## Tree-Juen Chuang (莊樹諄)

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#### **Education**

1988~1992: B.S., Department of Computer Science, Soochow University, Taiwan

1992~1998: Ph.D., Institute of Computer and Information Science, National Chiao Tung University, Taiwan (Ph.D. Thesis: "Compression, Encryption, and Hiding of Still Images")

1998~2003: Postdoctoral Fellow, Institute of Biomedical Sciences, Academia Sinica, Taiwan (military service)

#### Main position and relevant experience

- Research Fellow (2014~date), Associate Research Fellow (2007~2014), Assistant Research Fellow (2003~2007), Genomics Research Center, Academia Sinica
- Joint Professor, International Graduate Program for Biodiversity, National Taiwan Normal University
- Joint Professor, NTU-Academia Sinica Genomics and Systems Biology Degree Program, National Taiwan University

#### Fields of specialty (limit to fields related to research)

Bioinformatics, Comparative and Evolutionary Genomics/Transcriptomics, Post-transcriptional Regulation, *Trans*-splicing, Circular RNA, Gene Fusion, Imprinting, Systems Biology

#### Major awards and honors

- Project for Excellent Junior Research Investigators Award, Ministry of Science and Technology, Taiwan, 2014-2018.
- Pius XI Medal, the Pontifical Academy of Sciences, Vatican, 2012.
- Academia Sinica Research Award for Junior Research Investigators, 2007.
- Wu Ta-Yuo Memorial Award, National Science Council, 2007.
- Post-doctoral Research Award of National Health Research Institutes (NHRI, Taiwan), 2000.
- Academia Sinica Post-doctoral Fellowship, 1999-2000.
- Academic Paper Awards from the Image Processing and Pattern Recognition (IPPR) Society, 1998.

### Representative publications (selected publications) (\*corresponding author)

- Trees-Juen Chuang\*, Chan-Shuo Wu, Chia-Ying Chen, Li-Yang Hung, Tai-Wei Chiang, and Min-Yu Yang (2016) NCLscan: accurate identification of non-co-linear transcripts (fusion, trans-splicing, and circular RNA) with a good balance between sensitivity and precision. Nucleic Acids Research, 44(3), e29. (SCI: 9.112; Rank: 20/290)
- Chun-Ying Yu, Hsiao-Jung Liu, Li-Yuan Hung, Hung-Chih Kuo\* and <u>Trees-Juen Chuang\*</u>
  (2014) Is an Observed Non-co-linear RNA Product Spliced in *trans*, in *cis*, or just *in vitro*?

- Nucleic Acids Research, 42(14), 9410-9423. (SCI: 9.112; Rank: 20/290)
- Chan-Shuo Wu, Chun-Ying Yu, Ching-Yu Chuang, Michael Hsiao, Cheng-Fu Kao, Hung-Chih Kuo\* and <u>Trees-Juen Chuang\*</u> (2014) Integrative transcriptome sequencing identifies trans-splicing events with important roles in human embryonic stem cell pluripotency. Genome Research. 24(1), 25-36. (SCI: 14.630; Rank: 4/290) ==> highlighted in Nature Reviews Genetics 14, 822, 2013.
- <u>Trees-Juen Chuang</u>\* and Feng-Chi Chen\* (2014) DNA methylation is associated with an increased level of conservation at nondegenerate nucleotides in mammals. *Molecular Biology and Evolution*. 31(2), 387-396. (SCI: 9.105; Rank: 10/167)
- Yi-Ching Chen, Jen-Hao Cheng, Zing Tsung-Yeh Tsai, Huai-Kuang Tsai\* and <u>Trees-Juen Chuang\*</u> (2013) The Impact of *Trans*-Regulation on the Evolutionary Rates of Metazoan Proteins. *Nucleic Acids Research*, 13 (41), 6371-6380. (SCI: 9.112; Rank: 20/290)
- <u>Trees-Juen Chuang\*</u>, Feng-Chi Chen\*, Yen-Zho Chen (2012) Position-dependent correlations between the level of DNA methylation and the evolutionary rates of mammalian coding exons. *P Natl Acad Sci USA*, 109(39), 15841-15846. (SCI: 9.674; Rank: 4/57) ==> highlighted in A-IMBN (Asia-Pacific International Molecular Biology Network) Research
- Feng-Chi Chen, Chueng-Jong Chen, Wen-Hsiung Li, and <u>Trees-Juen Chuang\*</u> (2010) Gene family size conservation is a good indicator of evolutionary rates. *Molecular Biology and Evolution*, 27(8), 1750-8. (SCI: 9.105; Rank: 10/167)
- Yao-Ting Huang, Feng-Chi Chen\*, Chiuan-Jung Chen, Hsin-Liang Chen and <u>Trees-Juen Chuang\*</u> (2008). Identification and analysis of ancestral hominoid transcriptome inferred from cross-species transcript and processed pseudogene comparisons. *Genome Research* 18(7), 1163-1170. (SCI: 14.630; Rank: 4/290)
- Feng-Chi Chen, Shu-Miaw Chaw, Yun-Huei Tzeng, Sheng-Shun Wang, and <u>Trees-Juen</u>
  <u>Chuang\*</u> (2007). Opposite Evolutionary Effects between Different Alternative Splicing Patterns.
  *Molecular Biology and Evolution*, 24(7), 1443-6. (SCI: 9.105; Rank: 10/167)
- Feng-Chi Chen, Chueng-Jong Chen, and <u>Trees-Juen Chuang\*</u> (2007). INDELSCAN: a web server for comparative identification of species-specific and non-species-specific insertion/deletion events, *Nucleic Acids Research*, 35 (Web Server issue):W633-8. (SCI: 9.112; Rank: 20/290)
- Feng-Chi Chen, Chueng-Jong Chen, Wen-Hsiung Li\*, and <u>Trees-Juen Chuang\*</u> (2007). Human-specific insertions and deletions inferred from mammalian genome sequences. *Genome Research*, 17(1), 16-22. (SCI: 14.630; Rank: 4/290)
- ◆ Feng-Chi Chen, Sheng-Shun Wang, Chuang-Jong Chen, Wen-Hsiung Li and <u>Trees-Juen Chuang\*</u> (2006). Alternatively and Constitutively Spliced Exons are Subject to Different Evolutionary Forces. *Molecular Biology and Evolution*, 23(3), 675–682. (SCI: 9.105; Rank: 10/167)
- <u>Trees-Juen Chuang</u>, Wen-Chang Lin, Hurng-Chun Lee, Chi-Wei Wang, Keh-Lin Hsiao, Zi-Hao Wang, Danny Shieh, Simon C. Lin, and Lan-Yang Ch'ang\* (2003) "A Complexity Reduction Algorithm for Analysis and Annotation of Large Genomic Sequences," *Genome Research*, 13(2), 313-322. (SCI: 14.630; Rank: 4/290)

Title:

# Investigation of *trans*-splicing and *cis*-backsplicing (circular RNA) in the human transcriptome

#### Abstract:

High-throughput transcriptome sequencing has brought an unprecedented opportunity for globally investigating transcriptomes and thus detected numerous non-co-linear (NCL) transcripts, which comprised sequence segments that are topologically inconsistent with the reference genome. Regarding post-transcriptional events, non-co-linear transcripts can arise from trans-splicing or back-splicing in cis (or the so-called "circular RNA"). Detection of post-transcriptionally non-co-linear ("PtNCL") transcripts is usually severely hampered by several types of false positives such as sequence error, alignment error, experimental artifacts, and genetic rearrangements (or gene fusion events). I will first show a high level of false positive rate in previously-nominated NCL candidates. We demonstrated that trans-spliced and circular RNAs can share the same non-co-linear junction sites, and some PtNCL events and their splicing type of PtNCL isoforms (i.e., trans-spliced or circular RNAs) were evolutionarily conserved between species. After that, I will introduce the first reported trans-spliced large intergenic noncoding RNA – tsRMST, which can contribute to pluripotency maintenance of human embryonic stem cells by suppressing lineage-specific gene expression through the recruitment of NANOG and the PRC2 complex factor, SUZ12. Finally, I will introduce our recently developed tool -NCLscan, which can accurately identify NCL events, including *trans*-spliced, circular, and fusion transcripts, with a good balance between sensitivity and precision.

**Keywords:** Post-transcriptionally non-co-linear transcript; *cis-/trans*-splicing; Circular RNA; gene fusion; Embryonic stem cell; Next-generation sequencing; Bioinformatics

#### References: (\* corresponding author)

- 1. Chan-Shuo Wu, Chun-Ying Yu, Ching-Yu Chuang, Michael Hsiao, Cheng-Fu Kao, Hung-Chih Kuo\* and <u>Trees-Juen Chuang\*</u> (2014) Integrative transcriptome sequencing identifies *trans*-splicing events with important roles in human embryonic stem cell pluripotency. *Genome Research*. 24(1), 25-36.
- 2. Chun-Ying Yu, Hsiao-Jung Liu, Li-Yuan Hung, Hung-Chih Kuo\* and <u>Trees-Juen Chuang\*</u> (2014) Is an Observed Non-co-linear RNA Product Spliced in *trans*, in *cis*, or just *in vitro*? *Nucleic Acids Research*, 42(14), 9410-9423.
- 3. Iju Chen, Chia-Ying Chen and <u>Trees-Juen Chuang\*</u> (2015) Biogenesis, identification, and function of exonic circular RNAs. *WIREs RNA*, 6(5), 563-579.
- 4. <u>Trees-Juen Chuang\*</u>, Chan-Shuo Wu, Chia-Ying Chen, Li-Yang Hung, Tai-Wei Chiang. (2016) NCLscan: accurate identification of non-co-linear transcripts (fusion, *trans*-splicing, and circular RNA) with a good balance between sensitivity and precision. *Nucleic Acids Research*, 44(3), e29.