Секция «Вирусология»

Investigation of Echovirus 1 (Farouk) binding receptor using CRISPR-Cas knockout gene libraries

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Oncolytic viruses represent a new class of anticancer drugs [1]. These are naturally occurring non-pathogenic viruses and their derivatives modified by genetic engineering or bioselection to increase safety and enhance oncolytic properties [2]. The action of oncolytic viruses is based on their ability to selectively destroy tumor cells without affecting normal tissues and organs. These cells have selective sensitivity to viruses due to disruption of tissue architecture inside the tumor, increased permeability of tumor vessels, and frequent disturbances in interferon induction systems [3].

Multiple viruses of different families have demonstrated oncolytic properties and are considered as platforms for the development of oncoselective strains. Enteroviruses, a large family of small viruses containing single-stranded positive-sense RNA genome, are also promising candidates [5]. However, the effectiveness of their effects on different tumors is not completely predictable, which complicates their practical use. In this regard, molecular determinants of cancer cell sensitivity to enteroviruses need to be investigated [6-9].

In order to identify new markers of sensitivity for enterovirus infection, a knockout HEK293T cells were obtained using transduction by the pooled GeCKO 2 lentivirus libraries (Genome-Scale CRISPR Knock-Out) and infected with Echo1 Farouk strain, an oncolytic virus [11], at moi=1.The survived cell clones grew as colonies and were subcultured, followed by determination of the knocked out genes. In two sublines, a disruption of the *FCGRT* gene encoding neonatal Fc receptor (FcRn) was found. The FcRn was recently identified as an entry receptor for some human echoviruses [10].

The obtained cells were tested for sensitivity to various enterovirus strains: Echo1 (Farouk), Echo7, Echo11, Echo12 (Travis), Echo30, vaccine polioviruses types 1, 2, 3 (Sabin), non-pathogenic Coxsackie virus A7 and B5. We found that the *FCGRT* knockout resulted in a reduced sensitivity to Coxsackie A7 and Echo11, or the complete loss of sensitivity to Echo1, Echo7, and Echo12.

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