

Opis delovnega mesta mladega raziskovalca/ke (*Description of the Young Researcher's position*)

1. Članica UL (*UL member*):

Univerza v Ljubljani, Medicinska fakulteta

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

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3. Raziskovalno področje (*Research field*):

ARRS: 3.03 Medicina, Nevrobiologija. Raziskovalni program ARRS: Farmakologija in farmakogenomika

4. Opis delovnega mesta mladega raziskovalca/ke (*Description of the Young Researcher's position*):

Vključuje morebitne dodatne pogoje, ki jih mora izpolnjevati kandidat/ka za mladega raziskovalca/ko, ki niso navedeni v razpisu za mlade raziskovalce.

sl.: Raziskovalno delo mlade(ga) raziskovalke(ca) bo potekalo v Laboratoriju za molekularno in celično toksikologijo, na Inštitutu za farmakologijo in eksperimentalno toksikologijo. Pogoji za prijavo so:

- zaključen magistrski študij medicine, veterine, farmacije, biologije, biokemije, biotehnologije in kemije
- znanje angleškega jezika
- prednost pri izbiri bodo imeli kandidati(ke) z izkušnjami z delom v molekularni biologiji

Vsebina raziskovalnega dela: **Rezistenca na farmakološko zdravljenje pri raku jajčnikov**

Rak jajčnikov je kljub nizki pojavnosti najbolj smrtonosna maligna bolezen ženskega reproduktivnega sistema. Zaradi nespecifičnih znakov je pri večini bolnic tumor odkrit, ko je bolezen že v napredovalem stadiju. Čeprav je bil v zadnjem desetletju splošen trend zmanjševanja incidence in umrljivosti zaradi raka jajčnikov, pa je opaženo znatno povečanje incidence pri mlajših ženskah. Glavni razlog za slabo prognozo je poleg poznega odkritja bolezni, tudi rezistenca na farmakoterapijo. Kljub novim tarčnim zdravilom, kot so zaviralci poli (ADP-riboze) polimeraze (PARPi), ostaja karboplatin z dodanim paklitakselom standardno zdravljenje prve izbire za napredovali rak jajčnikov. Poleg tega so PARPi indicirani za vzdrževalno zdravljenje v prvi liniji in za recidive samo pri bolnicah, ki so se odzvale na zdravilo na osnovi platine. Ker je na platino rezistenten rak jajčnikov neozdravljiva bolezen, je osrednji cilj raziskav na tem področju razvoj novih strategij zdravljenja za premagovanje rezistence. Vendar merila za izbiro terapije niso povsem jasna, saj trenutno ni klinično validiranih molekularnih napovednih biooznačevalcev za zgodnjo napoved bolezni rezistentne na platino. Namen doktorske naloge ob ovrednotiti ustreznost komercialnih celičnih linij za raziskave novih potencialnih napovednih biooznačevalcev za zgodnjo rezistenco, kar bi omogočilo personaliziran pristop k zdravljenju teh bolnic. Na ta način bi se lahko izognili neučinkovitem zdravljenju in resnim neželenim učinkom

Metode dela: Uporabili bomo celične linije raka jajčnikov, katerih karakteristike so dobro opredeljene in so kot *in vitro* model še posebej dragocen v dobi personaliziranega zdravljenja. Vsaj povečajo verjetnost, da bodo zaključki, pridobljeni v *in vitro* okolju, prenosljivi na kliniko. Glavna metoda analize bo pretočna citometrija.

eng: The research work of the young researcher will take place in the Laboratory of Molecular and Cellular Toxicology, at the Institute of Pharmacology and Experimental Toxicology. The application requirements are:

- Master degree in medicine, veterinary medicine, pharmacy, biology, biochemistry, biotechnology, and chemistry
- knowledge of the English language
- candidates with work experience in molecular biology will be given preference

Content of the research work: **Resistance to pharmacotherapy in ovarian cancer**

Despite its low incidence, ovarian cancer is the deadliest malignant disease of the female reproductive system. Due to non-specific signs, the tumor is discovered in most patients when the disease is already in an advanced stage. Although there has been a general downward trend in ovarian cancer incidence and mortality over the last decade, a significant increase in incidence has been observed in younger women. The main reason for the poor prognosis is, in addition to the late detection of the disease, resistance to pharmacotherapy. Despite new targeted drugs such as poly (ADP-ribose) polymerase inhibitors (PARPi), carboplatin with added paclitaxel remains the standard first-line treatment for advanced ovarian cancer. In addition, PARPis are indicated for first-line maintenance therapy and for relapse only in patients who have responded to platinum-based therapy. Since platinum-resistant ovarian cancer is an incurable disease, the central goal of research in this area is the development of new treatment strategies to overcome resistance. However, the criteria for selecting therapy are not entirely clear, as there are currently no clinically validated molecular predictive biomarkers for the early prediction of platinum-resistant disease. Therefore, the aim of the doctoral thesis will be to evaluate the suitability of commercial cell lines for research to discover new potential predictive biomarkers for early resistance, which would enable a personalized approach to the treatment of these patients. In this way, ineffective treatment and serious side effects could be avoided.

Work methods: We will use ovarian cancer cell lines whose characteristics are well defined and are especially valuable as an *in vitro* model in the era of personalized treatment. At least, they increase the likelihood that conclusions drawn in an *in vitro* setting will be transferable to the clinic. The main method of analysis will be flow cytometry.