

**Recruitment for the Poznań Doctoral School of the Institutes of the Polish Academy of Sciences
at the Institute of Bioorganic Chemistry, PAS in Poznań
Procedure no. 13/2023/ICHB/PSD**

INSTITUTION: Institute of Bioorganic Chemistry, PAS
CITY: Poznań
POSITION: PhD student
POSITIONS AVAILABLE: 1 position
SCIENTIFIC DISCIPLINE: biological and related sciences
PUBLICATION DATE: **04.05.2023**
APPLICATION DEADLINE: **04.06.2023**
IBCH PAS WEBSITE: <https://portal.ichb.pl/homepage/>
PDS IPAS WEBSITE: <https://psd-ipan.ichb.pl/index.php/en/home/>

KEY WORDS: RNA structure, thermodynamics of modified RNA, pseudouridine, N1-methylpseudouridine, chemical mapping of RNA structure, IVT mRNA vaccines, Nanopore RNA sequencing

Principal Investigator: Prof Ryszard Kierzek

Research topic: Impact of RNA modifications on structure and function of natural RNA and vaccine-type in vitro transcribed mRNA (IVT mRNA)

I. Project description

RNAs are one of the most important biomolecules. In RNA, beside canonical nucleotides, are over 140 modified ones. The most abundant are N6-methyladenosine and pseudouridine. It is well established that different RNA biological functions are often related to their structure and for that reasons the knowledge about RNA structure is very important. In addition to many experimental systems of chemical mapping of RNA structure, there is also a method for predicting of RNA structure based on thermodynamic rules of RNA folding. Various programs are used for that prediction and RNAstructure is the leading one.

The aim of the research project is to determine full set of the thermodynamic parameters necessary to predict folding of RNAs containing the following modifications: pseudouridine (P), N1-methylpseudouridine (1MeP), 5-methoxyuridine (5moU) and 5-methylcytidine (5meC). The collected thermodynamic parameters will be implemented into the RNAstructure program and allow to predict folding of natural RNAs (with modifications at selected positions) and vaccine type RNAs (with P, 1MeP, 5moU and 5meC replacing all uridines or cytidines, respectively). The next stage of the project will be the chemical mapping of several RNAs containing the chosen nucleotides and the comparison of RNA structures predicted with the modified RNAstructure program and determined experimentally with chemical mappings. The project is also important for reason related with SARS-CoV-2 virus pandemic. The most effective IVT mRNA vaccines from Pfizer and Moderna carrying spike mRNA in which all uridines were replaced with N1-methylpseudouridine. Earlier studies have shown that the introduction of N1-methylpseudouridine into IVT mRNAs most significantly increases mRNA expression as well as stability of mRNA in the cellular environment and indicated the best immunological respond. Other modified nucleotides that also showed very promising features were: pseudouridine, 5-methoxyuridine and 5-methylcytidine. This was also the reason why the particular modified RNA nucleotides were selected for investigations in this project.

The research plan includes the following steps:

(1) synthesis of necessary modified phosphoramidites and RNA oligonucleotides containing pseudouridine, N1-methylpseudouridine, 5-methoxyuridine and 5-methylcytidine at specific positions,

(2) measurements of the thermodynamic stability of complementary duplexes and duplexes containing modifications within nonhelical RNA motifs. The project concerns determination of modified RNA thermodynamic parameters applicable to natural RNAs with modifications as well as to vaccine type RNAs. For each type of RNA modification, the next step will be calculation of respective thermodynamic parameters and their implementation into RNAstructure program,

(3) chemical mapping of two large fragments of the 28S subunit of the human ribosomal RNA (rRNA). Both model rRNAs contain 5 and 13 pseudouridine residues, respectively. They are selected from region of peptidyl transferase center (PTC) of rRNA. Based on the results of the chemical mapping, the RNAs secondary structure will be solved and compared with the structure predicted with the modified RNAstructure program. The comparison of both secondary structures will also serve for eventually improvement of the modified thermodynamic parameters and RNAstructure program,

(4) chemical mapping of two vaccine type RNAs. The selected RNAs are: subgenomic RNA M from SARS-CoV-2 virus (ca. 800 nt) and segment 4 mRNA from influenza A virus (ca. 1800 nt). For sgRNA M the chemical mapping will be performed on RNAs containing P, 1MeP, 5moU and 5meC, respectively. Also, segment 4 mRNA containing pseudouridine and N1-methylpseudouridine will be mapped. Next, their structures predicted with RNAstructure and determined based on chemical mapping will be compared,

(5) determination the structure of small RNA fragments containing modified pseudouridine and N1-methylpseudouridine by NMR and crystallographic methods. These studies are aimed at determining the interactions responsible for the significant stabilization of RNA structures by both modifications.

Overall, the project is important for understanding biological functions and the effects of modifications on RNA structure. The aspect of vaccine RNAs is extremely important also, as the effectiveness of the Pfizer and Moderna vaccines indicates that this is the right direction for the future development of IVT mRNA vaccines.

Additional information:

1. Research and doctoral theses shall be carried out within the project no. 2022/45/B/ST4/03586, entitled "Thermodynamics of modified RNAs. Impact of RNA modifications on structure and function of natural RNA and vaccine-type in vitro transcribed mRNA (IVT mRNA)", funded by National Science Center
2. PhD students shall receive a stipend in the gross amount of ca 4 300 PLN (3 800 PLN net), for the period of 44 months with possibility of extension
3. PhD students shall be subject to social insurance, pursuant to article. 6 section 1 passage 7b of the act of October 13th, 1998 on the social insurance system (Journal of Laws of 2019, item 300, 303 and 730).

II. Requirements for the candidates:

1. Master's degree in biology or related fields, or meeting the conditions indicated in Art. 186 sec. 2 of the Act of July 20, 2018. Law on Higher Education and Science (Journal of Laws of 2018, item 1668, as amended).
2. Experience in laboratory work in the field of molecular biology. Experience in the field of biology and biochemistry of nucleic acids are welcome.
3. Very good knowledge of the English language.
2. Knowledge of basic issues related to the research topic of the project.
3. High motivation for further development and the ability to work in a team.

III. Duties in project:

1. Thermodynamic stability studies of model duplexes and non-helical RNA structural motifs containing modifications present in RNA vaccines.
2. Chemical mapping of the secondary structure of influenza virus RNA and SARS-CoV-2 RNA containing pseudouridine, N1-methylpseudouridine and 5-methoxyuridine.
3. Analysis of the results obtained and preparation of publications on the conducted research.

IV. Required documents:

1. Application for admission to PDS IPAS along with the consent for processing personal data upon the recruitment procedure and a statement on having acknowledged the regulations of recruitment for PDS IPAS, using form downloaded from:
https://portal.ichb.pl/wp-content/uploads/2021/10/ICHBApplication_for_admission_202110.docx
2. Certified copy of the diploma confirming graduation or a certificate confirming graduation (in the case of diplomas issued by foreign higher education schools, diploma stipulated in article 326, section 2, passage 2 or article 327, passage 2 of the act of July 20th, 2018 – Law on Higher Education and Science (Journal of Laws of 2018, item 1668, as amended), entitling to apply for conferment of a doctoral degree in the state in where such a certificate was issued by the relevant higher education school. In the event when the candidate is not in possession of the aforementioned documents, he/she is obliged to submit them prior to admission to PDS IPAS. Additional information on foreign school diplomas are available at:
<https://nawa.gov.pl/en/recognition/recognition-for-academic-purposes/applying-for-admission-to-doctoral-studies>
3. Scientific CV encompassing track record of previous education and employment, information on involvement in scientific activities (participation in student research groups, attendance at scientific conferences, accomplished internships and training, awarded prizes and distinction) and list of publications.
4. Cover letter featuring a short description of research interests, achievements and justification for the intention to commence education at the doctoral school.
5. Certificates or other documents confirming the degree of proficiency in English, if the candidate is in possession of such materials.
6. Contact details of at least one, previous scientific supervisor or another researcher who is entitled to issue an opinion on the candidate.

V. Applications should be submitted via the eRecruiter portal at:

<https://system.erecruiter.pl/FormTemplates/RecruitmentForm.aspx?WebID=60be4ca01e404e31a7cb392a2a4f25d7>

VI. Submission deadline is **04.06.2023 r.**

VII. Criteria for evaluation of candidates:

1. Candidate's research achievements, pursuant to the grades obtained in the course of studies, scientific publications, awarded scholarships and distinctions resulting from conducting scientific research or student activities or other achievements.
2. Candidate's scientific and professional experience, pursuant to participation in conferences, workshops, training sessions and internships, implementation of research and commercial projects, involvement in scientific trusts and societies, international and professional mobility, experience in other sectors, including industry.
3. Candidate's knowledge on the following discipline: molecular biology and related sciences.
4. Knowledge of the subject matter described in the recruitment advertisement.

VIII. The recruitment procedure shall be concluded no later than **30.06.2023 r.**

IX. The description of the recruitment process is stipulated in the Regulations of Recruitment for PDS IPAS. Following the recruitment procedure, the unadmitted candidates shall be informed on the number of points obtained at both stages.

Incomplete applications will not be considered.

For additional information please contact the Principal Investigator:

Prof. Ryszard Kierzek, e-mail: rkierzek@ibch.poznan.pl

Information clause:

Pursuant to the stipulations of the regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation), further referred to as GDPR, we hereby inform that:

- *The Institute of Bioorganic Chemistry, Polish Academy of Sciences, seated in Noskowskiego St. 12/14, 61-704 Poznan; REGON 000849327, NIP 777-00-02-062 is the administrator of the collected personal data (further referred to as the Institute).*
- *The Administrator appointed a Data Protection Officer, who can be contacted in writing, via traditional mail, by sending a letter to the following address: Z. Noskowskiego St. 12/14, 61-704 Poznan, or by sending an e-mail to: dpo@ibch.poznan.pl.*
- *The personal data of the candidates is processed for the purposes of fulfilling the tasks of the administrator, associated with conducting the recruitment procedure for a vacant position.*
- *The legal basis for processing personal data is the Act of 26 June 1974 – The Labor Code, Act of 30 April 2010 on the Polish Academy of Sciences or the consent of the person whose data shall be subjected to processing.*
- *Your personal data shall be subjected to processing for period of 3 months upon the date of decision of the recruitment committee. Following this period, the data will be irretrievably and effectively destroyed.*
- *The personal data of the candidates shall not be transferred to any third country.*
- *The person whose data shall be subjected to processing has the right to:*
 - *request access to his/her personal data, and to amend it or delete it, pursuant to articles 15-17 of GDPR;*
 - *limit data processing, in the events stipulated in article 18 of GDPR;*
 - *data transferring, pursuant to article 20 of GDPR;*
 - *withdraw consent at any moment, without influencing compliance with the law of the processing that was executed prior to consent withdrawal;*
 - *file a complaint to the Inspector General for Personal Data Protection.*

Providing personal data in the scope stipulated in article 22 (1) of the Act of 26 June 1974 – The Labor Code is mandatory, whereas providing data in a broader scope is voluntary and requires consent for its processing.