**KRATEK OPIS PROGRAMA USPOSABLJANJA MLADEGA RAZISKOVALCA**

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Raziskovalno področje po šifrantu Javne agencije za raziskovalno dejavnost RS: Nevrobiologija

**Predviden potek usposabljanja mladega raziskovalca:**

Farmakogenomski biooznačevalci za odziv na klasična zdravila (male sintetične molekule) so razmeroma dobro raziskani. Vključujejo predvsem variante v genih za presnovo in transport zdravil (ksenobiotikov) ter se že vpeljujejo v klinično prakso. Variabilnost v odzivu na novejša biološka zdravila je slabše raziskana, hkrati pa predvsem na področju kroničnih imunskih bolezni prihajajo v uporabo vedno nova biološka zdravila za različne molekularne tarče, ki omogočajo izbiro in personalizirano zdravljenje.

V okviru programa usposabljanja bo mladi raziskovalec raziskal molekularne procese in mehanizme poteka bolezni in odziva na zdravljenje z novimi pristopi sistemske biologije in (bio)medicine, kjer težimo k čim bolj celostni obravnavi bioloških procesov. S pristopi sistemske medicine bomo preučevali molekularne mehanizme neodzivnosti na biološka zdravila pri kroničnih imunskih boleznih (kronična vnetna črevesna bolezen, revmatoidni artritis, luskavica, astma). Celovit in podroben vpogled v različne skupine biomolekul in njihovih povezav v signalna, metabolna in druga omrežja v celici na osnovi ogromnega števila podatkov, ki jih bomo pridobili z najsodobnejšo tehnologijo multi-omik, kot so genomika, transkriptomika, proteomika, epigenomika, metabolomika, bomo povezali s kliničnimi podatki. S pomočjo bioinformatske analize bomo razvili modele molekularne patogeneze in odkrili biooznačevalce za klasifikacijo bolnikov na osnovi molekularnih endotipov za spremljanje poteka bolezni in personalizirano medicino. Modele molekularno bioloških procesov bomo nadgradili z integracijo podatkov na različnih nivojih (organel, celica, tkivo, organ, organizem). Z integracijo molekularnih podatkov, kliničnih podatkov in podatkov vplivov okolja bomo izdelali napovedne modele za personalizirano medicino.

Raziskave bomo izvajali s pomočjo obsežne biobanke kliničnih vzorcev (DNA, RNA, proteini izolirani iz seruma, sline, blata, urina, brisov sluznic, različnih tkiv), ki vključuje preko 6000 bolnikov, in ki jo razvijamo v skladu z najvišjimi mednarodnimi standardi. Biobanka je povezana z obsežno zbirko kliničnih podatkov bolnikov, vključno z odzivom na zdravljenje. Večjo zanesljivost biooznačevalcev bomo dosegli s predhodnim procesiranjem kliničnih vzorcev za izolacijo posameznih celičnih podtipov. V ta namen skupaj z industrijo razvijamo novo tehnologijo za avtomatizirano, enostavno in cenovno ugodno ločevanje različnih podtipov celic. Novoodkrite biooznačevalce bomo tudi funkcijsko ovrednotili z in vitro celičnimi modeli temelječimi na primarnih celicah bolnikov. Poleg standardnih funkcionalnih celičnih modelov bomo razvijali tudi 3D organoidne modele in v končni fazi organe na čipu.

## **BRIEF DESCRIPTION OF THE YOUNG RESEARCHER TRAINING PROGRAM**

**Faculty:** University of Maribor, Faculty of Medicine

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**Ortelius Research field:** 47.3 Biochemistry (ID 49); 28.1 Medicine (ID 313)

**Short description of the training programme:**

Pharmacogenomic biomarkers for response to classical drugs (small synthetic molecules) are relatively well studied and are being translated into clinical practice. They mainly include variants in genes for drug (xenobiotic) metabolism and transport. New biologics aimed at various molecular targets are increasingly becoming available for chronic immune diseases, widening treatment options and enabling personalized treatment. However, patient response variability to newer biologics is not well understood.

Young researcher will use new systems biology and (bio)medicine approaches to investigate the molecular processes, mechanisms of disease progression and response to treatment in a in deeply comprehensive way. We will use systems medicine approach to study molecular mechanisms of non-response to biological drugs in chronic immune diseases (inflammatory bowel disease, rheumatoid arthritis, psoriasis, asthma). Comprehensive insight into different groups of biomolecules, their signaling and other cellular networks will be obtained from the large amount state-of-the-art multi-omics technology (genomics, transcriptomics, proteomics, epigenomics, metabolomics) data. We will use bioinformatics analyses for generation of molecular pathogenesis models and the discovery of biomarkers for patient classification based on molecular endotypes that will aid in personalized medicine and disease progression monitoring. Models of molecular processes will be upgraded by integrating data from different sources (organelle, cell, tissue, organ, organism). Predictive models for personalized medicine will be generated by integrating molecular data, clinical data and environmental risk factors.

We will use our extensive biobank of clinical samples (DNA, RNA, proteins isolated from serum, saliva, faeces, urine, mucosal swabs, various tissues), which already includes over 6000 patients, and which is being regulary upgraded according to the highest international standards. Our biobank includes comprehensive clinical data for each patient, including treatment response. We will develop protocols for isolation of individual cell subtypes to discover more reliabile cell type specific biomarkers. For translation of the cell type specific biomarkers into clinical practise, automated, simple and cost-effective separation of different cell subtypes technology should be developed, such as one we are currently developing in collaboration with our industry partners. The newly discovered biomarkers will be functionally evaluated using in vitro cell models based on patients' primary cells. In addition to standard functional cell models, 3D organoid models will be developed and finally, organ-on-a-chip systems.