Computational Toxicology Specialty Section (CTSS)

Veritas ex machina

Virtual Event, SOT 2021
2021 CTSS Election Results

Congratulations to our new members of CTSS leadership!

• Vice-President Elect: Minjun Chen
• Secretary: Fjodor Melnikov
• Councilor: Anne Loccisano
• Postdoctoral Rep: Adrian Green
Thank you for your service on the CTSS Leadership Team!

- Past President: Lisa Beilke
- Secretary: Joel Cohen
- Councilor: Minjun Chen
- Postdoctoral Rep: David Edmondson
CTSS Past- President Recognition

- Founder of the CTSS in 2018
- Lead the team last year in finalizing CTSS by-laws
- Supported the development of webinars and membership communications
- Remained a critical partner and active guiding CTSS mission
CTSS Membership Growth

Members strong in 2021: 261
(c.f. 164 members in 2019)

http://www.toxicology.org/groups/ss/ctss/
2021 Membership by Employment Sector

- Industry: 41.0%
- Academia: 19.2%
- Government: 14.6%
- Consulting: 11.5%
- CRO: 5.4%
- Research Institute: 3.4%
- Student: 3.1%
- Other: 1.9%

SOT | Society of Toxicology
Creating a Safer and Healthier World by Advancing the Science and Increasing the Impact of Toxicology

Annual Meeting & ToxExpo
VIRTUAL EVENT • MARCH 2021

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Follow CTSS on LinkedIn

Join our LinkedIn group and stay up to date with the latest news and events!

https://www.linkedin.com/groups/13858870/

Veritas ex machina
CTSS Treasury Report

<table>
<thead>
<tr>
<th>Description</th>
<th>Income</th>
<th>Expense</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019 balance</td>
<td>$8765</td>
<td></td>
</tr>
<tr>
<td>CTSS dues &amp; interest</td>
<td>$5466</td>
<td></td>
</tr>
<tr>
<td>2019-20 Industry Donations</td>
<td>$14,000</td>
<td></td>
</tr>
<tr>
<td>SOT 2020 Meeting Costs</td>
<td></td>
<td>$0</td>
</tr>
<tr>
<td>SOT 2020 Awards</td>
<td>$274</td>
<td></td>
</tr>
<tr>
<td>SOT 2021 Meeting Costs (est.)</td>
<td></td>
<td>$0</td>
</tr>
<tr>
<td>SOT 2021 Awards</td>
<td>$3,100</td>
<td></td>
</tr>
<tr>
<td>sub-totals</td>
<td>$28,231</td>
<td>$3,374</td>
</tr>
<tr>
<td>Total</td>
<td>$24,857</td>
<td></td>
</tr>
</tbody>
</table>

Thank you to a number of generous donations, CTSS is in the black for the year.
This SOT Scholarship Fund Endowment was established in July 2019 by his students, friends, colleagues, and family. Dr. Alarie, a longtime member of the SOT, has made significant contributions to the fields of inhalation toxicology and computational toxicology. During his career as a Professor at the University of Pittsburgh, he advised, trained, encouraged, and supported many students in the field of toxicology.

This award provides $2,500 to a motivated trainee or young investigator from an underrepresented group that is working in the field of computational toxicology and shares Dr. Alarie’s passion for science. The award must be used for the professional development of the trainee/young investigator.

SUSTAINABLE FUND WITH OVER $103,000 as of Q1 2021

- Dr. Michelle Shaper PhD; Department of Labor (DOL)
- Dr. Heather Burleigh-Flayer PhD DABT; ex-PPG Industries
- Dr. Yves Alarie PhD; University of Pittsburgh (emeritus)
12 Scientific Sessions were received and ranked

- Anne Loccisano
- Adams Amantana
- Mark Gosink
- David Szabo
- Joel Cohen
- Nigel Greene
- Patricia Ruiz
“Industrial Applications of Artificial Intelligence in Toxicology”
- Monday, March 15, 2021, 11:15 AM US EST
- Co-chaired by Catrin Hasselgren (Genentech) and Nigel Greene (AstraZeneca)
- Speakers: Alex Amberg (Sanofi); Fangyao Hu (Genentech); Marinka Zitnik (Harvard Uni); Andreas Bende (Cambridge)

"Application of Computational Genomic Approaches to Address Toxicity Mechanisms and Prediction"
- Wednesday, March 24, 2021, 11:45 AM - 2:30 PM U.S. EST
- Co-chaired by Mark M Gosink (Pfizer) and Minjun Chen (NCTR/FDA)
- Speakers: Roland Grafström (Karolinska Institutet/Sweden); Baitang Ning (NCTR/FDA); David Rouquié (Bayer/France); Jean-Claude Marshall (Pfizer/USA); Jiri Aubrecht (Sarepta Therapeutics/USA)
• The Society of Toxicology Scientific Planning Committee (SPC) makes the final decision on acceptance, NOT the CTSS.
  – Each SOT SPC member scores half the proposals independently without knowing scores from other SPC members.
  – The average score for each proposal is calculated, and the top third proposals have high probability of being accepted.
  – Most of the discussion is about the middle third (on the bubble).

• You want to be in the top third, which means you have to help SOT SPC members who are not computational toxicologists understand the significance of your proposal.

• CTSS committee will help you if you ask!

With thanks to Abby Li
Contribute to the Continuing Education Program!

• Opportunity to connect with and teach attendees about your specialty
• Submission deadline is May 17, 2021
• $500 stipend to help support each speaker!

www.toxicology.org/2022
Topics of Interest

- Applied Organ-on-a-Chip
- Biologics
- **Computational Analysis Including Machine-Learning and AI**
- Endocrine
- Exposure Toxicology Including NAMs and Mixtures
- Gene/Cell-Based Therapies
- *In Vitro* and *In Vivo* High-Throughput Screening Challenges and Best Practices
- Immunotoxicology
- Microbiome
- Nanotoxicology (Imaging and Drug Delivery)
- **QSAR**
- Regulatory Guidelines and Practices
- Reproductive and Developmental Toxicology
- Single Cell Approaches

www.toxicology.org/2022
CTSS Webinar Series
Past webinars

- Government and Academic initiatives with AOPs, Endocrine Predictions, and Deep Neural Network Modeling
  CTSS Award Winners: Sara Vliet, PhD, Mary Schleiff, Dong Wang PhD

- Artificial Intelligence in the Design of Safer Medicines—Science or Science Fiction?
  Nigel Greene, PhD

- Computational Methods in Next-Generation Risk Assessment of Consumer Products
  Steve Gutsell, PhD

- US FDA Experience in the Regulatory Application of (Q)SAR Modeling
  Naomi Kruhlak, PhD

- An Introduction to In Silico Toxicology
  Glenn Myatt, PhD & Donna Macmillan, PhD

Educational Webinars
on CTSS Website
CTSS Webinar Series
Upcoming webinars

- **April 7, 2021, 11 am EST**
  Advanced Tissue Imaging and AI Data Analysis: Opportunities/Challenge for Supporting Drug Discovery
  Richard Goodwin, PhD & Matthew Jacobsen, PhD, AstraZeneca

- **May 21, 2021 (IVAM joint Webinar – pending SOT approval)**
  State of the Science: QSAR Modeling of Skin Sensitization
  Vinicius Alves, Ph.D, UNC-Chapel Hill, Emily Golden, Johns Hopkins U, Glenn Myatt, Leadscope

- **June 23, 2021 11 am EST**
  Application of *In Vitro* and *In Silico* Data in Predictive Modeling of Human Organ Toxicity
  Ruili Huang, PhD, National Center for Advancing Translational Sciences (NCATS), National Institutes of Health (NIH)

- **August 5, 2021, 11 am EST**
  Moving from One-Size-Fits-All to Fit-for-Purpose TTC Values
  Speakers: Ron Brown, PhD, Risk Sciences Consortium and Grace Patlewicz, PhD, US EPA
CTSS Award Process

- Award Committee: Nigel Greene, Kevin Cross, Patricia Ruiz, David T Szabo, Minjun Chen
- All members are required to recuse themselves from potential conflicts of interest
CTSS Paper of the Year Award
“A cross-industry collaboration to assess if acute oral toxicity (Q)SAR models are fit-for-purpose for GHS classification and labelling”, Regulatory Toxicology and Pharmacology, 2020

CTSS Student Travel Award
Alexander Blanchette (Texas A&M University)
Abstract title: “A Bayesian Method for Population-wide Cardiotoxicity Hazard and Risk Characterization Using an In Vitro Human Model”

CTSS Postdoctoral Travel Award
Kiara Fairman (FDA National Center for Toxicology Research)
A cross-industry collaboration to assess if acute oral toxicity (Q)SAR models are fit-for-purpose for GHS classification and labelling

Glenn J. Myatt
VP, Informatics
Leadscope (an Instem company)

March 16, 2021
A cross-industry collaboration to assess if acute oral toxicity (Q)SAR models are fit-for-purpose for GHS classification and labelling

Research reported in this publication was supported by the National Institute of Environmental Health Sciences of the National Institutes of Health under Award Number R44ES026909. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Collaborators in this project included:
- Catrin Hasselgren. Genentech
- Jean Lord. Ultragenyx
- Joel Bercu, Melissa Masuda-Herrera, Alejandra Trejo-Martin. Gilead Sciences
- Jessica Graham. Bristol Myers Squibb
- Matthew Schmitz. AbbVie Inc
- Lawrence Milchak, Colin Owens. 3M
- Sunya Hari Lal, Richard Marchese Robinson, Sarah Whalley. Syngenta
- Phillip Bellion, Anna Vuorinen. DSM Nutritional Products
- Kamila Gromek. Galapagos
- William A. Hawkins. GlaxoSmithKline
- Iris van de Gevel, Kathleen Vriens. Janssen Pharmaceutical Companies of Johnson & Johnson
- Raymond Kemper, Russell Naven. Vertex Pharmaceuticals Inc.
- Pierre Ferrer. Texas A&M University

https://doi.org/10.1016/j.yrtph.2020.104843
Use of acute toxicity test (AOT)

- International compound registrations
- Define labeling information
  - safety data sheets (SDS)
  - containers
- Guide how a chemical should be packaged, labeled and/or transported
AOT (Q)SAR Models and 3Rs

• An AOT (Q)SAR model offers an animal-free alternative
• If an alternative model predicts AOT as reliably as an in vivo study, the alternative method should be preferred and supported
• A reliable AOT in silico model could complement an existing laboratory study (reduce and refine)
Study design

- Collaborators were given access to the acute toxicity (Q)SAR models from Leadscope (both statistical-based and expert rule-based methodologies)
- Each collaborator collected historical information on chemicals where rat AOT study had been performed, including
  - Information on the study protocol
  - Study parameters
  - Results
- Chemicals were then loaded into the (Q)SAR software and prediction results were generated
- The experimental and predicted results were collected and analyzed from all collaborators

https://doi.org/10.1016/j.yrtph.2020.104843
Results

“...percentage of correct or more conservative predictions, based on a comparison of experimental and predicted GHS categories, was approximately 95%...”

Table 2
Table showing counts of how the consensus model predicts for the different GHS categories.

<table>
<thead>
<tr>
<th>Predicted</th>
<th>Cat. 1</th>
<th>Cat. 2</th>
<th>Cat. 3</th>
<th>Cat. 4</th>
<th>Cat. 5</th>
<th>NC</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental</td>
<td>5⁵</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Cat. 1</td>
<td>5</td>
<td>1⁶</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Cat. 2</td>
<td>1</td>
<td>29</td>
<td>52⁷</td>
<td>40</td>
<td>2</td>
<td>2</td>
<td>126</td>
</tr>
<tr>
<td>Cat. 3</td>
<td>4</td>
<td>43</td>
<td>115</td>
<td>269⁸</td>
<td>38</td>
<td>8</td>
<td>468</td>
</tr>
<tr>
<td>Cat. 4</td>
<td>1</td>
<td>15</td>
<td>54</td>
<td>196</td>
<td>99²</td>
<td>12</td>
<td>247</td>
</tr>
<tr>
<td>Cat. 5</td>
<td>3</td>
<td>48</td>
<td>164</td>
<td>343</td>
<td>126⁹</td>
<td>25³</td>
<td>709</td>
</tr>
<tr>
<td>Cat. 5 or NC</td>
<td>9</td>
<td>32</td>
<td>119</td>
<td>227</td>
<td>116</td>
<td>87¹</td>
<td>590</td>
</tr>
<tr>
<td>NC</td>
<td>28</td>
<td>187</td>
<td>509</td>
<td>978</td>
<td>346</td>
<td>133</td>
<td>2181</td>
</tr>
</tbody>
</table>

a Indicates where a correct prediction is made.
b Where chemicals were identified as > 2000 mg/kg they were placed in category “Cat. 5 or NC” and not in Cat.5 or NC.
c Not including inconclusive predictions.

https://doi.org/10.1016/j.yrtph.2020.104843
A cross-industry collaboration to assess if acute oral toxicity (Q)SAR models are fit for purpose for GHS classification and labeling.

https://doi.org/10.1016/j.jyrph.2020.104843
Conclusions

“...rapid and cost-effective alternative approach...”

“...potential to reduce or eliminate the use of in vivo testing...”

“... broad range of chemicals...”

“... importance of an expert review...”

“... scientifically rational, reasonable and conservative approach to hazard identification.”

https://doi.org/10.1016/j.yrtph.2020.104843
A Bayesian Method for Population-Wide Cardiotoxicity Hazard and Risk Characterization Using an In Vitro Human Model

Alexander Blanchette, BS
Doctoral Candidate – Weihsueh Chiu Lab
Environmental Cardiotoxicity Data-Gap

- Cardiovascular disease is a leading cause of death worldwide and in the US
- Some links from environmental exposures to CVD have been established, but little known about most compounds
- No testing requirements for cardiovascular effects under current TSCA guidelines

Population Variability Data-Gap

- Interspecies variability typically addressed in risk assessments through the use of default uncertainty factors
- Recognized need for chemical-specific data to replace the default uncertainty factors.

\[
Rfd = \frac{POD}{UF_H \times UF_A}
\]

Replace with \( TDVF_{05} \)

\[UF_{H,TK}^{10^{1/2}}\]

\[UF_{H,TD}^{10^{1/2}}\]
Our Solution

In vitro- In Silico Method

Compounds from Multiple Chemical Classes (n=136)

<table>
<thead>
<tr>
<th>Chemical Class</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIPA Pharmaceuticals</td>
<td>15</td>
</tr>
<tr>
<td>Other Pharmaceuticals</td>
<td>39</td>
</tr>
<tr>
<td>Environmental Chemicals (e.g., pesticides, PAHs, industrial chemicals, flame retardants)</td>
<td>82</td>
</tr>
</tbody>
</table>

Population-Based iPSC-Derived Cardiomyocyte Model (n = 43 individuals)

In Vitro Concentration-Response Screening

Bayesian Population Concentration-Response Modeling

Markov Chain Monte Carlo Sampling

Posterior Distributions

Model Evaluation and Predictions

Population-Based Hazard and Risk Characterization

Hazard Characterization
- Active/Inactive for each chemical and endpoint
- Critical endpoint for each chemical
- Point of departure (POD) for each endpoint
- Population variation in toxicodynamic sensitivity

Risk Characterization
- Margin of safety for pharmaceuticals
- Margin of exposure for environmental chemicals
- Separate estimates for population median and sensitive individual


See Burnett et al. (2019) for details
Hazard Characterization

Most common critical endpoints:
- QT Prolongation and Asystole for CiPA compounds
- -chronotropes for other pharmaceuticals
- + chronotropes for environmental chemicals

Risk Characterization

- Cardiotoxic risk from environmental compound exposure is low
- Cardiotoxic risk from pharmaceutical dosing is higher in comparison

Population Variability Characterization

Most common critical endpoints:
- QT Prolongation and Asystole for CiPA compounds
- -chronotropes for other pharmaceuticals
- + chronotropes for environmental chemicals
Study Key findings:

1. Functional phenotype $TDV_{0.05}$ values often exceed the default $UF_{H,TD}$

2. There is little risk of adverse cardiovascular outcomes as a result of exposure to environmental chemicals at current estimated levels

Our *in vitro-in silico* model can:

- Quantify the degree of chemical-specific TD variability for pharmaceuticals and environmental chemicals
- Derive chemical-specific estimations of risk while still accounting for population variability
- Help close ever-widening data gap of chemicals with insufficient or no data on cardiotoxicity and its population variation in susceptibility
Pregnancy PBPK Modeling of UGT Substrate Labetalol: An Application of Parameter Contribution Analysis to Guide Predictive Performance of Life Stage Models

Kiara Fairman, Pharm.D., M.S.¹, Miao Li, Ph.D.¹, Annie Lumen, Ph.D.¹

1.Division of Biochemical Toxicology, National Center for Toxicological Research, U.S. Food and Drug Administration, Jefferson, AR 72079, USA
Corresponding Authors: Kiara Fairman (Kiara.Fairman@fda.hhs.gov); Annie Lumen (Annie.Lumen@fda.hhs.gov)

Disclaimer: The information in these materials is not a formal dissemination of information by FDA and does not represent agency position or policy.
BACKGROUND

*Fuchsia indicates lumped compartments with multiple tissues contributing to one compartment's growth

Full structure of minimalistic dynamic pregnancy PBPK model
RESULTS
Pregnancy Model Performance and Simulation

Plasma profiles of labetalol for a simulated oral dose of 300 mg in a pregnant woman without UGT activity change for trimesters 1, 2 & 3 and non-pregnancy superimposed over each other on a logarithmic scale.

Parameter contributions in predicting AUC changes for labetalol across trimesters 1, 2, 3.
RESULTS

Table 1. Model predictions compared to AUC calculated from clinically observed CL/F. 300mg Orally every 12 hours. No change in clearance from non-pregnancy input.

<table>
<thead>
<tr>
<th>Trimester</th>
<th>CI/F fold change</th>
<th>% drop in observed AUC</th>
<th>PBPK model predicted % drop in AUC</th>
<th>Uncaptured AUC</th>
<th>Captured AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>1.4</td>
<td>28.5%</td>
<td>16.2%</td>
<td>43.3%</td>
<td>56.7%</td>
</tr>
<tr>
<td>2nd</td>
<td>1.6</td>
<td>37.5%</td>
<td>41.8%</td>
<td>11.5%</td>
<td>88.5%</td>
</tr>
</tbody>
</table>

Labetalol plasma concentrations for trimesters 1, 2, and 3 and non-pregnancy superimposed on a logarithmic scale for 300mg oral dose with UGT activity change.

Proposed quantitative activity change of UGT1A1 and UGT2B7 throughout pregnancy.

Table 2. Model predictions compared to calculated AUC from clinically observed CL/F. 300mg Orally every 12 hours. UGT1A1 and UGT2B7 estimated changed included.

<table>
<thead>
<tr>
<th>Trimester</th>
<th>CI/F fold change</th>
<th>% drop in observed AUC</th>
<th>PBPK model predicted % drop in AUC</th>
<th>Uncaptured AUC</th>
<th>Captured AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>1.4</td>
<td>28.6%</td>
<td>28.6%</td>
<td>0.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>2nd</td>
<td>1.6</td>
<td>37.5%</td>
<td>37.4%</td>
<td>0.2%</td>
<td>100.2%</td>
</tr>
</tbody>
</table>
CONCLUSIONS

• The life-stage PBPK model initially captured 60-90% of the total AUC changes at for trimesters 1 & 3 with the remaining possibly attributed to pregnancy related changes in UGT-mediated clearance capturing 100%.

• Progesterone influence of UGT1A1 allowed for greater certainty in the estimated equation, whereas UGT2B7 was estimated to increase AUC capture in trimesters with reported PK values available for comparison.

• Sensitivity coefficient guided parameter contribution analysis identified the primary physiological determinants of pregnancy PK for labetalol and quantified the extent of their contributions.

• Such contribution analysis could help determine the confidence of life-stage model predictions, especially in data sparse life-stages, where there are uncertainties in model input parameters and help prioritize parameterization of life-stage PBPK models in the future.

ACKNOWLEDGEMENTS

• Annie Lumen, PhD
• Miao Li, PhD

• Computational Toxicology Specialty Section
• Office of Women’s Health
• FDA National Center for Toxicological Research

FUNDING & DISCLAIMER

We acknowledge support of this work and the fellowship for Kiara Fairman from the FDA Office of Women’s Health through the Oak Ridge Institute for Science and Education. We also acknowledge the support of the FDA National Center for Toxicological Research.

The information in these materials is not a formal dissemination of information by FDA and does not represent agency position or policy.

References will be provided upon request.
2021 Best SOT-CTSS Abstract Awards
Top 3

- David Filipovic from Michigan State University for the SOT abstract: “Accurate Tissue-Specific In Silico Genome-Wide Prediction of Aryl Hydrocarbon Receptor Binding” (Abstract No. 2537)

- Suguna Dev Sakkiah from the FDA’s NCTR for the SOT abstract: “Elucidating Interactions between SARS-Co-V-2 Trimeric Spike Protein and ACE2 Using Homology Modeling and Molecular Dynamics Simulations” (Abstract No. 2999)

- Ting Li from the FDA’s NCTR for the SOT abstract: “Deep Learning-Powered Drug-Induced Liver Injury Prediction Using Model-Level Representation” (Abstract No. 2518)
2021 CTSS Abstract Awards

- Farida Akhtari from NIEHS (Abstract no. 2985)
- Shagun Krishna from NIEHS (Abstract no. 2561)
- Cathy Lester from Procter & Gamble (Abstract no. 2553)
- Robert Pullen III from Sanofi (Abstract no. 2995)
- David Rouquie from Bayer SAS (Abstract no. 2788)
- Elizabeth Shipp from Corteva Agriscience (Abstract no. 2792)
- Leihong Wu from the FDA’s NCTR (Abstract no. 2545)

All abstracts can be viewed on our SOT planner and referenced on our CTSS website.
2021 Winner of the Yves Alarie Diversity Award

Shagun Krishna, PhD
National Toxicology Program/NIEHS
Early Investigator

SOT Abstract: High-Throughput Screening to Predict hERG inhibition

Shagun Krishna, Alexandre Borrel, Ruili Huang, Jinghua Zhao, Menghang Xia, and Nicole Kleinstreuer
Division of the National Toxicology Program, National Institute of Environmental Health Sciences (NIEHS), Research Triangle, NC, USA, 2Independent Consultant, France, Division of Preclinical Innovation, National Center for Advancing Translational Sciences (NCATS), Bethesda MD 20892-4874, USA
High-Throughput Screening to Predict hERG inhibition

Shagun Krishna
Division of the National Toxicology Program, NIEHS

Annual CTSS Award Reception, SOT 2021
16 March 2021
Cardiovascular (CV) disease is the leading cause of death for people of most ethnicities in the United States.

A potentially significant but underappreciated risk factor contributing to the development and severity of CV disease is exposure to bioactive substances in our environment.

The human ether-a-go-go related gene (hERG) potassium channel plays a pivotal role in cardiac rhythm regulation, especially in the repolarization of cardiac action potential, and can lead to prolongation of the QT interval.

An evaluation of the effect of environmental chemicals on hERG channel function can help inform the potential public health risks of these compounds.

To assess the effect of environmental chemicals on hERG channels, the Tox21 federal research program has screened a collection of 9667 chemicals using a cell-based thallium influx assay in a quantitative high throughput screening (qHTS) format.
Results: Clustering

**Assay description**
- Thallium influx assay in U2OS cells
- Tox21 library 7871 unique chemicals
- 15 Point concentration response

**Assay outcome**
- 896 Active
- 6975 Inactive

**Data processing**
- 559 Active
- 6627 Inactive

**Structural activity patterns**
- SOM
- Hierarchical Clustering

**Workflow**

**Structure-based SOM**

**Hierarchical Clustering**
Results: Classification Models

Q = Accuracy
SP = Specificity
SE = Sensitivity
MCC = Matthew’s correlation coefficient
Qb = Balanced Accuracy

QSAR Classification Models

Validation: External Test Set (PubChem Assay)
• Approximately 7.8% of the Tox21 chemical library demonstrated hERG inhibitory potential.

• Structure-based models have the capability to predict new chemical structures that may disrupt hERG activity and cause cardiotoxicity.

• Multiple machine learning algorithms were applied, and random forest model was found to outperform other models.

• Ongoing work involves enrichment of active chemicals by including data from CHEMBL datasets and construction of regression models.
Volunteer Opportunities

• GET INVOLVED with CTSS
• Several CTSS Committees need you:
  ✓ Sessions
  ✓ Awards
  ✓ Newsletter
  ✓ Webinars
  ✓ Events
  ✓ Endowment Fund

Are you interested in participating as invited speaker for our future CTSS webinars? Do you have colleagues who might be a great fit? We welcome nominations, including yourself, for anyone with interest and expertise in computational toxicology, applications, methods development and cutting-edge topics. Please submit your nominations to Catrin Hasselgren
March 27-31, San Diego

- Events: CTSS Luncheon/Reception
- What topics would be of interest?
Thank you for attending the 2020-2021 CTSS Annual Reception and we look forward to seeing you at next year’s meeting in San Diego!!