

**IBCH PAS RECRUITMENT PROCEDURE NO. 7/2023/SN
FOR THE POSITION OF A POSTDOCTORAL RESEARCH ASSISTANT**

INSTITUTION: Institute of Bioorganic Chemistry, Polish Academy of Sciences,
Department of Structural Chemistry and Biology of Nucleic Acids
CITY: Poznań
POSITION: postdoctoral research assistant (post-doc)
POSITIONS AVAILABLE: 1
SCIENTIFIC DISCIPLINE: chemistry
PUBLICATION DATE: **16 May 2023**
APPLICATION DEADLINE: **16 June 2023**
WEBSITE: <https://portal.ibch.poznan.pl/homepage>

KEY WORDS: RNA structure, thermodynamics of modified RNA, pseudouridine, N1-methylpseudouridine, chemical mapping of RNA structure

Principal Investigator: Prof. Ryszard Kierzek

Research topic: Effect of RNA modifications on the structure and functions of natural RNAs and in vitro transcribed vaccine mRNAs (IVT mRNA).

We offer the position of postdoctoral research assistant (post-doc) within the project 2022/45/B/ST4/03586 entitled "Thermodynamics of modified RNAs. The influence of RNA modifications on the structure and functions of natural RNAs and in vitro transcribed vaccine mRNAs (IVT mRNA)" funded by the National Science Center.

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.

II. Requirements for the candidates:

1. A PhD degree in chemistry, biochemistry, structural biology or related discipline.*
2. Experience in the chemical synthesis of nucleic acids and their components,
3. Experience in structural studies of nucleic acids and their components,
4. Well-documented research output in the form of research papers.
5. Ability to make responsible decisions without supervision and adaptability to teamwork
6. Good command of English, enabling efficient communication and preparation of research papers.

*In accordance with the requirements of the National Science Center, only those candidates who received their PhD degree no earlier than 7 years prior to the date of employment within the research project, excluding parental or related leaves governed by the stipulations of the Labor Code, rehabilitation period associated with rehabilitation allowances or other rehabilitation benefits, are eligible for recruitment. In such cases, the aforementioned 7-year period shall be extended by additional 18 months for every descendant or adoptee. Female applicants may choose the way of justifying breaks in their research career, which is more favorable in a given case.

Pursuant to the regulations of the National Science Center, only those candidates are eligible for the position who obtained their PhD degree at an institution other than the Institute of Bioorganic Chemistry, PAS, or accomplished at least a 10-month long, continual and documented post-doctoral internship at an institution other than the host institution, in a country other than the country where the doctoral degree was conferred.

III. Job Responsibilities:

1. Chemical synthesis of modified oligonucleotides,
2. Thermodynamic stability studies of modified oligonucleotides,
3. Studies of the secondary structure of modified nucleic acids,
4. Participation in the preparation of scientific manuscripts
5. Supervising the work of students and doctoral students.

IV. Required documents:

1. Cover letter of application to the Director of IBCH PAS featuring contact details to at least two referees.
2. Copy of the doctoral diploma.
3. CV featuring information on the candidate's scientific track record, including:
 - the list of papers published in journals listed in the Web of Science (WoS) database, stating the IF in accordance with WoS, number of citations and the H-index.
 - list of patents;
 - information on the previously managed projects or participation in project implementation;
 - information on the accomplished research internships;
 - information on the awarded prizes and distinctions.

V. Applications should be submitted via the eRecruiter portal

<https://system.erecruiter.pl/FormTemplates/RecruitmentForm.aspx?WebID=cd8a79a61be944d6950786f22e327f6e>

VI. The submission deadline is 16 June 2023**VII. Selection of candidates:**

Following preliminary verification, on the basis of the application documents, selected candidates will be invited to an interview, as a result of which a candidate recommended for employment shall be appointed. The main criteria, taken into consideration during the selection of the candidates, will be: (i) research output (research papers published), (ii) compliance of the previous experience with the tasks planned within the framework of the project, (iii) experience gained during a long-term, foreign internship.

VIII. The recruitment procedure shall be concluded no later than on 30 June 2023.**IX. Start and duration of the position.**

Employment is available instantly (depending on the result of the recruitment procedure). The position is available for the period of 24 months, with possible extension.. The estimated gross salary is ca. 8 150 PLN/month.

X. Employment shall take place in compliance with the provisions of the Labor Code of Poland.

For more details, please contact: prof Ryszard Kierzek, 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.