Laboratoire de Chémo-Biologie Synthétique & Thérapeutique CBST
UMR 7199 | Université de Strasbourg – CNRS

CONFERENCE

Lundi 30 juin 2025 à 14h30
Faculté de Pharmacie
Amphi Métais

Versatility of Unnatural Nucleic Acids: Synthesis, Properties, and Applications in Chemical Biology

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La professeure Lo sera disponible le lundi matin et après-midi à la Faculté de Pharmacie. Si vous souhaitez la rencontrer, merci de contacter : alexandre.specht@unistra.fr ou frederic.bolze@unistra

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Abstract

In recent decades, natural nucleic acids have been extensively engineered and utilized in various applications due to their programmability, synthetic accessibility, and diverse functionality. However, the inherent limitations of natural oligonucleotides, such as their narrow chemical repertoire and susceptibility to nuclease degradation, have prompted the development of modified oligonucleotides with expanded functionalities at the nucleobase, sugar, and/or phosphate backbone levels. In this talk, I will present our recent progress in α-L-threose nucleic acid (TNA) research, encompassing its synthesis, chemical structure, physical and biological properties, as well as its diverse applications. TNA is an artificial nucleic acid analog that has been discovered to form stable antiparallel Watson−Crick duplex structures with complementary strands of itself, RNA, and DNA. TNA possesses a backbone composed of an unnatural four-carbon sugar, α-L-threose, with phosphodiester linkages connecting at the 2’ and 3’ vicinal positions of the sugar ring. Due to the chemical simplicity of threose sugar relative to ribose sugar and its ability to exchange genetic information between TNA and RNA, TNA has attracted significant interest as a potential RNA ancestor. My talk will begin with a historical account of the discovery of TNA, followed by discussions on the synthetic methods employed for its production and the distinctive features of its chemical structure. The thermodynamics and biocompatibility of TNA will also be presented. Furthermore, we will explore the potential of TNA-based antisense oligonucleotides as targeted treatments and diagnostic modalities in medicine, as well as the applications of TNA-based oligonucleotides in new materials for biomolecular detection.

References

1. P. Li, S. Zheng, H. M. Leung, L. S. Liu, T. J. H. Chang, A. Maryam, F. Wang *, Y. R. Chin *, **P. K. Lo**.* "TNA-Mediated Antisense Strategy To Knockdown Akt Genes For Triple-Negative Breast Cancer Therapy" *Small Methods* **2024**, 2400291.
2. P. Li, C. Zhu, L. S. Liu, T.J.H. Chang, H. C. Chu, Z. Li, Z. Mao, F. Wang, **P. K. Lo.*** “Ultra-stable threose nucleic acid-based biosensors for rapid and sensitive nucleic acid detection and in vivo imaging” *Acta Biomaterialia*, **2024**, 177, 472-485.
3. 6. D. Y. Tam, + P. Li, + L. S. Liu, F. Wang, H. M. Leung, **P. K. Lo**.* “Versatility of Threose Nucleic Acids: Synthesis, Properties, and Applications in Chemical Biology and Biomedical Advancements” *Chemical Communications* **2024**, 60, 11864 - 11889.
4. F. Wang, L. S. Liu, P. Li, C. H. Lau, H. M. Leung, Y R. Chin, C. Tin, **P. K. Lo***. “Cellular Uptake, Tissue Penetration, Biodistribution, and Biosafety of Threose Nucleic Acids: Assessing In Vitro and In Vivo Delivery” *Materials Today Bio* **2022**, *15*, 100299.

5. F. Wang, P. Li, H. C. Chu, **P. K. Lo**. “Nucleic Acids and Their Analogues for Biomedical Applications” *Biosensors* **2022**, 12(2), 93.
6. F. Wang, L. S. Liu, P. Li, H. M. Leung, D. Y. Tam, **P. K. Lo**. “Biologically Stable Threose Nucleic Acid-Based Probes for Real-Time microRNA Detection and Imaging in Living Cells” *Molecular Therapy - Nucleic Acids* **2022**, *27*, 787-796.
7. F. Wang, L. S. Liu, C. H. Lau, T. J. H. Chang, D. Y. Tam, H. M. Leung, C. Tin, **P. K. Lo**. “Synthetic α-L-Threose Nucleic Acids Targeting BcL-2 Show Gene Silencing and in Vivo Antitumor Activity for Cancer Therapy” *ACS Applied Materials & Interfaces* **2019**, *11*, 38510-38518.
8. L. S. Liu, H. M. Leung, D. Y. Tam, T. W. Lo, S. W. Wong, **P. K. Lo**. “α-L-Threose Nucleic Acids as Biocompatible Antisense Oligonucleotides for Suppressing Gene Expression in Living Cells” *ACS Applied Materials & Interfaces* **2018**, 10, 9736-9743.

Biography of Presenting Author:

Prof. Peggy Lo is currently an Associate Professor in the Department of Chemistry at City University of Hong Kong. She obtained her BSc degree (First Class) and MPhil degree from Hong Kong Baptist University, respectively. She then pursued her PhD degree in the Department of Chemistry at McGill University in Canada. Following her doctoral studies, she conducted postdoctoral research at Harvard University in the United States until her return to Hong Kong in 2012. Peggy Lo has received several prestigious awards, including the Dream Chemistry Awards Top 5 in the Institute of Physical Chemistry Polish Academy of Science in Poland in 2013, The President's Awards in 2016, and the Excellent Teaching Award in 2024. She has also won the Gold Medal at the 48th International Exhibition of Inventions Geneva for her innovative invention project "TNA-Based Probes for miRNA Detection". Her research area is highly interdisciplinary, encompassing chemistry, biology, nanotechnology, and materials science. She focuses on developing multifunctional nano-sized materials and applying them in biomedical and technological applications.