

Šifra projekta / Project code Z3-4501

Sprožitev imunogene celične smrti z DNA senzorskim sistemom, ki prepozna genomski podpis, značilen za rakave celice

Induction of immunogenic cell death by a DNA sensor system that recognizes a genomic signature specific to cancer cells

Vodja projekta / Project manager: dr. Taja Železnik Ramuta

1. VSEBINSKI OPIS PROJEKTA / CONTENT DESCRIPTION OF THE PROJECT:

Imunogena celična smrt lahko sproži prirojeni in pridobljeni imunski odziv, kar se že izkorišča pri razvoju strategij za izboljšanje terapij raka, saj tovrstni odzivi okrepijo terapevtski učinek konvencionalnih terapij, kot sta kemoterapija in radioterapija. Kljub potencialu, ki ga tovrsten pristop kaže, študije opozarjajo tudi na tveganje, ki ga prinaša aktivacija imunogene celične smrti v normalnih tkivih, kar lahko vodi k hudim poškodbam. Cilj našega projekta je razviti DNA senzorski sistem, ki bo na podlagi prepoznavanja genomskega podpisa, značilnega za rakave celice, sprožil imunogeno celično smrt.

Pristop, ki bi omogočal sprožitev imunogene celične smrti le v celicah, ki vsebujejo tarčno DNA, bi pomembno izboljšal specifičnost in s tem varnost terapije. Tumorsko mikrookolje pomembno vpliva na lastnosti rakavih celic in njihovo dovzetnost za zdravljenje, zato bomo testirali specifičnost in učinkovitost DNA senzorskega sistema v 2D in 3D večceličnih *in vitro* modelih.

Immunogenic cell death can initiate the innate and adaptive immune response, which has been exploited for improving the efficiency of cancer treatments, since immune responses reinforce the therapeutic effects of conventional anticancer therapies, such as chemotherapy and radiotherapy. These approaches show promising potential, but at the same time studies warn that activation of immunogenic cell death in normal tissues may induce severe damage. The aim of our project is to develop a DNA sensor system, which will be based on the recognition of cancer-specific genomic signature to induce immunogenic cell death. An approach that would enable the induction of immunogenic cell death only in cells carrying target DNA, would significantly improve specificity and consequently the safety of the treatment. The tumor microenvironment importantly affects the properties of cancer cells and their susceptibility to treatment, hence we will test the specificity and efficiency of the DNA sensor system in 2D and 3D multicellular *in vitro* models.

a. osnovni podatki glede financiranja / basic information on funding:

Projekt financira ARRS v okviru cenovne kategorije B v obsegu 1700 letnimi urami za obdobje 2 let. Pričetek financiranja je 1. 10. 2022.

The project is co-financed by ARRS with 1700 annual hours of price class B for a period of 2 years. Funding starts on October 1, 2022.

b. sestava projektne skupine s povezavami na SICRIS / composition of the project team with links to SICRIS

Nosilka podoktorskega projekta / Holder of the postdoctoral project:

Taja Železnik Ramuta; SICRIS št. 39124

<https://cris.cobiss.net/ecris/si/sl/researcher/45144>

2. faze projekta in njihova realizacija / project phases and their realization

Projekt bo potekal v sledečih fazah:

- Načrtovanje in razvoj DNA senzorskega sistema, ki temelji na proteazi ter cilja tarčno sekvenco,
- Načrtovanje in razvoj efektorja imunogene celične smrti,
- Vzpostavitev signalne kaskade za ojačanje signala za sprožitev celične smrti,
- Ocenjevanje specifičnosti in učinkovitosti DNA senzorskega sistema na monoceličnih ter večceličnih sesalskih in vitro modelih.

The project will be carried out in the following phases:

- Design and development of a protease-based DNA sensor system that targets a selected genomic signature,
- Design and development of an immunogenic cell death effector,
- Establishment of a signal amplification cascade for improved induction of cell death,
- Evaluation of the specificity and efficiency of a DNA sensor system on monocellular and multicellular mammalian in vitro models.

3. bibliografske reference, ki izhajajo neposredno iz izvajanja projekta / bibliographic references arising directly from the implementation of the project

4. Vir financiranja / funding agency



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