Curriculum Vitae

Name
Cheng-Chung Lee

Current Position
Associate Research Fellow
The Ph.D. Program for Translational Medicine, Taipei Medical University, Taipei, Taiwan

Email address
chengung@tmu.edu.tw

Education & Professional Experiences (Times New Roman, 11 point)

Education
2003–2008 Ph.D., Institute of Biochemistry and Molecular Biology, School of Life Sciences, National Yang Ming University, Taiwan
2000–2002 M.S., Graduate Institute of Biotechnology, College of Agriculture and Natural Resources, National Chung Hsing University, Taiwan
1996–2000 B.S., Department of Chemistry, College of Science, Tamkang University, Taiwan

Professional Experience
2008–2019 Institute of Biological Chemistry (IBC), Academia Sinica, Taipei, Taiwan — Postdoctoral Fellow; Senior Research Scientist (Taiwan Protein Project, TPP Flagship A3)
2020–2022 Senior Research Scientist, Genomics Research Center (TSPA), Academia Sinica, Taipei, Taiwan

Technology Transfer & Awards
2022 Technology Transfer: Antibodies to Interleukin-1β licensed to BioLegend, Inc.
2025 Future Tech Award: Revolutionary CAR-sEVs for Precision Medicine
2025 National Innovation Award: Heavy-Chain Antibody–Drug Conjugate Targeting CEACAM6

Research Interests (Times New Roman, 11 point)
Structural protein and antibody engineering, AI-driven binder design, and translational biologics development.

Selected Publications (※3-5 major papers)

1. Lu YT, Chen TY, Lin HH, Chen YW, Lin YX, Le DC, Huang YH, Wang AHJ, Lee CC*, Ling TY*. Small extracellular vesicles engineered using click chemistry to express chimeric antigen receptors show enhanced efficacy in acute liver failure. *J Extracell Vesicles.* 2025 Feb;14(2):e70044. doi: 10.1002/jev2.70044.
2. Lee CC, Kuo WC, Chang YW, Hsu SF, Wu CH, Chen YW, Chang JJ, Wang AHJ. Structure-Based Development of a Canine TNF-α-Specific Antibody Using Adalimumab as a Template. *Protein Sci.* 2024 Feb;33(2):e4873. doi: 10.1002/pro.4873.
3. Pao PJ, Hsu MF, Chiang MH, Chen CT, Lee CC*, Wang AHJ*. Structural basis of an epitope tagging system derived from Haloarcula marismortui bacteriorhodopsin I D94N and its monoclonal antibody GD-26. FEBS J. 2022 Feb;289(3):730-747. doi:

10.1111/febs.16184.
4. Lee CC, Su YC, Ko TP, Lin LL, Yang CY, Chang SSC, Roffler SR, WangAHJ. Structural basis of polyethylene glycol recognition by antibody. *J Biomed Sci.* 2020 Jan 7;27(1):12. doi: 10.1186/s12929-019-0589-7.
5. Lee CC, Maestre-Reyna M, Hsu KC, Wang HC, Liu CI, Jeng WI, Lin LL, Wood R, Chou CC, Yang JM, Wang AHJ. Crowning Proteins: Modulating the Protein Surface Properties using Crown Ethers. *Angew Chem Int Ed Engl.* 2014 Nov 24;53(48):13054-8. doi: 10.1002/anie.201405664.

Lecture Title

Structural Basis of Antibody-Mediated B-to-Z DNA Transition: Relevance to Autoimmunity.

Abstract (500 words maximum)

Anti-nuclear antibodies are central to autoimmune disease, yet the structural principles governing DNA recognition remain incompletely understood. DNA is not a static molecule; beyond the canonical right-handed B-form, it can adopt alternative conformations such as left-handed Z-DNA. This raises a fundamental question: does DNA topology influence antigenicity?

Here, we present the structural basis by which an antibody stabilizes the B-to-Z transition, providing a framework for understanding conformational DNA recognition in autoimmunity. Z-DNA is a left-handed double-helical form implicated in transcriptional regulation, immune responses, viral infection, bacterial biofilm formation, and autoimmune diseases. However, its intrinsic instability under physiological conditions has hindered detailed structural and functional investigation.

Although antibodies are known to recognize nucleic acids, the mechanisms by which they detect and stabilize dynamic DNA conformations remain unclear. In this study, we provide atomic-level structural insights into antibody-mediated B-to-Z DNA transition. A Z-DNA-specific chimeric Fab fragment (cZ22-Fab) derived from Z22 antibody was engineered and characterized. cZ22-Fab induces a concentration-dependent B-to-Z transition in CG-repeat DNA, establishing a stable 2:1 Fab/DNA stoichiometry. The crystal structure of the cZ22-Fab/Z-DNA complex reveals a left-handed, backbone-tracking recognition mode in which the antibody engages the zigzag phosphate backbone through phosphate-clamp interactions and base contacts. Notably, a 5′-end C-hanging Z-DNA duplex formed by $dC(GC)_3$ and stabilized by cZ22-Fab was observed. Structure-guided mutagenesis confirmed key residues for Z-DNA binding, and analysis of additional Z-DNA-forming sequences further defined the recognition features.

Collectively, these findings provide molecular insight into the mechanism of antibody-mediated Z-DNA formation and stabilization, highlighting broader implications for conformational DNA recognition and its relevance to autoimmunity.