Jui-Hua Hsieh

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Summary of Expertise

- Experienced in both structure- and ligand-based drug design: docking, homology modeling, pharmacophore modeling, QSAR analysis, clustering, and machine learning methods.
- Excellent cheminformatics development skills
- Knowledgeable in both *in vitro* high throughput screening (HTS) and virtual screening
- Familiar with bioinformatics tools (e.g., R/bioconductor packages): gene selection and GO/pathway enrichment analysis
- Solid knowledge in pharmacology, medicinal chemistry, and biology

Computational Skills

- Programming Languages: R, Perl, C/C++, Matlab, UNIX shell, Python, and Java.
- Software:
  - Cheminformatics: Pipeline Pilot and Discovery Studio (Accelrys); KNIME, Leadscope; MOE (CCG)
  - Docking: Glide and Induced Fit (Schrödinger); OMEGA and FRED (OpenEye)
  - Data visualization and plotting: R/ggplot2 and Spotfire

Education

- **Ph.D., Pharmaceutical Sciences (Cheminformatics), Aug. 2005 – Jan. 2011**

  University of North Carolina at Chapel Hill, Chapel Hill, NC

  - Dissertation: Cheminformatics Approaches to Structure Based Virtual Screening: Methodology Development and Applications
  - Advisor: Alexander Tropsha

- **National Taiwan University, Taipei, Taiwan**

  B.S., Pharmacy, Sept. 1999 - June 2003

  - Licensure, Pharmacist, the Union of Pharmacist Association, R.O.C., September 2003. (No. 029160)

Research Experiences

- **Research Fellow, Aug. 2013 – Current & Visiting Fellow, Sept. 2011 – Aug. 2013**

  National Institute of Environmental Health Sciences, Division of National Toxicology Program, Biomolecular Screening Branch, Durham, NC

  Mentors: Drs. Raymond Tice & B. Alexander Merrick

  - Applied statistical approaches to monitor Tox21 quantitative HTS (qHTS) assay robustness and to investigate the influence of compound source on activity variation
  - Developed a comprehensive data analysis pipeline for Tox21 Phase II qHTS assays
  - Developing web sites hosting data from qHTS assays, facilitating data/method accessibility.
  - Applied bioinformatics and cheminfomatics approaches to understand the perturbed biological functions/pathways/genes and enriched substructures of hits in Tox21 qHTS assays
  - Developed compound prioritization strategy for *in vivo* rat oral acute toxicity testing based on *in vitro* qHTS cytotoxicity assays
  - Developing compound prioritization strategy for genotoxicity testing based on both *in vitro* qHTS genotoxicity assays and chemical structures
  - Collaborating biologists, facilitating qHTS assay results interpretation

- **Visiting Scholar, Mar. 2011 – Aug. 2011 & Research Assistant, Apr. 2007 – Feb. 2011**

  University of North Carolina at Chapel Hill, Division of Medicinal Chemistry and Natural Products, Chapel Hill, NC

  Advisor: Alexander Tropsha

  - Developed novel conceptual density functional theory (DFT) descriptors to characterize intermolecular interactions in protein-ligand structures
  - Developed structure-based, target-specific scoring functions (i.e., pose filter) for over 13 protein targets to improve hit rate in virtual screening
  - Developed a cheminformatics-force field scoring function to improve ligand binding affinity prediction
  - Constructed QSAR models for AmpC β-lactamase, applied them to virtual screening, and identified confirmed hits
  - Derived QSAR models to identify selective, potent activated cdc42-associated kinase 1 (ACK1) inhibitors
  - Constructed histone deacetylase 8 (HDAC8) structure-based pharmacophore models to facilitate conformer search in virtual screening
  - Constructed human GPCR adenosine A_{2A} receptor homology model; attended GPCR Dock 2008 competition
  - Other structure-based virtual screening projects
    - Glyceraldehydes-3-phosphate dehydrogenase (GAPDH)
    - Mer kinase

- **Research Assistant, June 2009 – Aug. 2009**

  GlaxoSmithKline, Computational and Structural Chemistry group, Summer Talent Identification Program Collegeville, PA

  Mentor: Dr. Zheng Yang

  - Derived QSAR models of efflux properties of Gram-negative bacteria, applied them to virtual screening, and identified confirmed hits
  - Curated in-house antibiotics efflux and penetration data for model building
  - Proposed new templates with low efflux property based on the model-descriptor interpretation

- **Research Assistant, July 2004 – May 2005**

  National Health Research Institutes, Division of Biotechnology and Pharmaceutical Research, Jhunan, Taiwan

  Mentor: Dr. Su-Ying Wu

  - Implemented Structural interaction fingerprint (SIFt)-based method for virtual screening
  - Analyzed binding interactions of Hepatitis C virus (HCV) NS3 Protease inhibitors
  - Conducted the structure-based virtual screening project (Dengue 2 NS3 protease)

- **Research Assistant, Sept. 2003 – Mar. 2004**

  Academia Sinica, Institute of Atomic and Molecular Science, Taipei, Taiwan

  Mentor: Dr. Dah-Yen Yang

  - Docking training
  - Administration

Teaching Experiences

- **Teaching Assistant, Jan. 2006 – May. 2007**

  University of North Carolina at Chapel Hill, School of Pharmacy, Chapel Hill, NC

  - Helped prepare teaching materials in pharmaceutical care lab
  - Graded quizzes and assignments

- Assisted Pham D. students with preparing presentations

Grants and Awards

- **Best Poster Award**, Oct. 2013, OpenTox USA InterAction Meeting, RTP, NC
- **TraCS $2K Grant (2KR100915),** Feb. 2010 – Feb. 2011, Design of Novel Therapeutic Agents against Mer Kinase for Cancer Treatment, Jui-Hua Hsieh (PI)

Publication

- **Peer-reviewed Journals**
  - Chang X., Kleinstreuer N., Ceger P., **Hsieh J-H.**, Allen D., and Casey W. (2014). Application of Reverse Dosimetry to Compare In vitro and In vivo Estrogen Receptor Activity. **Appl In Vitro Toxicol.** (accepted)
  - Hsu C-W., Zhao J., Huang R., **Hsieh J-H.**, Hamm J., Chang X., Houck K., Xia M. (2014). Quantitative High-Throughput Profiling of Environmental Chemicals and Drugs that Modulate Farnesoid X Receptor. **Sci Rep.** *4*, 6437.
  - Wang C., Gong B., Bushel P.R., Thierry-Mieg J., Thierry-Mieg D., Xu J., Fang H., Hong H., Shen J., Su Z., Meehan J., Li X., Yang L., Li H., Labaj P.P., Kreil D.P., Megherbi D., Gaj S., Caiment F., van Delft J., Kleinjans J., Scherer A., Devanarayan V., Wang J., Yang Y., Qian H.R., Lancashire L.J., Bessarabova M., Nikolsky Y., Furlanello C., Chierici M., Albanese D., Jurman G., Riccadonna S., Filosi M., Visintainer R., Zhang K.K., Li J., **Hsieh J-H.**, Svoboda D.L., Fuscoe J.C., Deng Y., Shi L., Paules R.S., Auerbach S.S., Tong W. (2014). The concordance between RNA-seq and microarray data depends on chemical treatment and transcript abundance. **Nat Biotechnol.** *32*, 926-32.
  - Huang R., Sakamuru S., Martin M.T., Reif D.M., Judson R.S., Houck K.A., Casey W., **Hsieh J-H.**, Shockley K.R., Ceger P., Fostel J., Witt K.L., Tong W., Rotroff D.M., Zhao T., Shinn P., Simeonov A., Dix D.J., Austin C.P., Kavlock R.J., Tice R.R., and Xia M. (2014). Profiling of the Tox21 10K compound library for agonists and antagonists of the estrogen receptor alpha signaling pathway. S**ci Rep.** *4*, 5564.
  - Zhang, J., **Hsieh, J-H**., Zhu, H. (2014). Profiling Animal Toxicants by Automatically Mining Public Bioassay Data: A Big Data Approach for Computational Toxicology. **PloS one** *9*, e99863
  - Tang, H., Wang, X.S., **Hsieh, J.-H.**, and Tropsha, A. (2012). Do crystal structures obviate the need for theoretical models of GPCRs for structure-based virtual screening? **Proteins: Struct, Funct, Bioinf** *80*, 1503–1521.
  - **Hsieh, J.-H.**, Yin, S., Wang, X.S., Liu, S., Dokholyan, N.V., and Tropsha, A. (2012). Cheminformatics Meets Molecular Mechanics: A Combined Application of Knowledge-Based Pose Scoring and Physical Force Field-Based Hit Scoring Functions Improves the Accuracy of Structure-Based Virtual Screening. **J Chem Inf Model** *52*, 16–28.
  - **Hsieh, J.-H.**, Yin, S., Liu, S., Sedykh, A., Dokholyan, N.V., and Tropsha, A. (2011). Combined Application of Cheminformatics- and Physical Force Field-Based Scoring Functions Improves Binding Affinity Prediction for CSAR Data Sets. **J Chem Inf Model** *51*, 2027–2035.
  - **Hsieh, J.-H.**, Wang, X.S., Teotico, D., Golbraikh, A., and Tropsha, A. (2008). Differentiation of AmpC beta-lactamase binders vs. decoys using classification kNN QSAR modeling and application of the QSAR classifier to virtual screening. **J Comput Aided Mol Des** *22*, 593–609.
- **Selected Abstracts/Posters**
  - **Hsieh, J-H.**, Kleinstreuer N., Franzosa J., Sedykh A., and Tice R. (2014). Identifying Structural Alerts Based on Zebrafish Developmental Morphological Toxicity. **2nd ToxCast Data Summit**, RTP, NC
  - **Hsieh, J.-H.**, Sedykh, A., Behl M., Huang R, Xia M, Tice R. (2014). A Data Analysis Pipeline for Tox21 Phase II Quantitative High Throughput Screening Assays and Its Application to Toxicity Profiling of Flame Retardants. **9th World Congress on Alternatives and Animal Use in the Life Sciences**, Prague, Czech Republic

- **Hsieh, J.-H.,** Sedykh, A., Behl M., Huang R, Xia M, Tice R. (2013). A Data Analysis Pipeline for Tox21 Phase II Quantitative High Throughput Screening Assays and Its Application to Toxicity Profiling of Flame Retardants. **Society of Toxicology (SOT)'s 53nd Annual Meeting**, Phoenix, AZ
- **Hsieh J.-H.,** Witt K., Smith-Roe S., Huang R., Xia M., and Tice R. (2013). Evaluating Tox21 quantitative high throughput screening (qHTS) genotoxicity assays for compound prioritization. **FutureTox II meeting**, RTP, NC
- **Hsieh, J.-H.,** Sedykh, A., Behl M., Huang R, Xia M, Tice R. (2013). A Data Analysis Pipeline for Tox21 Phase II Quantitative High Throughput Screening Assays and Its Application to Toxicity Profiling of Flame Retardants. **OpenTox USA InterAction Meeting**, RTP, NC
- **Hsieh, J.-H.**, Sedykh, A., Huang R, Xia M, Tice R. (2012). Compound Toxicity Profiling and Prioritization: Using Tox21 Phase I Quantitative High Throughput Screening (qHTS) Cytotoxicity Data. **Society of Toxicology (SOT)'s 52nd Annual Meeting**, San Antonio, TX
- La M., **Hsieh, J.-H.**, and Tice. R. (2012). Does Source Matter? The Influence of Chemical Supplier on Quantitative High Throughput Screening (qHTS) Data. **NIH Summer Internship Program Poster Session**, Durham. NC
- **Hsieh, J.-H.** & Yang Z. (2010). Pharmacophore Fingerprint-based Support Vector Machine Model Building for Antibiotics Influx and Efflux Properties against Gram-Negative Bacteria to Overcome Multi-Drug Resistance. **American Chemical Society Spring 2010 National Meeting**, San Francisco, CA
- **Hsieh, J.-H.**, Yin, S., Liu, S., Sedykh, A., Dokholyan, N.V., and Tropsha, A. (2010). Combination of Force-Field Scoring Functions and Cheminformatics-Based Pose Filters for Virtual Screening. **American Chemical Society Spring 2010 National Meeting**, San Francisco, CA
- **Hsieh, J.-H.**, Wang, X.S., Zhang S., Golbraikh A., and Tropsha A. (2008). Differentiation of Binding and Geometric Decoys Generated from Molecular Docking Using Cheminformatics Approaches. **American Chemical Society Spring 2008 National Meeting**, New Orleans, LA
- **Hsieh, J.-H.**, Wang, X.S., Golbraikh A., and Tropsha A. (2008). Differentiation of AmpC β-lactamase Binding Decoys by kNN Classification QSAR and the Use of QSAR Models for Virtual Screening. **University Research Day**, Chapel Hill, NC
- **Hsieh, J.-H.**, Wang, X.S., Golbraikh A., and Tropsha A. (2008). Differentiation of AmpC Beta-lactamase "Hit List"Decoys by kNN Classification QSAR and its Application for Database Mining. **Recruitment Weekend for Pharmaceutical Sciences**, Chapel Hill, NC
- **Hsieh, J.-H.**, Wang, X.S., Zhang S., and Tropsha A. (2007). Accurate Differentiation of Docking Decoys using Quantitative Structure - Binding Affinity Relationship (QSBAR) Classification Models with ENTess Chemical Geometrical Descriptors. **Microsoft eScience Workshop**, Chapel Hill, NC