

J1-1711 Receptorji na osnovi načrtovanih proteinskih origamijev: funkcionalizirane načrtovane proteinske nanostrukture za prepoznavanje izbranih tarč

Designed protein origami based receptors: functionalized designed protein nanostructures for the recognition of the selected targets

Vodja projekta:

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1. VSEBINSKI OPIS PROJEKTA:

Pred kratkim smo razvili inovativno strategijo za načrtovanje novih tipov enoverižnih proteinskih zvitij, ki temeljijo na v definiranem zaporedju povezanih dimernih modulih, ki tvorijo ovite vijačnice. Ti moduli se samosestavijo v načrtovano poliedrske nanostrukture, katere robovi predstavljajo rigidne dimerne ovite vijačnice. *De novo* načrtovane poliedrske nanostrukture predstavljajo proteinski origami, ki temelji na dimernih obvitih vijačnicah (ang. coiled-coil protein origami (CCPO)). Za CCPO so značilni robustnost pri načrtovanju ter raznolike lastnosti, zato so CCPO primerne za številne biomedicinske aplikacije v diagnostiki, preventivi in pri terapijah. Ena izmed obetavnih možnosti je funkcionalizacija sintetičnih polipeptidov z načrtovano arhitekturo z biospecifičnimi molekulami s tarčnim prepoznavanjem.

Osnovna inovativna ideja predloga projekta je načrtovanje in produkcija CCPO nanostruktur, ki so trikotne oblike, ter njihova funkcionalizacija z različnimi lektini, ki bodo delovali kot senzor za prepoznavanje glikanov. Lektini so namreč proteini, ki biospecifično prepoznavajo molekule različnih glikanov. En primer je prepoznavanje glikozilacijskega vzorca PSA (ang. prostate-specific antigen), ki je biomarker pri raku na prostati (PCa, ang. prostate cancer). Čeprav imajo analize glikanov z lektini določene omejitve (nizka specifičnost, nizka afiniteta), je velika prednost uporabe lektinov dejstvo, da se lektini lahko uporabijo za interakcijo z glikani, ki so še vedno vezani na proteine ali na celice. Kakorkoli, interakcije glikan-protein igrajo ključno vlogo pri virusnih okužbah, adheziji celic, in pri diferenciaciji ter napredovanju različnih bolezni, in so zato zelo zanimive za številne diagnostične in terapevtske aplikacije.

Recently a pioneering strategy for the design of new types of a single-chain protein folds was devised in our group based on the sequential arrangement of concatenated coiled-coil dimer forming modules that self-assemble into a polyhedral cage with edges composed of rigid coiled-coil (CC) dimers. *De novo* designed polyhedral nanostructures represent a new type of modular folds that we named coiled-coil protein origami (CCPO). Due to their robustness and versatile designable shapes and properties, designed CCPO possess a great potential for numerous biomedical applications for diagnostics, prevention and therapy. One of the outstanding opportunities is to exploit the CCPOs with designed architecture as the scaffolds for functionalization with biospecific recognition molecules that recognize the selected targets.

The innovative idea of this project proposal is to design and produce trigonal-shaped CCPOs, functionalized by different lectins that can act as glycans recognition sensor. Lectins are proteins that can act as biospecific recognition molecules for different glycans. One such example is recognition of the glycosylation pattern of a prostate-specific antigen (PSA), a biomarker of a prostate cancer (PCa). Although the analysis of glycans by lectins has some limitations (low specificity, low affinity), the

main advantage of using lectins is the fact that lectins can be applied for interaction with glycans still attached to proteins or even intact cells. However, glycan-protein interactions play a pivotal role in viral and bacterial infections, cell adhesion, and the differentiation and progression of various diseases and are thus of great interest for many diagnostic and therapeutic applications.

a. osnovni podatki glede financiranja:

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b. sestava projektne skupine s povezavami na SICRIS

Na Kemijskem inštitutu v projektne skupini sodelujejo:

17915	dr. Gradišar Helena	http://www.sicris.si/search/rsr.aspx?lang=slv&id=10174
6628	dr. Jerala Roman	http://www.sicris.si/search/rsr.aspx?lang=slv&id=5855
38163	Aupič Jana	http://www.sicris.si/search/rsr.aspx?lang=slv&id=44051
37987	dr. Lapenta Fabio	http://www.sicris.si/search/rsr.aspx?lang=slv&id=43857
17917	dr. Majerle Andreja	http://www.sicris.si/search/rsr.aspx?opt=1&lang=slv&id=10176
38275	Perčič Anja	http://www.sicris.si/search/rsr.aspx?lang=slv&id=44168
38337	Strmšek Žiga	http://www.sicris.si/search/rsr.aspx?lang=slv&id=44236

2. faze projekta in njihova realizacija

Projekt se izvaja v treh fazah:

1. Načrtovanje in produkcija trikotnih polipeptidnih nanostruktur, ki so sestavljene iz modulov, ki tvorijo ovite vijačnice (CC) in imajo različno geometrijo
- 2: Primerjalna analiza različnih strategij za funkcionalizacijo polipeptidnih nanostruktur
- 3: Pot do uporabe funkcionaliziranih nanostruktur za diagnostiko in prognozo pri raku na prostati (ang. Prostate cancer, PCa)

The project is implemented in three phases:

- 1: Design and production of triangular polypeptide nanostructures composed of coiled-coil (CC) modules with different geometry
- 2: Benchmarking of different strategies for the functionalization of polypeptide nanostructure
- 3: Towards application of functionalized nanostructures for prostate cancer (PCa) diagnostics and prognosis

3. bibliografske reference, ki izhajajo neposredno iz izvajanja projekta,

AUPIČ, Jana, LAPENTA, Fabio, STRMŠEK, Žiga, MERLJAK, Estera, PLAPER, Tjaša, JERALA, Roman. Metal ion-regulated assembly of designed modular protein cages. *Science advances*. 17 Jun. 2022, vol. 8, iss. 24, str. 1-12. ISSN 2375-2548. DOI: [10.1126/sciadv.abm8243](https://doi.org/10.1126/sciadv.abm8243). [COBISS.SI-ID [114422019](https://www.cobiss.si/record/114422019)]

MERLJAK, Estera, GOLOB URBANC, Anja, PLAPER, Tjaša, JERALA, Roman. Coiled coils as versatile modules for mammalian cell regulation. *Synthetic biology and engineering*. 2023, vol. 1, article no. 10006, str. 1-10, ISSN 2958-9053. <https://dirros.openscience.si/lzpisGradiva.php?id=16583>, DOI: [10.35534/sbe.2023.10006](https://doi.org/10.35534/sbe.2023.10006). [COBISS.SI-ID [151685635](https://www.cobiss.si/record/151685635)]

4. logotip ARRS in drugih sofinancerjev



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