

J3-1746 Vloga celične smrti v različnih aktivacijskih poteh inflammasoma NLRP3 in njena uporaba za inovativno imunoterapijo raka

The functional role of cell death in different NLRP3 inflammasome activation pathways and its application for innovative cancer immunotherapy

Vodja projekta:

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1. VSEBINSKI OPIS PROJEKTA:

Citokin interleukin-1 β (IL-1 β) je eden najpomembnejših citokinov pri aktivaciji in uravnavanju naravne in pridobljene imunosti. Že več kot 25 let vemo, da iz celice ne prehaja po klasični poti. V zadnjih nekaj letih so raziskave nakazale, da se iz celice sprošča pasivno, ob celični smrti, imenovani piroptoza, pri kateri zaradi cepitve gasdermina D (GSDMD) pride do nastanka por v celični membrani. Zadnje raziskave pa nakazujejo, da se IL-1 β lahko sprosti tudi iz živih celic. V okviru projekta bomo raziskali aktivacije inflammasoma NLRP3, pri katerih pride do sproščanja IL-1 β , razlikujejo pa se v potrebi po celični smrti. Z načrtovanjem natančno regulirane tvorbe por gasdermina D bomo vzpostavili sistem za sproščanje citokinov. V zadnjem delu projekta bomo preverili uporabnost načrtovane piroptoze v celicah. Načrtovani sintetični sistem bomo testirali v pogojih *in vivo* za namene imunoterapije raka.

The cytokine IL-1 β is one of the most important cytokines in the initiation and harmonization of innate and adaptive immunity. For more than 25 years it is known that IL-1 β cannot be secreted via conventional secretion system. In the past several years, IL-1 β was believed to be released from cells passively upon cell death, called pyroptosis, which is triggered by formation of gasdermin D (GSDMD) pores in the plasma membrane. Recent reports suggest that IL-1 β can also be released from living cells. We plan to investigate this important issue by comparing the mechanisms of inflammasome activation, where IL-1 β is released, but these pathways diverge in their requirement for cell death. Further, by designing tightly regulated cleavage of gasdermin D and pore formation we plan to establish controlled cytokine release. Finally, we propose to use designed pyroptosis *in vivo* for cancer immunotherapy.

a. osnovni podatki glede financiranja:

Projekt financira ARRS v okviru cenovne kategorije C za obdobje treh let v obsegu 2.469 letnimi urami. Pričetek financiranja je 1. 7. 2019.

b. sestava projektne skupine s povezavami na SICRIS

Na Kemijskem inštitutu v projektne skupini sodelujejo:

14360	Dr. Benčina Mojca	http://www.sicris.si/search/rsr.aspx?lang=slv&id=8380
23563	Dr. Hafner Bratkovič Iva	http://www.sicris.si/search/rsr.aspx?lang=slv&id=16734
6628	Dr. Jerala Roman	http://www.sicris.si/search/rsr.aspx?lang=slv&id=5855
21426	Dr. Manček Keber Mateja	http://www.sicris.si/search/rsr.aspx?lang=slv&id=13349
38275	Perčič Anja	http://www.sicris.si/search/rsr.aspx?lang=slv&id=44168
50616	Praznik Arne	http://www.sicris.si/search/rsr.aspx?lang=slv&id=46785

2. faze projekta in njihova realizacija

Raziskovanje mehanizmov aktivacije inflammasoma. In vitro sistemi za sproščanje citokinov, aplikacija znanja in vivo.

3. bibliografske reference, ki izhajajo neposredno iz izvajanja projekta

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