

The induction of mice lung tumors by HeLa cells and regression by human papillomavirus type HPV16 E2 protein

N.I. Rekoslavskaya*, A.V. Tretyakova, J.V. Nurminskaya, A.A. Chemezova

Siberian Institute of Plant Physiology and Biochemistry of SB RAS, Irkutsk, Russia

* *rekoslavskaya@sifibr.irk.ru*

Motivation and aim: In 2022, there were 20 million new cases of cancer and 9.7 million deaths from cancer worldwide. It is predicted that by 2050 this number will increase by 77% to 35 million. One of the reasons for the increase in carcinogenesis is the enhanced spread of viral carcinogens, such as human papillomaviruses (HPVs) with a high carcinogenic risk. In a plant expression system based on RdRP CMM, the HPV16 E2 tumor suppressor was synthesized, which induced the synthesis of T lymphocytes capable of causing regression of lung tumors in mice.

Materials and methods: The method for synthesizing HPV16 E2 in a plant viral expression system based on tomato fruits transgenic for the gene *hvp* 16 E2 has been used. To induce lung tumors in mice, HeLa cancer cells were used, which caused tumor formation the day after inoculation. The induction of synthesis of cellular immune components was studied using the Elispot procedure in T lymphocytes of the blood, lungs and in splenocytes.

Results: For the first time, a case of tumor formation in the lungs of mice was discovered when inoculated with human HeLa cancer cells *in vivo* and *ex vivo*. Studying the induction of the oncobiomarkers generation in T lymphocytes in a mice lung model in the presence of HeLa cells has promise the earlier recognition of the initiation of cancer development, timely diagnosis and therapy. It was known that “early protein” of human papillomavirus type 16 E2 exhibited tumor supersuppressor properties. The purpose of the work was to study the correlation between the generation of known oncobiomarkers: protein of cell proliferation and tumor proliferation Ki-67, oncomarker of lung tumor pyruvate kinase isoform M1, checkpoint receptor oncobiomarkers PD-1 and PD-L1 in T lymphocytes from blood, lungs and spleen affected with HeLa cells and blocking effect of 16 E2 on tumors arising after inoculation with HeLa. “Early” protein HPV 16 E2 was synthesized in plant viral expression system based on transgenic tomato fruit with the *hvp*16 E2 gene. Analyses were done mainly via Elispot technique. Oncosupersuppressor HPV16 E2 has blocked the generation of T lymphocytes that expressed of oncomarkers Ki-67, PKM1, PD-1 and PD-L1 in peripheral mononuclear blood cells and in isolated lungs but not in splenocytes inoculated with HeLa cells. Therefore, for early diagnosis and of the recognition of tumor initiation, T lymphocytes of the blood and lungs should be used. It is assumed that HPV16 E2 has a high affinity and rapidly interacts with the fraction of isolated HeLa nuclei. It is assumed that HPV16 E2 performs reparative activity and thereby causes blocking of carcinogenesis

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