

Kratek opis usposabljanja mladega raziskovalca (*Short description of the Young Researcher's training*)

1. Raziskovalna organizacija (*Research organisation*):

Univerza v Ljubljani, Medicinska fakulteta (University of Ljubljana, Faculty of Medicine)

2. Ime, priimek in elektronski naslov mentorja (*Mentor's name, surname and email*):

Vita Dolžan, vita.dolzan@mf.uni-lj.si

3. Šifra in naziv raziskovalnega področja (*Research field*):

1.05.00 Naravoslovje Biokemija in molekularna biologija
1.05.00 Nature sciences Biochemistry and molecular biology

4. Kratek opis usposabljanja mladega raziskovalca (*Short description of the Young Researcher's training*):

Navedite tudi morebitne druge zahteve, vezane na usposabljanje mladega raziskovalca (npr. znanje tujih jezikov, izkušnje z laboratorijskim delom, potrebne licence za usposabljanje...).

slo:

Mladi raziskovalec se bo posvetil preučevanju molekularnih mehanizmov, ki vplivajo na dovzetnost za okužbo s SARS-CoV-2, na težavnost in zaplete bolezni, ter na odgovor na določeno simptomatsko zdravljenje.

Interindividualne razlike v dovzetnosti in poteku okužbe s SARS-CoV-2 so lahko deloma posledica genske variabilnosti genov, vključenih v mehanizem vstopa SARS-CoV-2, zlasti genov *ACE2* in *TMPRSS2*. Polimorfizmi *ACE2* so že bili povezani s hipertenzijo in srčnimi boleznimi, te komorbidnosti pa tudi povečujejo tveganje za hujše oblike COVID-19. Okužba lahko povzroči tudi prekomerno nastajanje vnetnih citokinov zgodnjega odziva, kar vodi v neurejen in pretiran akutni sistemski imunski odziv in resnejši potek COVID-19. Ker genska variabilnost genov imunskega odziva in njihovih regulatornih mrež vpliva na vnetni fenotip, lahko vpliva na resnost in izid bolezni in tudi na odziv na imunomodulatorno zdravljenje.

Kandidat bo preverjal hipotezo, da genetski in epigenetski dejavniki omogočajo zgodnjo napoved povečanega tveganja za hujši potek bolezni COVID-19 in pojav zapletov, pa tudi zgodnjo napoved odgovora na določeno zdravljenje.

Kandidat bo izoliral in analiziral nukleinske kisline (DNA, RNA) iz krvnih vzorcev bolnikov s COVID-19. Z molekularno genetskimi metodami bo preverjal prisotnost pogostih funkcionalnih genetskih sprememb v ključnih genih, povezanih z okužbo s SARS-CoV-2 in z imunskim odgovorom, pa tudi genetske spremembe v njihovih regulatornih omrežjih, predvsem transkripcijskih faktorjih in nekodirajoči RNA. Na podlagi genetskih, epigenetskih in kliničnih podatkov bo z metodami strojnega učenja pripravil napovedne modele poteka in poznih posledic bolezni in odgovora na zdravljenje.

Raziskovalno delo bo potekalo v sodelovanju med Laboratorijem za farmakogenetiko Inštituta za biokemijo in molekularno genetiko, UL MF in Kliniko za infektivne bolezni in vročinska stanja UKC Ljubljana. Pri raziskavah bo mladi raziskovalec uporabljal širok razpon molekularno genetskih pristopov, metode za izolacijo in analizo DNA in RNA, kot tudi različna bioinformacijska in biostatistična orodja. V času opravljanja doktorskega dela se bo mladi

raziskovalec udeležil tudi več strokovnih izpopolnjevanj doma in v tujini, zato je potrebno aktivno znanje angleškega jezika.

eng:

The young researcher will focus on the studies of molecular mechanisms that influence the development and the course of SARS-CoV-2 infection, the severity and complications of the disease, and the response to specific symptomatic treatment.

Interindividual differences in susceptibility and outcomes of SARS-CoV-2 infection may be partly due to genetic variability of genes involved in SARS-CoV-2 entry mechanism, especially ACE2 and TMPRSS2. ACE2 polymorphisms were associated with hypertension and heart disease and these comorbidities increase the risk for more severe COVID-19. The infection may induce overproduction of early response proinflammatory cytokines that leads to dysregulated and excessive acute systemic immune response and more severe course of COVID-19. As genetic variability of immune response genes and their regulatory networks affects the proinflammatory phenotype, it could influence disease severity, outcome and immunomodulatory treatment response.

The following hypothesis will be tested: genetic and epigenetic biomarkers enable early prediction of increased risk for severe course of COVID-19 and development of complications as well as early prediction of response to a particular symptomatic treatment.

The candidate will extract and analyze nucleic acids (DNA, RNA) from blood samples of patients with COVID-19 and use molecular genetic methods to investigate common functional genetic alterations in key host genes associated with SARS-CoV-2 infection and the immune response, as well as genetic changes in their regulatory networks, primarily transcription factors and noncoding RNA. Based on genetic, epigenetic and clinical data, machine learning algorithms will be used to prepare predictive models of the course and late complications of the disease and the response to treatment.

Research work will be performed in collaboration between the Pharmacogenetics Laboratory at the Institute of Biochemistry and Molecular Genetics, UL MF and Clinic for infectious diseases, University Clinical Centre Ljubljana. The young researcher will use a wide range of molecular genetics research techniques, methods for DNA and RNA isolation and analysis, as well as bioinformatic and biostatistic tools. In the course of the PhD study the young researcher will participate at international research and professional meetings, training courses and collaborative studies, therefore fluent knowledge of the English language is required.