Curriculum Vitae

Name
Shin-Fu Chen

Current Position
Assistant Professor, Department of Biochemistry and Molecular Biology, College of Medicine, Chang Gung University, Taiwan.

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Education & Professional Experiences

2025/08- Present	Assistant Professor, Department of Biochemistry and Molecular Biology, College of Medicine, Chang Gung University, Taiwan.
2025/02- 2025/07	Postdoctoral Fellow, National Taiwan University, Taipei, Taiwan
2019/09- 2024/09	Postdoctoral Fellow, Department of Biochemistry and Molecular Biology, McGovern Medical School, University of Texas Health Science Center at Houston, Houston, TX, USA
2009/09- 2018/06	PhD, Institute of Biochemistry and Molecular Biology, College of Medicine, National Taiwan University, Taipei, Taiwan
2005/09- 2009/06	BSc, School of Nutrition and Health Sciences, Taipei Medical University, Taipei, Taiwan

Research Interests
Molecular mechanisms of transcriptional regulation
Assembly and regulation of macromolecular complexes
Structural and functional impacts of disease-associated mutations
Structure-based drug development

Selected Publications

1. Ti-Chun Chao[†], **Shin-Fu Chen**[†], Hee Jong Kim, Hui-Chi Tang, Hsiang-Ching Tseng, An Xu, Leon Palao III, Subash Khadka, Tao Li, Mo-Fan Huang, Dung-Fang Lee, Kenji Murakami[#], Thomas G Boyer[#], Kuang-Lei Tsai[#] (2024) Structural basis of the human transcriptional Mediator regulated by its dissociable kinase module. *Mol Cell. 84*(20), 3932–3949.e10 ([†]co first author)
2. Ko-Ting Liu, **Shin-Fu Chen**, Nei-Li Chan (2024) Structural insights into the assembly of type IIA topoisomerase DNA cleavage-religation center. *Nucleic Acids Res.*, gkae657.
3. Jose J Gorbea Colón[†], Leon Palao[†], **Shin-Fu Chen**, Hee Jong Kim, Laura Snyder, Yi-Wei Chang[#], Kuang-Lei Tsai[#], Kenji Murakami[#] (2023) Structural basis of a transcription pre-initiation complex on a divergent promoter. *Mol Cell.* 83(4):574-588.e11. ([†]co first author)
4. **Shin-Fu Chen**, Nan-Lan Huang, Jung-Hsin Lin, Chyuan-Chuan Wu, Ying-Ren Wang, Yu-Jen Yu, Michael K. Gilson[#] and Nei-Li Chan[#]. (2018) Structural Insights into the Gating of DNA Passage by the Topoisomerase II DNA-Gate. *Nat. Commun.* 9, 3085.

5. Ying-Ren Wang, **Shin-Fu Chen**, Chyuan-Chuan Wu, Yi-Wen Liao, Te-Sheng Lin, Ko-Ting Liu, Yi-Song Chen, Tsai-Kun Li[#], Tun-Cheng Chien[#], and Nei-Li Chan[#]. (2017) Producing irreversible topoisomerase II-mediated DNA breaks by site-specific Pt(II)-methionine coordination chemistry. *Nucleic Acids Res.* 45, 10861-10871.

Lecture Title

Structural Insights into the Regulation of Human Transcription by the Mediator Complex and its Kinase Module

Abstract (500 words maximum)

The precise assembly and regulation of large macromolecular complexes are central to gene expression and cellular homeostasis. In eukaryotic transcription, the Mediator complex serves as a key integrative platform that relays regulatory signals from transcription factors to RNA polymerase II (Pol II). Human Mediator consists of a core complex (cMED) and a reversibly associated Mediator kinase module (MKM), composed of CDK8, Cyclin C, MED12, and MED13. Although MKM is known to inhibit Mediator-dependent transcription, the structural basis of this repression has remained poorly understood.

In this talk, I will present cryo-EM structures of the complete human Mediator complex, together with biochemical and functional analyses, to elucidate how the kinase module regulates Mediator function. The MKM is anchored to cMED through interactions involving MED12 and MED13. Our data support a mechanism in which transcriptional repression is mediated not by steric occlusion from the MKM rigid body itself, but by deployment of the MED13 intrinsically disordered region (IDR) to occupy key binding sites on cMED. In particular, the MED13 IDR occludes the Pol II C-terminal domain (CTD)-binding surface, thereby preventing Pol II recruitment and suppressing transcriptional activation.

These findings reveal an IDR-mediated regulatory strategy by which a dissociable module dynamically controls access to functional interfaces within Mediator. This mechanism provides new insight into transcriptional regulation and highlights potential avenues for structure-guided therapeutic intervention.