

PONTIFICIA ACADEMIA SCIENTIARVM

THE AWARD  
OF THE  
PIUS XI GOLD MEDAL

2012



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*The aim of the Pontifical Academy of Sciences, which was founded on 28 October 1936 by the Holy Father Pius XI, is to honour pure science, wherever this may be found, to ensure its freedom, and to support the research essential for the progress of applied science.*

*On 28 October 1961, on the occasion of the 25<sup>th</sup> anniversary of the foundation of the Pontifical Academy of Sciences, the Holy Father John XXIII established the Pius XI Gold Medal in honour of the founder of the Academy. The medal should be awarded to a young scientist who has already gained an international reputation.*

*The Council of the Academy unanimously decided to award the “Pius XI Gold Medal” for the year 2012 to*

**Prof. TREES-JUEN CHUANG**

*in recognition of his great merits as a scholar and the important contribution of his research to scientific progress.*



**TREES-JUEN CHUANG**



## BIOGRAPHICAL DATA

*Full Name:* Trees-Juen Chuang

*Designation:* Associate Research Fellow

*Professional Address:*

Genomics Research Center, Academia Sinica  
128, Sec. 2, Academia Road, Nankang  
Taipei 11529, Taiwan

*Date of Birth:* 15 December 1970

*Place of Birth:* Taipei, Taiwan

*Wife and Children:* Married to Min-Chin Hsu; Pei-Hsun Chuang and Pei-Yao Chuang

*Academic Qualifications:*

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).

*Scientific Discipline:*

Computer Science, Image Processing, Pattern Recognition, Compression and Encryption.

*Specialty & Research Field of Interest:*

Bioinformatics and Computational Biology, Genome Annotation, Comparative and Evolutionary Genomics/Transcriptomics, Post-transcriptional Event.

*Current Professional Activity/Occupation:*

- 2007–: Associate Research Fellow, Genomics Research Center, Academia Sinica.
- 2003-2007: Assistant Research Fellow, Genomics Research Center, Academia Sinica.
- 2012–: Joint Associate Professor, International Graduate Program for Biodiversity, National Taiwan Normal University.
- 2010–: Joint Associate Professor, NTU-Academia Sinica Genomics and Systems Biology Degree Program, National Taiwan University.
- 2007–: Joint Associate Professor, Department of Bioinformatics, Asia University.
- 2006–: Adjunct Associate Professor, NYMU-Academia Sinica Genomics Science Degree Program, National Yang-Ming University.
- 2005–: Adjunct Associate Professor, Graduate Institute of Life Sciences, National Defense Medical Center.

*Research Evaluation:*

- Editorial Board of ISRN Bioinformatics, Hindawi Publishing Corporation (2011–).
- Associate Editor, BMC Genomics, BioMed Central, London (2010–).
- Supervisory Board, Bioinformatics Society Taiwan (2007-2009)
- Significant Publications of Academia Sinica (2004, 2006, and 2010).
- Referee for various international journals (*Nucleic Acids Res.*, *PLoS Computational Biology*, *PLoS One*, *Genome Biology*, *BMC Genomics* *BMC Bioinformatics*, *BMC Evol. Biol.*, *BMC Plant Biol.*, *Gene*, *J. Bioinform. Comput. Biol.*, *Int. J. of Evol. Biol.*, ...).

*Honors:*

- Laureate of the Academic Paper Awards from the Image Processing and Pattern Recognition (IPPR) Society, 1998.
- Laureate of the Academia Sinica Post-doctoral Fellowship, 1999-2000.
- Laureate of the Post-doctoral Research Award of National Health Research Institutes (NHRI, Taiwan), 2000.



Laureate of the Wu Ta-Yuo Memorial Award, National Science Council, 2007.

Laureate of the Academia Sinica Research Award for Junior Research Investigators, 2007.

*Pattern:*

Pattern to “A Complexity Reduction Algorithm for Analysis and Annotation of Large Genomic Sequences” (Patent no: TW238854).

*Invitation to Prominent Laboratory or International Meeting:*

Jun. 2010-Jul. 2010; Sep. 2011-Oct. 2011, Prof. Alexandre G. de Brevin’s Lab., INSERM UMR-S 665, DSIMB, INTS, Université Paris Diderot – Paris 7, Paris, France (Taiwan-France Orchid Program).

September 2010, International Primatological Society XXIII Congress Kyoto 2010, Kyoto University, Japan.

Mar. 2009-Apr. 2009, Prof. Hao Li’s Lab., Department of Biochemistry and Biophysics, University of California, San Francisco, USA.

Nov. 2003-Dec. 2003, Prof. Wen-Hsiung Li’s Lab., Department of Ecology and Evolution, University of Chicago, Chicago, USA.

## COMPARATIVE AND EVOLUTIONARY GENOMICS/TRANSCRIPTOMICS: FROM ENCIPHERING TO DECIPHERING

Before 1998, T.J. Chuang's work was mainly devoted to the following fields of computer science: Image/Signal Processing, Image Compression/Encryption/Hiding, Pattern Recognition, and Progressive Communication. To increase the security level of image transmission, T.J. Chuang, while working in Ja-Chen Lin's laboratory, has proposed several algorithms for enciphering images. After T.J. Chuang received the Ph.D. degree in 1998, he changed his research interests from computer science to life science and devoted himself to deciphering genetic code. T.J. Chuang's research includes the following four topics:

### 1. *Identification of gene structures and alternatively spliced variants (ASVs)*

T.J. Chuang developed a homology-based algorithm named CRASA (Complexity Reduction Algorithm for Sequence Analysis) for a framework annotation of expressed genes in the genome, which efficiently reduced the data complexity and performed gene identification on the basis of the same species EST-to-genome alignments (Chuang *et al.*, 2003, *Genome Res.*). On the basis of cross-species comparisons, several pipelines/Web interfaces, including PSEP (Chuang *et al.*, 2004, *Bioinformatics*), ESTviewer (Chen *et al.*, 2005, *Bioinformatics*), ENACE (Chen *et al.*, 2006, *BMC Bioinformatics*), and PGAA and RiceViewer (Chen *et al.*, 2007, *Plant Physiol.*), were further developed for identification of novel genes/ASVs in mammals or plants. Experimental validations also supported the effectiveness of these methods.

### 2. *Analysis of conflicting arguments in evolution*

T.J. Chuang's group first addressed a controversy on whether alternatively spliced exons (ASEs) evolve faster than constitutively spliced exons (CSEs). By examining the synonymous (Ks) and non-synonymous (Ka) substitution rates in human-mouse orthologous

exons, ASEs were shown to have higher  $K_a$  values and higher  $K_a/K_s$  ratios than CSEs, indicating faster amino-acid-level evolution in ASEs. Meanwhile, the majority of ASEs have lower  $K_s$  values than CSEs. With reference to the substitution rate in introns, the  $K_s$  values in ASEs were shown to be close to the neutral substitution rate, whereas the synonymous substitution rate in CSEs has likely been accelerated (Chen *et al.*, 2006, *Mol. Biol. Evol.*). The effects of multiple features of ASEs on the  $K_A/K_S$  ratio test were also examined (Chen *et al.*, 2006, *BMC Bioinformatics*). Furthermore, different ASE patterns were shown to undergo opposite selection pressure, with CSEs in-between, suggesting that evolutionary analyses of AS should take into consideration the effects of different splicing patterns. (Chen *et al.*, 2007, *Mol. Biol. Evol.*; *BMC Evol. Biol.*). T.J. Chuang's group also addressed the controversy on whether duplicate genes evolve more slowly than singletons by considering gene family size conservation (Chen *et al.*, 2010, *Mol. Biol. Evol.*). Recently, T.J. Chuang tries to address another controversy on whether DNA methylation is correlated with increased or decreased protein evolutionary rates. The preliminary result reveals differential correlations between DNA methylation and the evolutionary rates of coding exons in different genic positions.

### 3. Genomic/Transcriptomic variations between human and non-human primates

T.J. Chuang's group inferred human-specific (HS) insertions/deletions (indels) using multiple sequence alignments of mammalian genomes and thus identified >840,000 "small" indels, which affected more than 7,000 human genes (>11,000 transcripts). Functional analysis revealed that HS indels might have contributed to human unique traits by causing changes at the RNA and protein level (Chen *et al.*, 2007, *Genome Res.*; *Nucleic Acids Res.*). HS indels were further suggested to have been associated with human adaptive changes at both the species level and the subpopulation level (Chen *et al.*, 2009, *Genome Biol. Evol.*). On the basis of processed pseudogenes (PPGs), which are reverse transcribed ancient transcripts present in the current genome, T.J. Chuang's group also showed that chimpanzee PPGs can be applied to identification of novel human exons/ASVs and inference of the ancestral hominoid transcriptome and chimpanzee exon loss events (Huang *et al.*, 2008, *Genome Res.*).

#### 4. *Post-transcriptional events in human embryonic stem cells (hESCs)*

Post-transcriptional events embrace cis-splicing, trans-splicing, RNA editing, and so on. T.J. Chuang's preliminary results have shown that lineage-specific ASVs (or cis-splicing events) can play important roles in proliferation divergence between human and non-human primate ESCs during early neural differentiation. In addition, T.J. Chuang's group identified and confirmed several trans-spliced RNAs in hESCs, including the first reported trans-spliced large intergenic non-coding RNA. The preliminary results showed that these trans-spliced RNAs are all highly expressed in human pluripotent stem cells and differentially expressed during hESC differentiation. As well, trans-splicing may be significantly associated with the maintenance of pluripotency of hESCs. Like cis-/trans-splicing, RNA editing also lead to the generation of multiple transcript isoforms from a single gene, increasing the complexity of transcriptome/proteome. T.J. Chuang and his laboratory may, within the next few years, develop new computational tools to minimize potential false positives while detecting post-transcriptional events and provide insights into the role of these events in pluripotency maintenance of hESCs and lineage differentiation.

## SELECTED PUBLICATIONS

### *Computer Science*

- Trees-Juen Chuang and Ja-Chen Lin (1998). A New Algorithm for Lossless Still Image Compression. *Pattern Recognition*, 31(9), 1343-1352.
- Trees-Juen Chuang and Ja-Chen Lin (1998). A New Approach to Image Encryption. *Journal of Electronic Imaging*, 7(2), 350-356.

### *Life Science*

- Trees-Juen Chuang, 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.
- Trees-Juen Chuang, Feng-Chi Chen, and Meng-Yuan Chou (2004). A comparative method for identification of gene structures and alternatively spliced variants. *Bioinformatics* 20, 3064-3079.
- Feng-Chi Chen, and Trees-Juen Chuang (2005). ESTviewer: a web interface for visualizing mouse, rat, cattle, pig and chicken conserved ESTs in human genes and human alternatively spliced variants. *Bioinformatics* 21, 2510-2513.
- Feng-Chi Chen, Sheng-Shun Wang, Chuang-Jong Chen, Wen-Hsiung Li and Trees-Juen Chuang (2006). Alternatively and constitutively spliced exons are subject to different evolutionary forces. *Molecular Biology and Evolution*, 23(3), 675-682.
- Feng-Chi Chen, Chueng-Jong Chen, Wen-Hsiung Li, and Trees-Juen Chuang (2007). Human-specific insertions and deletions inferred from mammalian genome sequences. *Genome Research*, 17(1), 16-22.

- Feng-Chi Chen, Chueng-Jong Chen, and Trees-Juen Chuang (2007). INDELSCAN: a web server for comparative identification of species-specific and non-species-specific insertion/deletion events, *Nucleic Acids Research*, 35:W633-8.
- Feng-Chi Chen, Shu-Miaw Chaw, Yun-Huei Tzeng, Sheng-Shun Wang, and Trees-Juen Chuang (2007). Opposite Evolutionary Effects between Different Alternative Splicing Patterns. *Molecular Biology and Evolution*, 24(7):1443-6.
- Feng-Chi Chen, Sheng-Shun Wang, Shu-Miaw Chaw, Yao-Ting Huang, and Trees-Juen Chuang (2007). Plant gene and alternatively spliced variant annotator: a plant genome annotation pipeline for rice gene and alternatively spliced variant identification with cross-species expressed sequence tag conservation from seven plant species. *Plant Physiology*, 143(3), 1086-1095.
- Yao-Ting Huang, Feng-Chi Chen, Chiuan-Jung Chen, Hsin-Liang Chen and Trees-Juen Chuang (2008). Identification and analysis of ancestral hominoid transcriptome inferred from cross-species transcript and processed pseudogene comparisons. *Genome Research* 18(7), 1163-1170.
- Feng-Chi Chen, Yen-Zho Chen, and Trees-Juen Chuang (2009). CNVdb: a database of copy number variations across vertebrate genomes. *Bioinformatics* 25(11), 1419-1421.
- Feng-Chi Chen, Chueng-Jong Chen, Wen-Hsiung Li, and Trees-Juen Chuang (2010). Gene family size conservation is a good indicator of evolutionary rates. *Molecular Biology and Evolution*, 27(8), 1750-8.
- Sean Chun-Chang Chen, Trees-Juen Chuang, Wen-Hsiung Li (2011). The relationships among microRNA regulation, intrinsically disordered regions, and other indicators of protein evolutionary rate. *Molecular Biology and Evolution*, 28(9), 2513-20.
- Trees-Juen Chuang, Feng-Chi Chen, Yen-Zho Chen (2012). Position-dependent correlations between the level of DNA methyla-

tion and the evolutionary rates of mammalian coding exons.  
*Proc. Natl. Acad. Sci. USA*. Revised. Editor's request.

Chan-Shuo Wu, Chun-Ying Yu, Ching-Yu Chuang, Michael Hsiao, Cheng-Fu Kao, Chung-Hsuan Chen, Hung-Chih Kuo and Trees-Juen Chuang (2012). Transcriptome sequencing identifies trans-splicing events important for human pluripotency (manuscript submitted).

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