

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

1. Raziskovalna organizacija (*Research organisation*):

Univerza v Ljubljani, Fakulteta za farmacijo (University of Ljubljana, Faculty of Pharmacy)

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

Izr. prof. dr. Žiga Jakopin (ziga.jakopin@ffa.uni-lj.si)

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

1.09 Farmacija (*Pharmacy*)

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:

Kot posledica pogoste uporabe produktov za osebno nego se v okolje sproščajo številne spojine kot so UV filtri, konzervansi (parabeni), alkilfenoli in njihovi etoksilati ter bisfenoli, ki so bili toksikološko ovrednoteni in lahko dokazano delujejo kot endokrini motilci. Tekom procesa dezinfekcije v čistilnih napravah ali na primer med dezinfekcijo bazenov lahko iz teh spojin nastanejo monohalogenirani in dihalogenirani transformacijski produkti. Kljub temu, da je nastanek tovrstnih spojin bil dokazan, pa obstaja še velikanska luknja v znanju o toksikološkem profilu teh spojin, pri čemer so še posebej slabo poznane njihove endokrine in imunomodulatorne lastnosti. Cilj usposabljanja bo torej raziskati, kako mono- ali dihalogeniranje modulira toksične učinke osnovnih spojin.

Mladi raziskovalec bo v prvi fazi vključen v sintezo raznih halogeniranih transformacijskih produktov, ki nastajajo pri halogeniranju komponent izdelkov za osebno nego. Nato bo z uporabo celičnih testov na primarnih celicah in celičnih linijah proučil imunomodulatorno in endokrino delovanje sintetiziranih spojin. Raziskovalna skupina izr. prof. Jakopina je sicer nedavno z uporabo *in silico* metod izračunala, kako mono- ali dihalogeniranje teroetično vpliva na vezavo transformacijskih produktov UV filtrov, parabenov, alkil fenolov in bisfenolov na jedrne receptorje. Pri tem so odkrili, da lahko omenjena transformacija olajša vezavo na nekatere izmed jedrnih receptorjev, kar bi se lahko odrazilo v bolj izrazitem endokrinem delovanju spojin. Ti podatki bodo pomembno izhodišče za delo mladega raziskovalca, še posebej v smislu usmerjanja in prioritizacije testov na reporterske celične linije, ki izražajo ustrezne receptorje. V sklopu sodelovanja med skupino izr. prof. Jakopina in prof. Emanuela Corsini (Universita degli studi di Milano, Italija) so proučevali imunomodulatorno delovanje UV filtrov na različnih vrstah imunskih celic in jih ovrednotili v smislu vpliva na izločanje citokinov, izražanje površinskih označevalcev, kar bo tudi predstavljalo dobro osnovo za delo mladega raziskovalca, ki bo na uveljavljenih modelih ovrednotil še delovanje halogeniranih derivatov.

Mladi raziskovalec bo v okviru svoje disertacije sintetiziral načrtovane transformacijske

produkte in jih toksikološko ovrednotil z različnimi *in vitro* testi ter primerjal njihovo delovanje z delovanjem osnovnih spojin. Zaželeno je, da ima kandidat/kandidatka za mladega raziskovalca predhodno praktično znanje s področja sinteze organskih spojin in biološkega vrednotenja spojin z *in vitro* testi.

eng:

As a consequence of frequent use of personal care products, many compounds such as UV filters, preservatives (parabens), alkylphenols and their ethoxylates and bisphenols, which have been thoroughly toxicologically evaluated and proved to be endocrine disruptors, are being released into the environment. During the process of disinfection in wastewater treatment plants or for example during the disinfection of pools, monohalogenated and dihalogenated transformation products may be formed from these compounds. Despite the fact that the formation of such compounds is well known, there is still a huge knowledge gap in toxicological profile of these compounds, with their endocrine and immunomodulatory properties being particularly poorly understood. The aim of the training will therefore be to investigate how mono- or dihalogenation modulates the toxic effects of parent compounds.

In the first phase, the young researcher will be involved in the synthesis of various halogenated transformation products shown to form during the halogenation of components of personal care products. The young researcher will then study the immunomodulatory and endocrine activity of the synthesized compounds using cell assays on primary cells and cell lines. Research group of Assoc. Prof. Jakopin has recently employed *in silico* methodology to calculate how mono- or dihalogenation affects the binding of transformation products of UV filters, parabens, alkyl phenols and bisphenols to nuclear receptors. It has been predicted that such transformation may facilitate binding to some of the nuclear receptors, which could be reflected in a pronounced hormone disrupting activity of these compounds. The obtained data will serve as an important starting point for the young researcher's work, especially in terms of directing and prioritizing assays, i.e. to allow for the use of suitable reporter cell lines expressing nuclear receptors. As part of the collaboration between groups of Assoc. Prof. Jakopin and prof. Emanuela Corsini (Universita degli studi di Milano, Italy) the immunomodulatory action of UV filters on different types of immune cells has been examined and they were evaluated for their effect on cytokine secretion, expression of surface markers. These preliminary results will also provide a good basis for the work of a young researcher, who will evaluate the activity of halogenated derivatives using the established models.

As part of his/her dissertation, the young researcher will synthesize the designed transformation products and investigate their toxicological profile in various *in vitro* models in comparison to the corresponding parent compounds. It is desirable that the candidate for the young researcher has prior practical knowledge of synthesis of organic compounds and their biological evaluation *in vitro*.