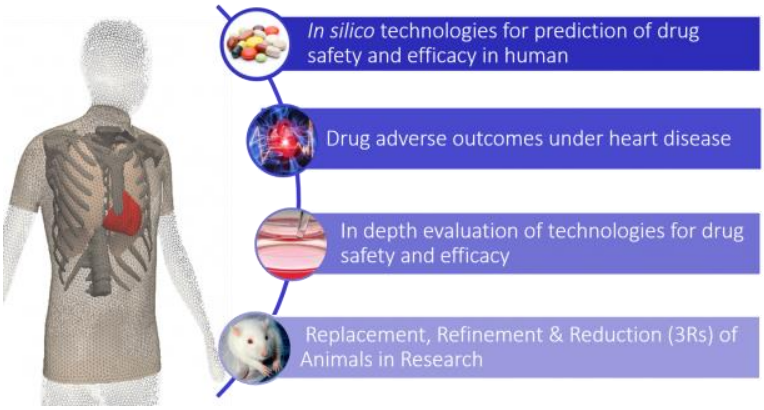
"In Silico Human Drug Safety and Efficacy" Newsletter



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The project "In silico human-based methodologies for evaluation of drug safety and efficacy" officially started on September 2016. The main goal of this initiative is to accelerate the use of *in silico* methodologies for the evaluation of drug safety and efficacy in academic, industrial, regulatory and clinical settings. The coordinated action of these four sectors aims to improve the efficiency of drug testing through the use of human-based computer models, refined and evaluated using experimental and clinical recordings. Through this project, we will work towards the replacement of animal experiments in the drug development process, and the development of a more reliable and accurate process for drug safety testing. The team is formed by a partnership across industry, academia, hospitals and regulatory agencies from 14 different countries.
The webpage of the project is an open space to share knowledge, papers and models, and also a reference for experts on *in silico* methodologies for drug safety and efficacy. We encourage all partners to get involved and send news, papers and models related to the project to insilicocardiotox@cs.ox.ac.uk, to keep the website alive.

LATEST NEWS

- Insilicocardiotox Mailing List **Privacy Notice** now available on our website!
  To comply with the General Data Protection Regulation (GDPR), a privacy notice explaining how we use and store your data is now available on our website.
- Human Cardiac **Model Repository** now available on our website!
  We recently added this page on our website, to group together all the human cardiac models published in literature, also including modified version representing specific diseased conditions. If there is a model you would like to add, please be in touch and we will update the page.
- Promote adoption of In Silico Trials through EMA's strategy on Regulatory Science to 2025 – **Sign the Petition**
  The VPH Institute together with the Avicenna Alliance, the Insigneo Institute for *in silico* Medicine and the University of Bologna has opened a petition to recommend EMA to include in the their strategy plan a more articulated role for *in silico* technologies. You can sign the petition here.
- Survey into opinions on the studies outlined within ICH S7 guidance – Deadline 30th of August
  The ICH S7 guidance describes nonclinical safety pharmacology studies as core battery, follow-up or additional studies. In order to ascertain how the guidance is used and the relevance of individual studies to current drug development portfolios, the Safety Pharmacology Society and NC3Rs have generated a short survey to gather high-level information on the opinions of individual scientists into the scope for revisiting the guidance. Participate here.
- Frontiers in Pharmacology's Special Issue – Deadline 15th of September
  Special Issue on "Perspectives on Antiarrhythmic Drug Therapy: Disappointing Past, Current Efforts and Faint Hopes".
- HESI Cardiac Program Awarded 3 Year Grant from FDA
  The HESI Cardiac Safety Committee has been awarded a multi-year U01 grant from the US FDA on the "Evaluation of Integrated Human-Relevant Approaches to Identify Drug Induced Cardiovascular Liabilities", starting in September 2019. This grant will support HESI in funding and managing novel, in vitro experimental studies to develop targeted mechanistic data to inform drug safety assessment for key cardiac "failure modes"
- INSPIRE - INnovation in Safety Pharmacology for Integrated cardiovascular safety assessment to REduce adverse events and late stage drug attrition – awarded a European Commission Horizon 2020: Research & Innovation Program grant
  INSPIRE aims to build on recent technological advances to improve risk prediction in safety pharmacology. With the involvement of leading pharmaceutical companies, universities, software and hardware suppliers, the research will translate into products and services for improved assessment of drug-induced cardiovascular toxicity and, ultimately, safer medicines for patients.

UPCOMING EVENTS

- Cardiac Mechano-Electric Coupling and Arrhythmias Workshop
  Freiburg (DE), 4-7 September, 2019.
- BioMedEng19 Conference
  London (UK), 5-6 September, 2019.
- Computing in Cardiology 2019
  Singapore (SG), 8-11 September 2019
- Safety Pharmacology Society 2019 Annual Meeting
  Barcelona (ES), 23-26 September 2019
- CompBioMed Conference 2019
  London (UK), 25-27 September, 2019
- IX Annual Meeting of the Italian Chapter of the European Society of Biomechanics (ESB-ITA)
  Bologna (IT), 30 September – 1 October, 2019
- Heart Rhythm Congress 2019
  Birmingham (UK), 6-9 October, 2019
- Biennial UC Davis Cardiovascular Symposium
  Davis (CA, US), 21-23 February, 2020

AWARDS

- PhD students Francesca Margara and Cristian Trovato have been awarded the 2019 Safety Pharmacology Society Student Travel Award
  They will present a poster about their research at the Safety Pharmacology Annual Meeting this September in Barcelona.
- Professor Yoram Rudy has been elected Fellow of the National Academy of Inventors of the United States of America
  The title was awarded for having demonstrated a prolific spirit of innovation in creating or facilitating outstanding inventions that have made a tangible impact on quality of life, economic development and the welfare of society.
- Professor Blanca Rodriguez has been elected Fellow of the ESC and EAMBES
  Fellow of the European Society of Cardiology (FESC) is a title of honour that is awarded to healthcare professionals who have made a significant contribution to cardiology, recognised throughout the cardiology community as a symbol of excellence. The European Alliance for Medical and Biological Engineering (EAMBES) represents the academic aspects and interests of Biomedical Engineering in Europe. The Division of Fellows is formed by individuals who have distinguished themselves by identifiable contributions or accomplishments in Medical and Biological Engineering and Science.

RECENT PUBLICATIONS

- A computational model of induced pluripotent stem-cell derived cardiomyocytes incorporating experimental variability from multiple data sources. Kernik DC, Morotti S, Duff HJ, Kurokawa J, Jalife J, Wu JC, Grandi E, Clancy CE. J Physiol 2019. doi: 10.1113/JP277724.
- A modeling and machine learning approach to ECG feature engineering for the detection of ischemia using pseudo-ECG. Ledezma CA, Zhou X, Rodriguez B, Tan PJ, Diaz-Zuccarini V. PloS One. 2019. doi: 10.1371/journal.pone.0220294.
- Antiarrhythmic mechanisms of beta blocker therapy. Grandi E, Ripplinger CM. Pharmacol Res. 2019. doi: 10.1016/j.phrs.2019.104274.
- Artificial intelligence for the electrocardiogram. Mincholé A, Rodriguez B. Nat Med. 2019. doi: 10.1038/s41591-018-0306-1.
- β-Adrenergic Receptor Stimulation and Alternans in the Border Zone of a Healed Infarct: An ex vivo Study and Computational Investigation of Arrhythmogenesis. Tomek J, Hao G, Tomková M, Carr C, Lewis A, Paterson DJ, Rodriguez B*, Herring N*, Bub G* (*shared senior authors). Front Physiol. 2019. doi: 10.3389/fphys.2019.00350.
- Computational modeling: What does it tell us about atrial fibrillation therapy? Grandi E, Dobrev D, Heijman J. Int J Cardiol. 2019. doi: 10.1016/j.ijcard.2019.01.077.
- Data-driven Identification of Stochastic Model Parameters and State Variables: Application to the Study of Cardiac Beat-to-beat Variability. Sampedro-Puente DA, Fernandez-Bes J, Virag L, Varro A, Pueyo E. IEEE J Biomed Health Inform. 2019. doi: 10.1109/JBHI.2019.2921881.
- Drug-induced Shortening of the Electromechanical Window is an Effective Biomarker for in Silico Prediction of Clinical Risk of Arrhythmias. Passini E, Trovato C, Morissette P, Sannajust F, Bueno-Orovio A, Rodriguez B. Br J Pharmacol. 2019. doi: 10.1111/bph.14786.

- Investigating the Complex Arrhythmic Phenotype caused by the Gain-of-function Mutation KCNQ1-G229D. Zhou X, Bueno-Orovio A, Schilling RJ, Kirkby C, Denning C, Rajamohan D, Burrage K, Tinker A, Rodriguez B*, Harmer SC*. (*shared senior author). Front Physiol. 2019. doi: 10.3389/fphys.2019.00259.
- Mechanisms Underlying Interactions Between Low-Frequency Oscillations and Beat-to-Beat Variability of Celullar Ventricular Repolarization in Response to Sympathetic Stimulation: Implications for Arrhythmogenesis. Sampedro-Puente DA, Fernandez-Bes J, Porter B, Van Duijvenboden S, Taggart P, Pueyo E. Front Physiol. 2019. doi: 10.3389/fphys.2019.00916.
- Transient outward K^+ current can strongly modulate action potential duration and initiate alternans in the human atrium. Ni H, Zhang H, Grandi E, Narayan S, Giles W. Am J Physiol-Heart C. 2019. doi: 10.1152/ajpheart.00251.2018.