

# THE DARK PROTEOME: MICROPROTEINS AS NEW FRONTIERS IN CANCER BIOLOGY AND THERAPY

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**DATE: 26 March 2025 (Wednesday)**

**TIME: 14:00 - 15:00**

**VENUE: LT-11, John Chan Lecture Theatre, Yeung Kin Man Acad Building, CityU**

## Abstract:

Microproteins, encoded by small open reading frames (sORFs) have been historically overlooked and are rapidly reshaping our understanding of the proteome. However, large-scale, and confident identification of these microproteins has been technically challenging, compounded by the largely unknown functions of these entities. To address this issue, we have customized sample preparation and data analysis workflows and identified functionally important microproteins in cancer.

First, we compared more than ten methods and reported that size-exclusion chromatography (SEC) could simultaneously enrich and fractionate microproteins from complex proteomes. Next, we designed a Data-Independent Acquisition (DIA) workflow that leverages a fragmentation spectra predictor for the efficient construction of DIA libraries for microproteins, enabling sensitive identification of microproteins and high reproducibility. Using this optimized approach, we identified thousands of microproteins from cancer. Among them, a novel microprotein PPGLue encoded by a lncRNA, was significantly downregulated in drug-resistant HCC. In both in-situ cell assays and in-vivo animal tests, upregulation PPGLue restored the sensitivity of HCC and lung cancer cells to multiple drug treatments. PPGLue interacted with a phosphate, increasing the degradation of g-pg and intracellular accumulation of drug. We have also utilized other technologies to investigate biological functions of microproteins, such as CRISPR screening and AI-based bioinformatics.

Our work not only provides a robust workflow to identify novel proteins with multi-disciplinary technologies, deepens our understanding of human proteome, but also highlights the great potential of microprotein in cancer research and therapy.

## Speaker:

Professor Zhao Qian is currently an Associate Professor in the Department of Applied Biology and Chemical Technology at The Hong Kong Polytechnic University (PolyU). She obtained her Ph.D. in Chemistry from the University of Hong Kong and completed her postdoctoral training at the University of California, San Francisco. At PolyU, Prof. Zhao leads a research team dedicated to Functional Peptidomics, with a particular focus on peptides translated from small open reading frames (sORFs) and their presentation on cell membrane surfaces via MHC complexes. Her innovative work has resulted in over 30 SCI papers with 1,438 citations. Her publications include journals such as Nature Communications, Analytical Chemistry (AC), and Journal of the American Chemical Society (JACS), where she has served as the corresponding author. Her contributions to the peptidomics have been recognized with the awards "Rising Star in Proteomics and Metabolomics" in 2024 by Journal of Proteome Research and the "Rising Star in Mass Spectrometry" award in 2021 by Journal of the American Society for Mass Spectrometry. In the scientific community, Prof. Zhao serves as an editorial board member for Molecular & Cellular Proteomics, and as a council member of the global Human Proteome Organization (HUPO).

All are Welcome!

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