



POLISH NATIONAL AGENCY
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PROGRAMME

name of the unit: INSTITUTE OF ORGANIC CHEMISTRY, Lodz University of Technology		symbol: I-32 http://www.chorg.p.lodz.pl
head of the unit: Professor Elżbieta Sochacka	potential promoters: Grazyna Leszczynska, PhD, DSc, Associate Professor	contact person: Grazyna Leszczynska, PhD, DSc, tel: 42-631-31-50 grazyna.leszczynska@p.lodz.pl
scope of activities: <ul style="list-style-type: none">➤ Modified RNA nucleosides: synthesis, physicochemical and structural properties. Changes in the chemical status of modified nucleosides under stressful conditions of the cell.➤ Synthesis of model RNA and DNA oligomers for the study of cellular processes and the selection of inhibitors of pathogen replication.➤ Research on the molecular causes of human diseases based on the DNA or RNA damage/mutation➤ Epigenetic RNA modifications as an element of regulation of gene expression.➤ The role of post-transcriptional modifications in the control of gene expression in tumor cells➤ <i>In vitro</i> studies of the biological activity of the enzymes with increased expression in the tumor cells.➤ Development of sequencing methods for modified tRNA molecules		graphic material
present activities: <ul style="list-style-type: none">➤ Study of the physicochemical and structural properties of pathogenic mt-tRNAs bearing methionine to determine the molecular reasons of mitochondrial dysfunction enhancing symptoms of hypertension, type 2 diabetes and Leber's Hereditary Optic Neuropathy (LHON). In addition, a protocol for the synthesis of 5-formylcytidine (f5C) modified oligoribonucleotides has been developed.➤ Biological role of wobble selenonucleosides in bacterial tRNAs specific for Lys and Glu. This project requires the synthesis of 5-methylaminomethyl-2-selenouridine modified RNA oligomer (mnm5Se2U) and the study of CD and thermodynamic stability of the homoduplexes.➤ Structural studies of oligomers containing newly discovered modified ribonucleosides: S-geranyl-2-thiouridine (geS2U) and cyclic 6-threonylcarbamoyl adenosine (ct6A) in the tRNA anticodon loop.➤ Development of new, effective protocols for the synthesis of natural modified ribonucleosides, including t6A, 5-substituted uridines, 2-thiouridines, 2-selenouridines, 5-substituted cytidines. Studies of physicochemical and structural properties of nucleosides.➤ Determination of the reactivity of 2-thio and 2-selenouridines with hydrogen peroxide as a factor that mimics oxidative stress in the cell.		
Future activities: <ul style="list-style-type: none">➤ Studies on the regulatory role of epigenetic modifications of mRNA, namely 5-methylcytidine (m5C), 5-hydroxymethylcytidine (hm5C), 5-formylcytidine (f5C) and 5-carboxymethylcytidine (ca5C) on the translation process.		



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- *In vitro* studies of the 5-hydroxymethylcytidine-RNA metabolism pathway mediated by A3A and hSMUG1 enzymes which show increased expression in tumor cells.
- Research on the usefulness of new precursor compounds in the preparation of modified nucleosides.
- Study of the influence of 2-thiocytidine methylation on the translation process in bacterial tRNA molecules bearing arginine.

Keywords: modified tRNA nucleoside, modified oligoribonucleotides, anticodon arm, synthesis of RNA by phosphoramidite chemistry on solid-phase, biological activity of RNA

List of internship proposal in this research team:

Melanie Etheve-Quellejeu, University Paris Descartes

Ronald Micura, University of Innsbruck

List of attachments:

Publikacions from the last 3 years :

1. Skotnicki, K., Janik, I., Sadowska, K., Leszczynska, G., Bobrowski, K. Radiation-Induced Oxidation Reactions of 2-Selenouracil in Aqueous Solutions: Comparison with Sulfur Analog of Uracil. *Molecules* **2022**, 27(1), 133.
2. Zhou J, Lénon M, Ravanat JL, Touati N, Velours C, Podskoczyj K, Leszczynska G, Fontecave M, Barras F, Golinelli-Pimpaneau B "Iron-sulfur biology invades tRNA modification: the case of U34 sulfuration". *Nucleic Acids Res.* **2021**;49, 997-4007.
3. Leszczynska G, Cypryk M, Gistynski B, Sadowska K, Herman P, Bujacz G, Lodyga-Chruscinska E, Sochacka E, Nawrot B. "C5-substituted 2-selenouridines ensure efficient base pairing with guanosine; consequences for reading the NNG-3' synonymous mRNA codons", *Int. J. Mol. Sci.* **2020**, 21, 2882-2905;
4. Bartosik K, Debiec K, Czarnecka A, Sochacka E, Leszczynska G. „Synthesis of nucleobase-modified RNA oligonucleotides by post-synthetic approach”, *Molecules*, **2020**, 25, 3344-3381;
5. Kulik K, Sadowska K, Wielgus E, Pacholczyk-Sienicka B, Sochacka E, Nawrot B "Different Oxidation Pathways of 2-Selenouracil and 2-Thiouracil, Natural Components of Transfer RNA", *Int J Mol Sci.* , **2020**; 21(17), 5956.
6. Debiec K, Matuszewski M, Podskoczyj K, Leszczynska G, Sochacka E. „Chemical synthesis of oligoribonucleotide (ASL of tRNA^{Lys} T.brucei) containing a recently discovered cyclic form of 2-methylthio-N6-threonylcarbamoyladenine (ms2ct6A)." *Chem. Eur. J.* **2019**, 25, 13309-13317;
7. Borowski R, Dziergowska A, Sochacka E, Leszczynska G. „Novel entry to the synthesis of (S)- and (R)-5-methoxycarbonylhydroxymethyluridines – diastereomeric pair of wobble tRNA nucleosides", *RSC Adv.*, **2019**, 9, 40507-40512.

Scientific projects:

OPUS 13; NCN „Synthesis and structural studies of oligonucleotides with tRNA anticodon arm containing new modified nucleosides: ct6A, ms2ct6A, ges2U ”; term from 21.02. **2018** to 20.02.**2022** No. UMO-2017/25/B/ST5/00971;

OPUS 15 NCN „ Why did Nature introduce selenium to nucleosides at the wobble position of bacterial tRNAs?", term from 24.01.**2019** to 24.01.**2023**. No 2018/29/B/ST5/02509; formal agreement No. 1/2019 was written between the Institute of Organic Chemistry of the Lodz University of Technology and CBMIM PAN in Lodz, represented by professor Barbara Nawrot.