

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

1. Članica UL (*UL member*):

Univerza v Ljubljani, Fakulteta za kemijo in kemijsko tehnologijo
University of Ljubljana, Faculty of Chemistry and Chemical Technology

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

Martin Gazvoda, email: martin.gazvoda@fkkt.uni-lj.si

3. Raziskovalno področje (*Research field*):

1.04 Kemija (*Chemistry*), 1.05 Biokemija in molekularna biologija (*Biochemistry and molecular biology*)

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

slo:

Metode za natančne strukturne modifikacije biomolekul, ki omogočajo izboljšanje (oziroma spreminjanje) njihove aktivnosti in stabilnosti, postajajo vse pomembnejše. Takšne modificirane biomolekule, med njimi na primer proteine, je mogoče uporabiti kot katalizatorje za razvoj novih vrst reakcij ali kot zdravilne učinkovine v medicini. V ta namen lahko strukturo proteina spreminjamo z različnimi pristopi, med drugim z izražanjem rekombinantnih proteinov, ki omogoča njihovo *de novo* načrtovanje oziroma preoblikovanje, kot tudi s kemijsko sintezo, s katero lahko v proteine vgradimo strukturne fragmente, ki jih z orodji molekularne biologije ni mogoče uvesti.

Mladi raziskovalec bo v sklopu raziskovalnega dela razvijal nove metode za pripravo modificiranih proteinov preko opisanih pristopov in sicer z izražanjem rekombinantnih proteinov z uvedbo nenaravnih aminokislin ter sintezo proteinov z metodami kemijske ligacije. Prvi pristop bo temeljil na pripravi nenaravnih aminokislin in poskusu njihove vgradnje v proteine z izražanjem *in vivo*. V ta namen bomo preučevali modificirane ekspresijske seve *E. coli* in njihovo združljivost z različnimi vektorskimi konstrukti, ki bodo prilagojeni vgradnji sintetiziranih nenaravnih aminokislin v izbrane proteine. Drugi pristop bo uporabljal metode selektivnega povezovanja nezaščitenih peptidnih fragmentov za sintezo proteinov. Za ta namen bo mladi raziskovalec uporabljal znane pristope kemijske ligacije, poleg tega bo, s pomočjo racionalne zasnove reakcij preko mehanističnih predpostavk, poskušal razviti nove tovrstne metode. Peptide bomo pripravili z uporabo sinteznih metod na trdnem nosilcu, ki omogočajo njihovo sintezo z natančno določenim aminokislinskim zaporedjem in tudi vključitev različnih, nenaravnih strukturnih fragmentov. Preiskovani proteini bodo izbrani glede na njihovo dokazano biološko aktivnost, opisana komplementarna pristopa pa bosta vodila do različno modificiranih struktur, pri tem bo poudarek na spreminjanju aminokislinskih ostankov v aktivnem mestu proteina. Tako pripravljene proteine bomo okarakterizirali ter ovrednotili njihovo aktivnost in stabilnost v primerjavi z nativnimi oblikami.

Zaželeno je, da ima kandidat/kandidatka za mladega raziskovalca izkušnje z raziskovalnim delom, zlasti na področjih organske kemije in biokemije. Od kandidata/kandidatke se pričakuje aktivno znanje angleškega jezika.

eng:

Rational structural modifications of biomolecules, such as proteins, to improve (or alter) their activity and stability are becoming increasingly important, as they can be used, for example, as catalysts to unfold unprecedented types of transformations and as therapeutic agents in medicine. To this end, protein structure can be altered in a variety of ways, including expression of recombinant proteins that allow *de novo* design or redesign, or by chemical synthesis that can be used to incorporate structural fragments into proteins that are not possible by the means of molecular biology.

Young researcher will address these challenges by attempting to develop novel methods for selective modification of biomolecules through described approaches: recombinant protein expression using non-canonical amino acids and by chemical synthesis using chemical ligation methods. The first approach is based on the preparation of non-canonical amino acids and an attempt to incorporate them into proteins by *in vivo* expression. To this end, modified *E. coli* expression strains and their compatibility with various vector constructs designed for incorporation of synthesized unnatural amino acids into selected proteins will be studied. The second approach will use methods of selective ligation of unprotected peptide fragments for protein synthesis. The known methods of chemical ligation will be used, and young researcher will also attempt to develop new methods of this type by designing the reactions through mechanistic hypotheses. Peptides will be prepared on a solid support using synthesis methods that allow the preparation of peptides with a precisely defined amino acid sequence and also the incorporation of various unnatural structural fragments. The proteins studied will be selected on the basis of their demonstrated biological activity, and the complementary approaches described will result in variously modified structures, with emphasis on modification of amino acid residues in the active site of the protein. The modified proteins produced will be characterized and tested for activity and stability compared to their native forms.

It is desirable that the candidate has experience in research work, preferably in the fields of organic chemistry and biochemistry. The applicant should be fluent in English.