

# Naziv Projekta

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## Oznaka in naziv projekta

J4-70159 TheraPIK3 - Ciljno dvojno zdravljenje raka dojke z mutacijo PIK3CA z uporabo siRNK in biomimetičnih dostavnih sistemov

J4-70159 TheraPIK3 – Targeted Dual Therapy for PIK3CA-Mutated Breast Cancer Using siRNA and Biomimetic Delivery Systems

## Logotipi ARIS in drugih sofinancerjev



## Projektna skupina

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Sodelujoče raziskovalne organizacije: [Povezava na SICRIS](#)

Sestava projektne skupine: [Povezava na SICRIS](#)

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## Vsebinski opis projekta

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Rak dojke ostaja pomemben svetovni zdravstveni izziv, pri čemer se primeri z mutacijo PIK3CA ne odzivajo na standardne terapije in predstavljajo resne omejitve zdravljenja zaradi toksičnosti in razvoja odpornosti na zdravila. Cilj projekta TheraPIK3 je obravnavati te izzive z razvojem inovativne dvojne terapije za raka dojke z mutacijo PIK3CA, ki združuje strategije za utišanje genov s ciljnimi sistemi dostave za večjo specifičnost in učinkovitost. Predlagamo uporabo male interferenčne RNK (siRNK) za utišanje gena PIK3CA, ki je kritični regulator celične signalne poti PI3K, ki vpliva na mehanizme, ki vodijo v napredovanje raka in odpornost na terapijo. siRNK ponuja neprimerljivo specifičnost z neposrednim ciljanjem na informacijsko RNK (mRNK), zmanjševa neželene stranske učinke, s čimer preseže omejitve trenutnih terapij, t.j. zaviralcev PI3K na osnovi malih molekul. Vendar pa je zaradi nestabilnosti siRNK in slabega celičnega vnosa potreben razvoj naprednih dostavnih sistemov. Za premagovanje teh ovir TheraPIK3 predlaga biomimetično dostavno platformo z uporabo veziklov iz eritrocitnih membran (EMV). Ti vezikli posnemajo naravne celične membrane, kar zagotavlja vrhunsko biokompatibilnost, podaljšano cirkulacijo in zmanjšano imunogenost. EMV so zasnovani tako, da enkapsulirajo siRNK, hkrati pa ohranjajo njeno stabilnost in zmanjšajo izven tarčno dostavo. Platforma predstavlja novo strategijo v siRNK terapiji, s potencialom za revolucijo ciljnega zdravljenja raka. Specifičnost te terapije bo dodatno izboljšana z vključitvijo analogov neuropeptida Y (NPY), zasnovanih tako, da ciljajo na receptor NPY 1 (NPYR1), ki je prekomerno izražen v endokrino odpornih celicah raka dojke. Z uporabo računalniških simulacij bomo razvili nove NPY analoge z visoko afiniteto vezave in antagonističnimi učinki proti NPYR1. Ti analogi ne le izboljšajo aktivno ciljanje, ampak tudi dopolnjujejo terapijo siRNA z zaviranjem poti PI3K prek modulacije receptorja. Ta dvojna terapevtska strategija občutno zmanjša možnosti razvoja odpornosti na zdravljenje s hkratnim utišanjem izražanja PIK3CA in prekinitvijo celične signalne poti, ki je ključna za celično preživetje. Učinkovitost TheraPIK3 pristopa bo potrjena tako v 2D kot 3D celičnih modelih, vključno s 3D sferoidi, ki bolje posnemajo tumorsko mikrokoolje. Učinke te dvojne terapije na proliferacijo, migracijo, invazijo in sposobnost preživetja bomo primerjali med NPYR1-pozitivnimi in -negativnimi celicami raka dojke ter normalnimi celicami dojke. Z integracijo siRNK terapije z biomimetičnimi nanonosilci in ciljnimi peptidnimi analogi, TheraPIK3 zagotavlja celovito, inovativno rešitev za reševanje neizpoljenih potreb pri zdravljenju raka dojke. Ta projekt lahko bistveno izboljša zdravljenje raka, zmanjša toksičnost, premaga odpornost in izboljša rezultate bolnikov pri raku dojke z mutacijo PIK3CA.

Osnovni podatki sofinanciranja so dostopni na spletni strani [SICRIS](#).

## Faze projekta in opis njihove realizacije

1. Uporaba male interferenčne RNK (siRNK) za utišanje gena PIK3CA
2. Biomimetična dostava zdravil: eritrocitni membranski vezikli (EMV)
3. Aktivno ciljanje rakastih celic z novo tarčno molekulo

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