

# Yun-Ru (Ruby) Chen

陳韻如

## Current Position:

### Professor



#### Laboratory for Protein Misfolding and Neurodegenerative Diseases

Professor/Research Fellow

Division of Chemical Biology

Genomics Research Center

Academia Sinica

e-mail: [yrchen@gate.sinica.edu.tw](mailto:yrchen@gate.sinica.edu.tw)

website: <http://www.genomics.sinica.edu.tw/index.php/tw/chen-yun-ru-ruby->

office: +886-2-2787-1275; lab: +886-2-2789-8816

## Education:

1998-2003 (Ph.D.): Department of Molecular and Structural Biochemistry, North Carolina State University, USA (under Prof. A. Clay Clark's Laboratory)

1992-1996 (B.S.): Department of Agricultural Chemistry, National Taiwan University, Taiwan

## Professional Experience:

2022-2025 President-elect, Asia Pacific Protein Association (APPA)

2022-present: Adjunct Professor/ Adjunct Research Fellow, Biomedical Translation Research Center, Academia Sinica, Taiwan

2021-present Professor/Research Fellow, Genomics Research Center, Academia Sinica, Taiwan

2021-present Adjunct Professor, Dept. of Biochemical Science & Technology, National Taiwan University, Taiwan

2014-2021 Associate Research Fellow, Genomics Research Center, Academia Sinica, Taiwan

2015-2021 Adjunct Associate Professor, Dept. of Biochemical Science & Technology, National Taiwan University, Taiwan

2015-2019 The World Academy of Sciences (TWAS) Young Affiliate

2014-2017 Council Member of Asia Pacific Protein Association (APPA)

2007-2014 Assistant Research Fellow, Genomics Research Center, Academia Sinica, Taiwan

2006-2007 Postdoctoral Fellow, Genomics Research Center, Academia Sinica, Taiwan (Prof. Chi-Huey Wong Laboratory)

2004-2006 Postdoctoral Fellow, Dept. of Molecular Biology & Biochemistry, University of California, Irvine, USA (Prof. Charles C. Glabe Laboratory)

1998-1999 Teaching Assistant, Dept. of Molecular and Structural Biochemistry, North Carolina State University, USA

1996-1998 Research Assistant, Institute of Botany, Academia Sinica

## Research Interests:

**Protein Folding/Misfolding, Amyloids, and Neurodegenerative Diseases**

My research focuses on understanding the mechanism of protein misfolding diseases, amyloidosis, by various techniques including biochemical, biophysical, molecular, and cellular methods. Our long-term goal is to elucidate the disease mechanisms of amyloidosis in the aspects of protein folding and structure, pathogenic protein interactions, and relate the results to the medical consequences. We further utilize the knowledge to develop novel diagnostic means and therapeutic modalities. Many ageing-related neurodegenerative diseases such as *Alzheimer's disease (AD)* and *Parkinson's disease (PD)* belong to amyloidosis. Among them, AD is the most serious problem in the 21st century. Amyloidosis is caused by aggregation of misfolded proteins to form amyloid fibrils comprising specific cross- $\beta$  structures. Amyloid oligomers that exist in several neurodegenerative diseases imply a common toxicity mechanism in different neurodegenerative diseases. Currently, we are working on three amyloid and amyloid-like proteins and their interacting partners in neurodegenerative diseases. They are **amyloid- $\beta$**  ( $A\beta$ ) peptide and **tau** protein, the major substance in senile plaques and neurofibrillary tangles of AD patients respectively,  **$\alpha$ -synuclein**, the component of Lewy bodies in PD, and **TDP-43**, a novel inclusion found in a subtype of *frontotemporal lobar dementia (FTLD-U)*, *amyotrophic lateral sclerosis (ALS)*, and AD. We start from elucidating the mechanism of such aggregation and further developing the diagnostic method, antibodies, and small molecule inhibitors. Moreover, we study the structure, function, and interactions of the related glycan conjugates, precursor proteins, and modifiers. The major research interests are listed as follows:

- Protein folding and misfolding of amyloids in neurodegenerative diseases.
- Amyloid protein oligomerization and the toxicity mechanisms in neurodegenerative diseases.
- Interactions of proteins, glycans, and lipids with the proteins involved in pathogenesis of the neurodegenerative diseases.
- Drug screening, diagnostic, and therapeutic developments in neurodegenerative diseases.

## Honors:

- 2023 中華扶輪教育基金會 2022-23 年度「傑出/特殊人才」獎。Outstanding Award by Chung Hwa Rotary Education Foundation, 2022-2023.
- 2022 第 19 屆國家新創獎。「對抗漸凍人及相關神經退化疾病的結構專一型單株抗體」。  
The 19th National Innovation Award. "A novel conformation-dependent monoclonal antibody against ALS and related neurodegenerative diseases"
- 2021 第十九屆有庠科技論文獎 The 19<sup>th</sup> Y. Z. Hsu Scientific Paper Award, Far Eastern Y. Z. Hsu Science and Technology Memorial Foundation, 2021
- 2019 National China Youth Corps Youth Medal, Taiwan. 108 年度救國團青年獎章
- 2018 Selected work for Future Tech Exhibition "A novel potential therapeutic antibody to combat ALS and related neurodegenerative diseases". 技術團隊入選 2018 科技部未來科技展，作品"治療漸凍人及相關神經退化疾病的新穎抗體"
- 2018 年第 14 屆永信李天德青年醫藥科技獎 The 14<sup>th</sup> Young Investigator Award, TienTe Lee Biomedical Foundation
- 2017 Career Development Award, Academia Sinica 中央研究院前瞻計畫
- 2016 年中國化學會傑出青年化學家獎章 2016 Young Chemists Award of the Chemical Society, Taipei
- 104 年度科技部吳大猷先生紀念獎 2015 Ta-You Wu Memorial Award
- **2015 第三世界科學院年輕學者成員 TWAS Young Affiliate, 2015-2019, East & Southeast Asia and Pacific Region (International Award)**
- 2015 第十三屆有庠科技論文獎 The 13<sup>th</sup> Y. Z. Hsu Scientific Paper Award, Far Eastern Y. Z. Hsu Science and Technology Memorial Foundation, 2015

- 104 年度中央研究院年輕學者著作學獎 Academia Sinica Research Award for Junior Research Investigators, 2015
- **2015 Junior Faculty Award, the 12th International Conference on Alzheimer's Disease and Parkinson's Disease, 2015 (International Award)**
- 2014 財團法人吳健雄學術基金會 103 年度台灣女科學家新秀獎 Promising Women in Science Award, Wu Chieh Shiung Education Foundation, 2014
- 2013 中華民國生物物理學會 102 年度傑出年輕學者獎 Young Investigator Award, Biophysical Society of R.O.C., 2013
- 台灣臨床失智症學會財團法人立夫醫藥文教基金會學術獎第一名之指導教授 2012 和 2015，第二名之指導教授 2011，佳作指導教授 2014。 Taiwan Dementia Society, LiFu Medical Research Foundation Academic Award, Advisor of the 1<sup>st</sup> Price in 2012 and 2015, 2<sup>nd</sup> Price in 2011, excellent work in 2014.
- 台灣生物化學及分子生物學會年輕學者出國研習優秀論文獎助 The Taiwan Society for Biochemistry and Molecular Biology Traveling Fellowship, 2012  
2012 FAOBMB Congress

### **Publications in current position:**

1. Gary Jen-Wei Chen<sup>§</sup>, Ming-Yun Chang<sup>§</sup>, Xin-peng Lin, Yu-Jen Chang, and **Yun-Ru Chen\***. Tau destabilization accelerates fibrillization and modulates the seeding template effect. In preparation.
2. Yu-Jen Chang, Kai-Tai Lin, Orion Shih, Chi-Hua Yang, Ching-Yu Chuang, Ming-Han Fan, Yi-Chung Lee, Hung-Chih Kuo, Shang-Cheng Hung, Chi-Kuang Yao, U-Ser Jeng, **Yun-Ru Chen\***. Sulfated disaccharide protects membrane and DNA damages from poly-glycine-arginine in ALS. (2022) Submitted.
3. Wei-Wei Chang<sup>†</sup>, Yuh-Shen Lye<sup>†</sup>, Yao-Hsiang Shih<sup>†</sup>, Yu-Sheng Fang, Jeng-Jung Wu, Rong-Shou Chen, Justin Kwan, **Yun-Ru Chen\***. TDP-43-oligomer specific monoclonal antibodies identify TDP-43 oligomers in ALS patients and rescue abnormality in ALS mouse models. Submitted. (2022)
4. Tien-Ying Tsai<sup>§</sup>, Chun-Yu Chen<sup>§</sup>, Tien-Wei Lin, Tien-Chang Lin, Karan Chiu, Orion Shih, An-Chung Su, U-Ser Jeng, Hung-Chih Kuo, Chi-Fon Chang, and **Yun-Ru Chen\***. Amyloid Modifier SERF1a Interacts with PolyQ-expanded Huntingtin Exon 1 via Helical Interactions and Exacerbates PolyQ-induced Toxicity. Submitted.
5. Abnormal Auto-glycan Antibodies Predicts Preclinical Huntington's Disease by Ganglioside-focused Array. Tien-Wei Lin<sup>†</sup>, Jung-Kai Chang<sup>†</sup>, Yih-Ru Wu, Tsung-Hsien Sun, Yang-Yu Cheng, Chien-Tai Ren, Mei-Hung Pan, Kuo-Hsuan Chang, Hwai-I Yang, **Chiung-Mei Chen\***, **Chung-Yi Wu\***, and **Yun-Ru Chen\***. In revision.

### **Publications in current position:**

6. Jin-Lin Wu and **Yun-Ru Chen\***. Signal peptide stabilizes folding and inhibits misfolding of serum amyloid A. Protein Science. 31(12):e4485. (2022)
7. Wan-Chin Chiang<sup>§</sup>, Yu-Sheng Fang<sup>§</sup>, Yuh Shen Lye, Tzu-Yu Wong, Kiruthika Ganesan, Shih-

Han Huang, Lan-Yun Chang, Shih-Chieh Chou, **Yun-Ru Chen\***. Hyperphosphorylation-mimetic TDP-43 Drives Amyloid Formation and Possesses Neuronal Toxicity at the Oligomeric Stage. **ACS Chemical Neuroscience**. 13, 17, 2599–2612 (2022). (Selected as SI cover)

8. Jin-Lin Wu, Tung-Hung Su, Pei-Jer Chen, and **Yun-Ru Chen\***. Acute Phase Serum Amyloid A and its Prion-like Property as a Potential Serum Diagnosis Biomarker for Hepatocellular Carcinoma. **Scientific Reports**. 12:5799 (2022).
9. Yuh Shen Lye and **Yun-Ru Chen\***. TAR DNA-binding protein 43 Oligomers in Physiology and Pathology. Review. **IUBMB Life. Review**. 74(8):794-811 (2022)
10. Ming-Che Lee<sup>‡</sup>, Yi-Hung Liao<sup>‡</sup>, Shih-Hui Chen, and **Yun-Ru Chen\***. Amyloid- $\beta$  E22K Fibril in Familial Alzheimer's Disease is More Thermo-stable and Susceptible to Seeding. **IUBMB Life**. 74(8):739-747. (2021) (Cover Story)
11. Katrin H. P. Vu, Ming-Che Lee, Gerhard H. Blankenburg, Yu-Jen Chang, Ming-Lee Chu, Andreas Erbe, Leonardo Lesser-Rojas, **Yun-Ru Chen\***, and **Chia-Fu Chou\***. Time-evolved SERS signatures of DEP-trapped A $\beta$  and Zn<sup>2+</sup>A $\beta$  peptides revealed by a sub-10 nm electrode nanogap. **Analytical Chemistry**. 93(49):16320-16329 (2021) (Supplementary Cover Story)
12. Ya-Ling Chiang, Yu-Jen Chang, **Yun-Ru Chen\***, and **Ing-Shouh Hwang\***. Effects of dissolved gases on the amyloid fibril morphology. **Langmuir**. 37, 1, 516–523 (2021) (IF=3.882)
13. Yao-Hsiang Shih $\S$ , Ling-Hsien Tu $\S$ , Ting-Yu Chang, Kiruthika Ganesan, Wei-Wei Chang, Pao-Sheng Chang, Yu-Sheng Fang, Yeh-Tung Lin, Lee-Way Jin, and **Yun-Ru Chen\***. TDP-43 interacts with amyloid- $\beta$ , inhibits fibrillization, and worsens pathology in a model of Alzheimer's disease. **Nature Communications**. 11: 5950 (2020) (IF=14.919, times cited=25) (selected as annual important publication in Academia Sinica)  
Research Highlights in Press:
  - GRC: <https://www.genomics.sinica.edu.tw/index.php/tw/news/lastest-news/637-tdp-43>
  - Liberty Times 自由時報: <https://news.ltn.com.tw/news/life/paper/1415430>
  - UDN 聯合新聞網: <https://udn.com/news/story/7266/5047708>
  - 民視: <https://www.ftvnews.com.tw/news/detail/2020B27L04M1>
  - Radio Taiwan International 中央廣播電台 <https://www.rti.org.tw/news/view/id/2085768>
14. Phillip Smethurst, Emmanuel Risse, Giulia E. Tyzack, Jamie S. Mitchell, Doaa M. Taha, **Yun-Ru Chen**, Jia Newcombe, John Collinge, Katie Sidle and Rickie Patani\*. Distinct responses of neurons and astrocytes to TDP-43 proteinopathy in amyotrophic lateral sclerosis. **Brain**. 143 (2):430-440 (2020) (IF=13.501, times cited=30)
15. Shih-Ling Huang, Lien-Szu Wu, Min Lee, Chin-Wen Chang, Wei-Cheng Cheng, Yu-Sheng Fang, **Yun-Ru Chen**, Pei-Lin Cheng, Che-Kun James Shen\*. A Robust TDP-43 Knock-In Mouse Model of ALS. **Acta Neuropathologica Communications** (2020) 8(1):3. (IF=7.801, times cited=12)
16. Ling-Hsien Tu, Ning-Hsuan Tseng, Ya-Ru Tsai, Tien-Wei Lin, Yi-Wei Lo, Jien-Lin Charng, Hua-Ting Hsu, Yu-Sheng Chen, Rong-Jie Chen, Ying-Da Wu, Yi-Tsu Chan, Chang-Shi Chen, **Jim-Min Fang\***, and **Yun-Ru Chen\***. Rationally Designed Divalent Caffeic Amides Inhibit Amyloid- $\beta$  Fibrillization, Induce Fibril Dissociation, and Ameliorate Cytotoxicity. **European**

**Journal of Medicinal Chemistry**. 158: 393-404 (2018) (IF=6.514, times cited=4)

17. Chia-Jung Kuo, Hsu-Cheng Chiang, Chi-Ang Tseng, Chin-Fu Chang, Rajesh Kumar Ulaganathan, Tzu-Ting Ling, Yu-Jen Chang, Chiao-Chen Chen, Yun-Ru Chen, and Yit-Tsong Chen\*. A Lipid-Modified Graphene-Transistor Biosensor for Monitoring Amyloid- $\beta$  Aggregation. **ACS Applied Materials & Interfaces**. 10(15):12311-12316 (2018) (IF=9.229, times cited=13)
18. Ming-Che Lee, Wan-Cheng Yu, Yao-Hsiang Shih, Chun-Yu Chen, Zhong-Hong Guo, Shing-Jong Huang, Jerry C. C. Chan, and Yun-Ru Chen\*. Zinc ion rapidly induces toxic, off-pathway amyloid- $\beta$  oligomers distinct from amyloid- $\beta$  derived diffusible ligands in Alzheimer's disease. **Scientific Reports** 8, Article number: 4772 (2018) (IF=4.379, times cited=72)
19. Tien-Wei Lin, Chi-Fon Chang, Yu-Jen Chang, Yi-Hung Liao, Hui-Ming Yu, and Yun-Ru Chen\*. Alzheimer's Amyloid- $\beta$  A2T Variant and its N-terminal Peptides Inhibit Amyloid- $\beta$  Fibrillization and Rescue the Induced Cytotoxicity. **PLoS One**. 12(3):e0174561 (2017) (IF=3.240, times cited=25)
20. Smethurst, Phillip\*; Newcombe, Jia; Troakes, Claire; Simone, Roberto; Wadsworth, John; Hardy, John; Chen, Yun-Ru; Patani, Rickie; Sidle, Katie. In vitro prion-like mechanisms of TDP-43 in ALS. **Neurobiology of Disease**, 96:236-247 (2016) (IF=5.996, times cited=91)
21. Nguyen Quoc Thai, Ning-Hsuan Tseng, Mui Thi Vu, Tin Trung Nguyen, Huynh Quang Linh, Chin-Kun Hu\*, Yun-Ru Chen\*, and Mai Suan Li\*. Discovery of DNA dyes Hoechst 34580 and 33342 as good candidates for Alzheimer's disease: in silico and in vitro study. **Journal of Computer-Aided Molecular Design**, Aug;30(8):639-50 (2016) (IF=3.686, times cited=9)
22. Yu-Jen Chang, Nguyen Hoang Linh, Yao-Hsiang Shih, Hui-Ming Yu, Mai Suan Li\*, and Yun-Ru Chen\*. Alzheimer's Amyloid- $\beta$  Sequesters Caspase-3 in vitro via its C-terminal Tail. **ACS Chemical Neuroscience**, 7(8):1097-106 (2016) (IF=4.418, times cited=14)
23. Yu-Jen Chang, U-Ser Jeng, Ya-Ling Chiang, Ing-Shouh Hwang, and Yun-Ru Chen\*. The Glycine-Alanine Dipeptide Repeat from C9orf72 Hexanucleotide Expansions Forms Toxic Amyloids Possessing Cell-to-cell Transmission Properties. **J Biol. Chem.**, 291(10):4903-11. (2016) (IF=5.157, times cited=97)
24. Chia-Wei Lee, Lan-Ling Jang, Huei-Jyuan Pan, Yun-Ru Chen, Chih-Cheng Chen, and Chau-Hwang Lee. "Membrane roughness as a sensitive parameter reflecting the status of neuronal cells in response to chemical and nanoparticle treatments". **Journal of Nanobiotechnology**, 14:9. (2016) (IF=10.435, times cited=20)
25. Yi-Hung Liao and Yun-Ru Chen\*. A novel method for expression and purification of authentic amyloid- $\beta$  with and without 15N labels. **Protein expression and purification**, 113, 63-71. (2015) (IF=1.650, times cited=14)
26. Patricia F. Kao, Yun-Ru Chen, Xiao-Bo Liu, Charles DeCarli, William W. Seeley, and Lee-Way Jin\*. Detection of TDP-43 oligomers in frontotemporal lobar degeneration-TDP. **Annals of Neurology**, 78(2):211-21. (2015) (IF=10.422; times cited=24)

27. Yu-Sheng Fang, Kuen-Jer Tsai, Yu-Jen Chang, Patricia Kao, Rima Woods, Pan-Hsien Kuo, Cheng-Chun Wu, Jih-Ying Liao, Shih-Chieh Chou, Vinson Lin, Lee-Way Jin, Hanna S. Yuan, Irene H Cheng, Pang-Hsien Tu, and **Yun-Ru Chen\***. "Full-Length TDP-43 Forms Toxic Amyloid Oligomers that are Present in Frontotemporal Lobar Dementia-TDP Patients." **Nature Communications**, 5:4824 (2014) (IF=14.919; times cited=128, R/C=4/73, Multidisciplinary Sciences)  
Research Highlights in Press
- Alzforum News: <http://www.alzforum.org/news/research-news/does-tdp-43-oligomerize-and-coax-av-do-same>
  - PTS News Network 公視新聞: <https://www.youtube.com/watch?v=N1QNiBg4uFw#action=share>
  - CTS News Magazine 華視新聞雜誌專訪: <https://www.youtube.com/watch?v=aVIVrimF4J0&feature=youtu.be>
  - UDN 聯合新聞網專訪: <https://video.udn.com/news/254960>
  - United Daily News 聯合報
  - China Times 中國時報
28. Yu-Jen Chang and **Yun-Ru Chen\***. The Co-existence of an Equal Amount of Alzheimer's Amyloid- $\beta$  40 and 42 forms Structurally Stable and Toxic Oligomers through a Distinct Pathway. **FEBS Journal**, 281, 2674-2687 (2014) (IF=5.542, times cited=45)
29. Huei-Jyuan Pan, Ruei-Lin Wang, Jian-Long Xiao, Yu-Jen Chang, Ji-Yen Cheng, **Yun-Ru Chen**, and Chau-Hwang Lee\*. Using optical profilometry to characterize cell membrane roughness influenced by Amyloid-beta peptide and electric fields. **Journal of Biomedical Optics**, 19 (1):011009 (2014) (IF=3.170, times cited=9)
30. Man Hoang Viet, Chun-Yu Chen, Chin-Kun Hu, **Yun-Ru Chen\***, and Mai Suan Li\*. Discovery of Dihydrochalcone as a potential lead for Alzheimer's disease: in silico and in vitro study. **PLoS One**, 8(11):e79151. (2013) (IF=3.057, times cited=30)
31. Wei-Chieh Cheng\*, Chen-Yi Weng, Wen-Yi Yun, Shang-Yu Chang, Yu-Chun Lin, Fuu-Jen Tsai, Fu Yung Huang, **Yun-Ru Chen**. Rapid modifications of *N*-substitution in iminosugars: Development of new  $\beta$ -glucocerebrosidase inhibitors and pharmacological chaperones for Gaucher disease. **Bioorganic & Medicinal Chemistry**, 21(17) 5021-5028. (2013) (IF=3.641, times cited=30)
32. Rong-Jie Chen, Wei-Wei Chang, Yu-Chun Lin, Pei-Lin Cheng, and **Yun-Ru Chen\***. Alzheimer's Amyloid- $\beta$  Oligomers Rescue Cellular Prion Protein Induced Tau Reduction via Fyn pathways. **ACS Chemical Neuroscience**, 4(9):1287-96. (2013) (IF=4.418, times cited=29)
33. Yi-Ting Wang, Pan-Hsien Kuo, Chien-Hao Chiang, Jhe-Ruei Liang, **Yun-Ru Chen**, Shuying Wang, James C. K. Shen, and Hanna S. Yuan. The truncated C-terminal RRM domain of TDP-43 plays a key role in forming proteinaceous aggregates. **J Biol. Chem.**, 288 (13), 9049-57. (2013) (IF=5.157, times cited=95)
34. Winny Ariesandi, Chi-Fon Chang, Tseng-Erh Chen, and **Yun-Ru Chen\***. Temperature-dependent structural changes of Parkinson's  $\alpha$ -synuclein reveal the role of pre-existing oligomers in  $\alpha$ -synuclein fibrillization. **PLoS One**, 8(1):e53487. (2013) (IF=3.057, times cited=30)

35. Yi-Hung Liao, Yu-Jen Chang, Yuji Yoshiike, Yun-Chorng Chang\*, and **Yun-Ru Chen**\*. Negatively charged gold nanoparticles inhibit Alzheimer's amyloid- $\beta$  fibrillization, induce fibril dissociation, and mitigate neurotoxicity. **Small**, 8(23):3631-3639. (2012) (IF=13.281, times cited=251).
36. Wei-Ting Chen, Chen-Jee Hong, Ya-Tzu Lin, Wen-Han Chang, He-Ting Huang, Jih-Ying Liao, Yu-Jen Chang, Yi-Fang Hsieh, Chih-Ya Cheng, Hsiu-Chih Liu, **Yun-Ru Chen**\*, and Irene H Cheng \*. Amyloid-beta ( $A\beta$ ) D7H mutation increases oligomeric  $A\beta_{42}$  and alters properties of  $A\beta$ -zinc/copper assemblies. **PLoS One**, 7(4): e35807. (2012) (IF=3.240, times cited=108).
37. Chun-Lun Ni, Hoi-Ping Shi, Hui-Ming Yu, Yun-Chorng Chang, and **Yun-Ru Chen**\*. Folding Stability of Amyloid- $\beta_{40}$  Monomer is an Important Determinant of the Nucleation Kinetics in Fibrillization. **FASEB J.**, 25(4), 1390-401. (2011) (featured as a key scientific article in **Global Medical Discovery**) (IF=5.191, times cited=50)
38. Wei-Ting Chen, Yi-Hung Liao, Hui-Ming Yu, Irene Cheng, and **Yun-Ru Chen**\*. Distinct Effects of  $Zn^{2+}$ ,  $Cu^{2+}$ ,  $Fe^{3+}$ , and  $Al^{3+}$  on Amyloid- $\beta$  Stability, Oligomerization, and Aggregation: Amyloid- $\beta$  Destabilization Promotes Annular Protofibril Formation. **J Biol. Chem.**, 286 (11), 9646-56. (2011) (IF=5.157; times cited=183)
39. Ni-Shian Lin, John Ching-Hao Chao, Fang-Chieh Chou, Chi-Fon Chang, **Yun-Ru Chen**, Yu-Jen Chang, Shing-Jong Huang, Wei-Hsiang Tseng, and Jerry C. C. Chan. Molecular Structure of Amyloid Fibrils Formed by Residues 127 to 147 of the Human Prion Protein. **Chemistry - A European Journal**, 16(18), 5492-9 (2010) (IF=5.236, times cited=16)
40. Yuji Yoshiike, Ryoichi Minai, Yo Matsuo, **Yun-Ru Chen**, Tetsuya Kimura, Akihiko Takashima. Amyloid Oligomer Conformation in a Group of Natively Folded Proteins. **PLoS One**, 3(9), e3235 (2008) (IF=3.240, times cited=79)

### **Publications prior to current position:**

41. **Yun-Ru Chen**, Charles G. Glabe\*. Distinct Early Folding and Aggregation Properties of Alzheimer Amyloid- $\beta$  Peptide  $A\beta_{40}$  and  $A\beta_{42}$ : Stable Trimer or Tetramer Formation by  $A\beta_{42}$ . **J Biol. Chem.**, Aug 25;281(34):24414-22 (2006) (IF=5.157; times cited=262)
42. **Yun-Ru Chen**, A. Clay Clark\*. Substitutions of prolines examine their role in kinetic trap formation of the caspase recruitment domain (CARD) of RICK. **Protein Science**. Mar;15(3):395-409 (2006) (IF=6.725, times cited=9)
43. **Yun-Ru Chen**, A. Clay Clark\*. Kinetic traps in the folding/unfolding of procaspase-1 CARD Domain. **Protein Science**. Aug;13(8):2196-206. (2004) (IF=6.725, times cited = 24)
44. **Yun-Ru Chen**, A. Clay Clark\*. Equilibrium and Kinetic Folding of the  $\alpha$ -Helical Greek Key Protein Domain: Caspase Recruitment Domain (CARD) of RICK. **Biochemistry**, 42(20); 6310-6320. (2003) (IF=3.162, times cited = 23)
45. Pop C, **Chen YR**, Smith B, Bose K, Bobay B, Tripathy A, Franzen S, Clark AC\*. Removal of the pro-domain does not affect the conformation of the procaspase-3 dimer. **Biochemistry**. Nov 27; 40(47);14224-14235. (2001) (IF=3.162, times cited = 78)

46. Y. Y. Charng, C. W. Sun, S. L. Yan, S. J. Chou, **Y. R. Chen** and S. F. Yang\*. cDNA sequence of a putative ethylene receptor from carnation petals. **Plant Physiol.** 115. 863. (1997) (IF=8.340)

## Book Chapter

1. Chang, Y.J. and **Chen, Y.R.\*** (2017). "Folding and Misfolding of Amyloid- $\beta$  40 and 42 in Alzheimer's Disease" in Yuan, J.M and Zhou, H.X. (Ed.), "Biophysics and biochemistry of protein aggregation". Singapore, World Scientific.

## Conference Publication:

1. **Yun-Ru Chen\***. Recombinant TDP-43 Forms Toxic and Stable Amyloid-like Oligomers. **Alzheimer's and Dementia**, ISSN: 1552-5260, Vol: 6, Issue: 4, e44 (2010)

## Patent

1. US 9796778 B1. ANTIBODIES AGAINST PATHOLOGICAL FORMS OF TDP-43 AND USES THEREOF. **Yun-Ru Chen.** (2017.10.24-2035.9.14)
2. 台灣專利 I592423 B.可辨識致病性 TDP-43 之抗體及其用途 (2017.7.21-2035.3.8)

## Selected Presentations:

### Invited Oral Presentations since 2006 (Talk abroad) (Invited Talk in Major Scientific Conferences)

1. **Aug. 30-Sep. 01. NSRRC 2022 Annual Users' Meeting & Workshops.** NSRRC, Hsinchu, Taiwan. "Investigating Structure-function Relationship of Dipeptide Repeats in Neurodegenerative Diseases"
2. March 15-20. **The International conference on Alzheimer's and Parkinson's diseases AD/PD 2022, Barcelona, Spain.** (virtual) "TDP-43 Promotes Amyloid- $\beta$  Oligomerization via Interaction and Worsens Pathology in a model of Alzheimer's disease"
3. Nov. 30, 2021. **Dept. of Biomedical Sciences and Engineering, National Central University, Taoyuan, Taiwan.** "From Protein Misfolding to Translational Medical Research for Alzheimer's Disease and ALS"
4. Nov. 19 2021. **The 25th Biophysics Conference, National Cheng-Kung Univ., Tainan, Taiwan. Plenary Talk** "Investigation of misfolded TDP-43 oligomers and its role in Alzheimer's Disease"
5. Apr. 22, 2021. IUBMB focused meeting on "Neurodegenerative Diseases", Academia Sinica, Taipei, Taiwan." Investigation of the Role of TDP-43 in Alzheimer's Disease". Main Organizer. (Chair of the Organizing Committee)
6. Jul. 7, 2020 (postponed). **World Conference on Protein Science, Sapporo, Japan.** "TBA"
7. Nov. 17, 2019. THE TAIWAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY (TSMBM) annual symposium. "Neurodegenerative Diseases" Organizing committee. "TDP-43 Interacts with Amyloid- $\beta$  and Exacerbates Pathology of Alzheimer's Disease"
8. Oct. 3, 2019. **Asian Pacific Prion Symposium 2019, RIKEN, Wako, Saitama, Japan.** "Tau destabilization accelerates fibrillization and modulates the seeding template effect"
9. Jul. 29, 2019. **RIKEN Symposium: "Understanding the molecular basis of neuropsychiatric disorders", RIKEN Center for Brain Science, Wako, Saitama, Japan.** "Understanding Protein



Misfolding of TDP-43 and Dipeptide Repeats in FTD/ALS and Developing Therapeutic Potentials”

10. Jun. 13, 2019, **FASEB Summer Conference: The Protein Aggregation Conference: From Structure to In Vivo Sequelae, Snowmass Village, CO, USA.** “TDP-43 Interacts with Amyloid- $\beta$  and Exacerbates Pathology of Alzheimer’s Disease”
11. Mar. 27, 2019. **The 14th International conference on Alzheimer’s and Parkinson’s diseases AD/PD 2019, Lisbon, Portugal.** “TDP-43 interacts with amyloid- $\beta$  and exacerbates pathology of Alzheimer’s disease”.
12. Jan. 24, 2019. **RIKEN Symposium: “Recent Progress in Protein Conformation and Aggregation”, RIKEN Center for Brain Science, Wako, Saitama, Japan.** “From Protein Misfolding to Translational Medical Research for Alzheimer’s Disease and ALS”
13. Dec. 13, 2018. Frontier research in Alzheimer’s disease, Academia Sinica, Taipei, Taiwan. “Discovery of TDP-43 oligomer and the role in Alzheimer’s disease”
14. Dec. 2, 2018. **Asian Biophysics Association Symposium (ABA2018), Melbourne, Australia.** “Protein Misfolding and Therapeutics in Neurodegenerative Diseases”.
15. Nov. 24, 2018. **The 4th Taiwan International Congress of Parkinson’ Disease and Movement Disorders (4th TIC-PDMD), Taipei, Taiwan.** “TDP-43 aggregation and therapeutic development in neurodegenerative diseases”
16. Nov. 22, 2018. **Biomedical Lecture, Taipei Medical University, Taipei, Taiwan.** “From Protein Misfolding to Translational Medical Research for Alzheimer’s Disease and ALS”北醫 姆山生物醫學講座
17. Oct. 20, 2017. **Dept. of Neurology, National Taiwan University Hospital, National Taiwan University, Taipei, Taiwan.** “From Protein Misfolding to Translational Medical Research for Alzheimer’s Disease and ALS”
18. Aug. 18, 2017. **Inst. of Brain Science, National Yang-Ming University, Taipei, Taiwan.** “From Protein Misfolding to Translational Medical Research for Alzheimer’s Disease and ALS”
19. Jul. 12<sup>th</sup>, 2017. **The 5th Asia Pacific Protein Association Conference, 12th International Symposium of the Protein Society of Thailand, Bangsaen, Thailand.** “Understanding Amyloids in Neurodegenerative Diseases”.
20. May. 5, 2017. **Dept. of Biochemistry, National Yang-Ming University, Taipei, Taiwan.** “Understanding Amyloids and Finding Opportunities toward Combating Neurodegenerative Diseases”
21. Apr. 1, 2017. **The 13th International conference on Alzheimer’s and Parkinson’s diseases AD/PD 2017, Vienna, Austria.** “Understanding TDP-43 Oligomers and Dipeptide Repeats in Frontotemporal Dementia and Amyotrophic Lateral Sclerosis”
22. Mar. 24, 2017. **Osaka University/Genomics Research Center Workshop, Academia Sinica, Taipei, Taiwan.** “Understanding Amyloids in Neurodegenerative Diseases”.
23. Jan. 27, 2017. **IPR Seminar / RIKEN Symposium / MEXT Kakenhi “Nascent Chain Biology: New Frontiers in Protein Misfolding and Aggregation, Osaka University, Osaka, Japan.** “Understanding TDP-43 Oligomers and Dipeptide Repeats in Frontotemporal Dementia and Amyotrophic Lateral Sclerosis”
24. Jan. 12, 2017. **Inst. of Medical Sciences, Tzu Chi University, Hualien, Taiwan.** “Understanding Amyloid Oligomers and Finding Opportunities toward Combating Neurodegenerative Diseases: Stories of Amyloid- $\beta$  and TDP-43”
25. Nov. 2, 2016. **Dept. of Biomedical Engineering and Environmental Sciences, National Tsing Hua University, Hsinchu, Taiwan.** “Understanding Amyloid Oligomers and Finding Opportunities toward Combating Neurodegenerative Diseases”
26. Oct. 17, 2016. **The 23rd East Asia Joint Symposium, the 15th Cross-Strait Symposium on Biomedical Research and the 13th Symposium of the Frontiers of Biomedical Sciences,**

- Taipei, Taiwan.** “Full-length TDP-43 Forms Toxic Amyloid Oligomers in Frontotemporal Lobar Dementia-TDP Patients and Disturbs Amyloid- $\beta$  Fibrillization”
27. Oct. 7, 2016. **Sunney Chan Symposium: Membrane Proteins: Biochemistry, Diseases, and Energy. Academia Sinica, Taipei, Taiwan.** “Investigation of Pathogenic Proteins in Amyotrophic Lateral Sclerosis: TDP-43 and Dipeptide Repeats”
  28. Aug. 8, 2016. **Gordon Conference: Neurobiology of Brain Disorder, Girona, Spain.** “The Discovery of Toxic TDP-43 Oligomers in TDP-43 Proteinopathies” (The only speaker from Asia)
  29. Jul. 23, 2016. **生技展 BioTaiwan Exhibition, Taipei, Taiwan.** “A novel antibody for neurodegenerative diseases”
  30. May 9, 2016. **Dept. of Life Science, National Taiwan University, Taipei, Taiwan.** “Understanding Amyloid Oligomers and Finding Opportunities toward Combating Neurodegenerative Diseases”
  31. Apr. 20, 2016. **Taipei Medical University, Taipei, Taiwan.** “Understanding Amyloid Oligomers and Finding Opportunities toward Combating Neurodegenerative Diseases”
  32. Dec. 17, 2015. **神經疾病產學交流研討會, Academia Sinica, Taipei, Taiwan.** “Discovery of Amyloid Oligomers in Neurodegenerative Diseases”
  33. Nov. 27, 2015. **Dept. of Life Science, National Normal University, Taipei, Taiwan.** “Understanding amyloid oligomers and finding opportunities toward combating neurodegenerative diseases”
  34. Yun-Ru Chen. (Nov. 16, 2015). **Protein Structure and Function-Joint Symposium between the Institute for Protein Research (Osaka University) and the Research School of Chemistry (Australian National University), Australia National University, Canberra, Australia.** “Discovery of Amyloid Oligomers of TDP-43 in Neurodegenerative Diseases”
  35. Yun-Ru Chen. (Oct. 16, 2015). **RIKEN-Academia Sinica Joint Conference on Chemical Biology, Academia Sinica, Taipei, Taiwan.** “Understanding the Mechanism of Amyloid Formation: Stories of Amyloid- $\beta$  and TDP-43”
  36. Yun-Ru Chen. (Jun. 14, 2015). **Symposium of Taiwan Dementia Society, Taipei General Veteran Hospital, Taipei, Taiwan.** “An emerging new player in frontotemporal lobar dementia, amyotrophic lateral sclerosis, and Alzheimer’s disease”
  37. Yun-Ru Chen. (Apr. 23, 2015). **Dept. of Biochemical Science & Technology, National Taiwan University, Taipei, Taiwan.** “Understanding structure and function of amyloid- $\beta$  and TDP-43 oligomers and the opportunities toward combating neurodegenerative diseases”
  38. Yun-Ru Chen. (Mar. 21, 2015) **The 12th International conference on Alzheimer’s and Parkinson’s diseases AD/PD 2015, Nice, France.** “Full-length TDP-43 Forms Toxic Amyloid Oligomers that are Present in Frontotemporal Lobar Dementia-TDP Patients”
  39. Yun-Ru Chen. (Nov. 21, 2014) **The 2nd Korea-Taiwan International Biophysics Workshop, Pusan, Korea.** “Understanding the mechanism of amyloid Formation: Stories of Amyloid- $\beta$  and TDP-43”
  40. Yun-Ru Chen. (Nov. 7, 2014) **The 2nd Proteostasis & Disease Symposium, Wollongong, Australia.** “Full-length TDP-43 Forms Toxic Amyloid Oligomers that are Present in Frontotemporal Lobar Dementia-TDP Patients”
  41. Yun-Ru Chen. (Oct. 9, 2014) **National Tsing-Hua University Life Science Seminar Series, Taipei, Taiwan.** “Understanding the mechanism of amyloid Formation: Stories of Amyloid- $\beta$  and TDP-43.”
  42. Yun-Ru Chen. (Oct. 6, 2014) **Taipei General Veteran Hospital, Dept. of Neurology Seminar, Taipei, Taiwan.** “Understanding Amyloid- $\beta$  and TDP-43 Oligomers and the Opportunities toward Combating the Neurodegenerative Diseases.”
  43. Yun-Ru Chen. (March 21, 2014) **National Yang-Ming University Biomedical Seminar Series, Taipei, Taiwan.** “Understanding the Formation and Function of Amyloid Oligomers in

Neurodegenerative Diseases: Alzheimer's A $\beta$ , Parkinson's alpha-synuclein, and FTL-D-U/ALS's TDP-43."

44. Yun-Ru Chen. (May 15, 2013) **National Taiwan University Hospital Seminar Series, Taipei, Taiwan.** "Pathogenic Amyloid Proteins in Neurodegenerative Diseases."
45. Yun-Ru Chen. (Jun. 2013) **The 18<sup>th</sup> Biophysics Conference, Taipei, Taiwan. Young Investigator Award Lecture** "The Role of Amyloid Oligomers in Amyloid Fibrillization: Amyloid- $\beta$  in Alzheimer's Disease and  $\alpha$ -Synuclein in Parkinson's Disease."
46. Yun-Ru Chen. (May. 2013) **Frontier in Neurodegenerative Diseases and Beyond-From Basic to Translational, Taipei, Taiwan.** "Distinct, Toxic Oligomer Formation during Co-existence of Alzheimer's amyloid- $\beta$  40 and 42"
47. Yun-Ru Chen. (Oct. 2012) **Annual Meeting of Society of Neuroscience (SfN), New Orleans, Louisiana, USA.** "Distinct, Toxic Oligomer Formation during Co-existence of Alzheimer's amyloid  $\beta$  40 and 42"
48. Yun-Ru Chen. (Nov. 2011) **Annual Meeting of Taiwan Society of Biochemistry and Molecular Biology, Taiwan.** "Oligomerization and its Associated Toxicity in Amyloid- $\beta$  in Alzheimer's Disease".
49. Yun-Ru Chen. (June 14, 2010) **IPR Seminar: Cooperation in Protein Science between Asian and Pacific Countries, Osaka University, Osaka, Japan.** "Folding Stability and Native Conformation of Amyloid- $\beta$  Monomer are Important Determinants of the Nucleation Kinetics and Fibril Formation."
50. Yun-Ru Chen. (Jan. 28-29, 2010) **NCTS January Workshop on Critical Phenomena and Complex Systems, National Center for Theoretical Sciences and Inst. of Physics, Academia Sinica.** "The Conformation Stability and Aggregation Mechanism of Amyloid- $\beta$ ".
51. Yun-Ru Chen. (May 19-21, 2010) **15<sup>th</sup> Joint Biophysics Conference, Taipei, Taiwan.** "Folding Stability and Native Conformation of Amyloid- $\beta$  Monomer are Important Determinants of the Nucleation Kinetics and Fibril Formation".
52. Yun-Ru Chen. (April, 2009) **PepCon-2009, Seoul, Korea.** "The conformational Stability and Aggregation Mechanisms of Amyloid  $\beta$  in Alzheimer Disease".
53. Yun-Ru Chen. (Jun. 4-5, 2009) **Frontier of Protein Aggregation and Neurodegenerative Diseases, Taipei, Academia Sinica.** "The Conformation Stability and Aggregation Mechanism of Amyloid- $\beta$ ".
54. Yun-Ru Chen. (Jul. 27-28, 2009) **NCTS July Workshop on Critical Phenomena and Complex Systems.** "Conformational Stability of Amyloid- $\beta$  Predominantly Determines the Nucleation Phase of Fibrillization".
55. Yun-Ru Chen. (Oct. 12-13, 2007) **NCTS July Workshop on Critical Phenomena and Complex Systems.** "Equilibrium Folding and Aggregation of Wild Type and Familial Mutants of Amyloid- $\beta$  in Alzheimer's Disease".
56. Yun-Ru Chen. (August, 2007) **Neuroscience Society of Taiwan, Hua Lien, Taiwan.** "Equilibrium Folding and Aggregation Properties of Wild Type and Familial Mutants of Amyloid  $\beta$  in Alzheimer Disease".
57. Yun-Ru Chen. (Oct. 2006) **IBC conferences: Structural and Biochemical Properties of Prions and Amyloids, Academia Sinica.** "Distinct Equilibrium Folding Properties of Amyloid  $\beta$  peptide 40 and 42 prior aggregation: Stable Trimer or Tetramer Formation of A $\beta$ 42".

## Selected Poster Presentations

58. Yun-Ru Chen. (Jun. 5-9, 2016) The 16th Annual Meeting of the Protein Science Society of Japan, Fukuoka, Japan. “Glycine-Alanine Dipeptide Repeat from C9orf72 Hexanucleotide Expansions Forms Toxic Amyloids Possessing Cell-to-cell Transmission Property”.
59. Yun-Ru Chen. (June 17-22, 2012) **Gordon Research Conferences: Molecular & Cellular Neurobiology**, Hong Kong Univ. of Science and Technology, Hong-Kong, China. “Full-length human TDP-43 forms stable and toxic amyloid-like oligomers in vitro and in vivo”.
60. Yun-Ru Chen. (Nov. 25-29, 2012) **The 13<sup>th</sup> FAOBMB Congress**, Bangkok, Thailand. “Spherical Gold Nanoparticles Retard A $\beta$ 40 Fibrillation and Induce Fibril Fragmentation”
61. Yun-Ru Chen. (June 12-17, 2011) **FASEB Summer Research Conferences: The Basic Origins and Medical Consequences of Protein Aggregation**, Snowmass Village, CO, USA. “Folding Stability of Amyloid- $\beta$  Predominantly Determines Nucleation Kinetics in Fibrillization where Destabilization upon Zn<sup>2+</sup> and Al<sup>3+</sup> Binding Promotes Annular Protofibril Formation”.
62. Chun-Lun Ni, Hoi-Ping Shi, Yu-Jen Chang, Kuo-Ging Lin, Hui-Mei Yu, and **Yun-Ru Chen\***. (June 28-July 3, 2009) **FASEB Summer Research Conferences: Amyloid Fibril Formation and Protein Misfolding-Molecular Mechanisms and Cellular Effects**, Snowmass Village, CO, USA. Conformational Stability and aggregation mechanism of amyloid  $\beta$  in Alzheimer’s disease.
63. Yun-Ru Chen. (June, 2007) **Gordon Conference: Proteins**, New Hampshire, USA. Equilibrium Folding and Aggregation Properties of Wild Type and Familial Mutants of Amyloid  $\beta$  in Alzheimer Disease.

### Serving as Organizing Committee or Conference Chairs:

1. IUBMB focused meeting on “Neurodegenerative Diseases”, Biotech Park, Taipei, Taiwan, Feb 25-27, 2020. Main Organizer. (Meeting postponed to 2021.4.21-23)
2. TSMBM, Nov. 15-17, 2019. Chairing at session “Neurodegenerative Diseases”
3. Mini-symposium of “Frontier Research in Alzheimer’s Disease”, Academia Sinica, Taipei, Taiwan, Dec. 13, 2018. Organizing committee.
4. The 23<sup>rd</sup> Biophysics Conference, R.O.C., May 23-25, 2018, Taichung, Taiwan. Chairing at session: Frontiers of Protein Folding and Misfolding.
5. The 21<sup>st</sup> Biophysics Conference, R.O.C., May 7-10, 2016, Hsin-Chu,, Taiwan. Chairing at session: Frontiers of Protein Folding and Misfolding.
6. The 19<sup>th</sup> Biophysics Conference, R.O.C., May 7-10, 2014, Tainan, Taiwan. Chairing at session: Protein Folding and Misfolding.
7. The 3<sup>rd</sup> APPA (Asian-Pacific Protein Association) Conference, May 6-9, 2011, Shanghai Univ., Shanghai, China. Co-chairing at session 3: Protein Folding, Structure, and Dynamics.
8. Symposium of “Frontier of Protein Aggregation and Neurodegenerative Diseases”, Taipei, Academia Sinica, Jun. 4-5, 2009. Organizing Committee.
9. PepCon-2009, Seoul, Korea. April 2-4, 2009. Co-chairing at session 3-3: Promising Protein Therapeutics for CNS Disorders/ Neurodegenerations.

### Memberships:

- Protein Society
- ISTAART (International Society to Advance Alzheimer’s Research and Treatment)
- Society of Neuroscience
- APPA (Asian-Pacific Protein Association)
- Taiwan Society for Biochemistry and Molecular Biology 台灣生物化學及分子生物學會

- The Biophysics Society of Taiwan 中華民國生物物理學會
- The Neuroscience Society of Taiwan 中華民國基礎神經科學會

## Serving as President and Council Member

- President, Asia Pacific Protein Association (APPA) (2022.6-2025.7)
- Council member, Taiwanese Neuroscience Society. 台灣基礎神經科學學會理事(2020-present)
- Council member, The Biophysical Society of R.O.C. 中華民國生物物理學會理事(2016-present)
- Council member, The Taiwan Society for Biochemistry and Molecular Biology 台灣生物化學及分子生物學會理事 (2015-2020)
- Council member, APPA (Asia Pacific Protein Association) Representative of Taiwan. (2014.5-2017.7)
- Council member, APPA (Asia Pacific Protein Association) Deputy Representative of Taiwan. (2009-2014.5)

## Grant Review

- Ministry of Science and Technology grant proposals, Taiwan
- Ministry of Science & Technology grant proposals, Taiwan
- MRC grant proposals (Medical Research Council, UK)
- Univ. of California, Davis, Pilot project grant proposal (USA)

## Journal Editorial Board

### Associate Editor

- Frontiers in Pharmacology-Ethnopharmacology (2021.3- now)

### Journal Editorial Board

- Frontiers in Aging Neuroscience (2019.5- now)

### Journal Referee

- ACS Chemical Neuroscience
- ACS Nano
- Biochemistry
- BBA-Proteins and Proteomics
- Chem Com
- Frontiers in Aging Neuroscience
- Frontiers in Neuroscience
- Frontiers in Pharmacology
- International Journal of Biological Macromolecules
- JACS
- Journal of Inorganic Chemistry
- Journal of Physical Chemistry
- Neurochemistry International
- Small
- Scientific Reports

## Trained lab members as faculty

鄧薇妮 Winny Arisandi, PhD student (2007-2015). Faculty of Biotechnology, Atma Jaya University, Indonesia

杜玲嫻 Ling-Hsien Tu, Post Doctor (2014-2016). 台灣師範大學化學系, Assistant Professor, Department of Chemistry, National Taiwan Normal University

施耀翔 Yao-Hsiang Shih, Post Doctor (2015-2019). 高雄醫科大學解剖所 Department of Anatomy, School of Medicine, Kaohsiung Medical University

簡儀欣 Yi-Hsin Chien, Post Doctor (2015-2017). 逢甲大學材料科學與工程學系 Department of Materials Science and Engineering, Feng Chia University