and-Biological Products of the Russian Academy of Sciences, Moscow, Russia; (3) Gamaleya Research Center of Epidemiology and Microbiology, Moscow, Russia (4) Department of Surgery, Riga Stradins University, Riga, Latvia; (5) Microbiology and Tumor Biology Center, Karolinska Institutet, Stockholm, Sweden; (6) Biomedical Research and Study Center, Riga, Latvia; (7) Sechenov First Moscow State Medical University, Moscow, Russia;

Objectives

Patients with HIV have an increased incidence of oncological diseases. Tumorigenicity of HIV proteins per se has been suggested, however factual data confirming the concept are sparse. The aim of the study was to characterize the capacity of tumors formed by murine adenocarcinoma cells expressing HIV-1 reverse transcriptase (RT) to metastasize in liver.

Methods

Cell lines 4T1_luc2-RT1.3, 4T1_luc2-RT5.3 and 4T1_luc2-RT20.1 were generated from cell line 4T1-luc2 (Perkin Elmer) by transduction with lentivirus encoding HIV-1 RT at multiplicity of infection 1, 5 and 20, respectively. Mice were injected subcutaneously with 4T1_luc2-RT1.3 (n=9), 4T1_luc2-RT5.3 (n=8), 4T1_luc2-RT20.1 (n=7) and parental 4T1luc2 cells (n=8). By days 7-9 all formed solid tumors. Metastases were detected and evaluated in liver samples collected on day 21 after their formalin-fixation and paraplast-embedding. Area of metastases per sample was quantified in 25 microscope fields (400x) of hematoxylin-eosin-stained slides by computer-assisted morphometry using specialized NIS-Elements software (Nikon, Tokyo).

Results

Liver micrometastases were found in all study groups (nn per mouse±SD/mean size±SD): 56 in 4T1_luc2_RT1.3-implanted group (6.22 ± 1.72/632.69 ± 247.99 μm2); 103 in 4T1_luc2_RT5.3 (12.88 ± 1.64/546.61 ± 260.95 μm2); 114 in 4T1_luc2_RT20.1 group (16.29 ± 1.38/366.54 ± 162.57 μm2); and 27 in 4T1-luc2 control group(3.37 ± 3.2/699.35 ± 280.52 μm2). RT-expressing cell lines had higher frequency of metastasis formation compared to parental cells, although the metastases were smaller (both $p < 0.05$). The number of metastases per animal increased with increasing level of RT expression by the cell line, while the size of metastases decreased (both $p < 0,05$).

Conclusions

The most aggressive tumor variant was formed by 4T1_luc2_RT.20.1 cell line expressing high levels of HIV-1 RT, although these tumors tended to form smaller metastases compared to the

parental cell line. This new data is an evidence of a direct tumorigenic potential of HIV-1 antigens. Foundation: RFBR №17_54_30002/17_04_0583, VACTRAIN#692293.