Cross-Species Extrapolation: Opportunities in a 21st-Century Regulatory Nonanimal Testing World

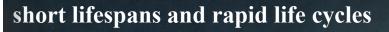
Q&A DISCUSSION

<u>CHAIR:</u> BRITT MCATEE, PH.D. PPG INDUSTRIES <u>MODERATOR:</u> CARLIE LALONE, PH.D. US ENVIRONMENTAL PROTECTION AGENCY

cheap and readily available



easy maintenance and good breeding capabilities



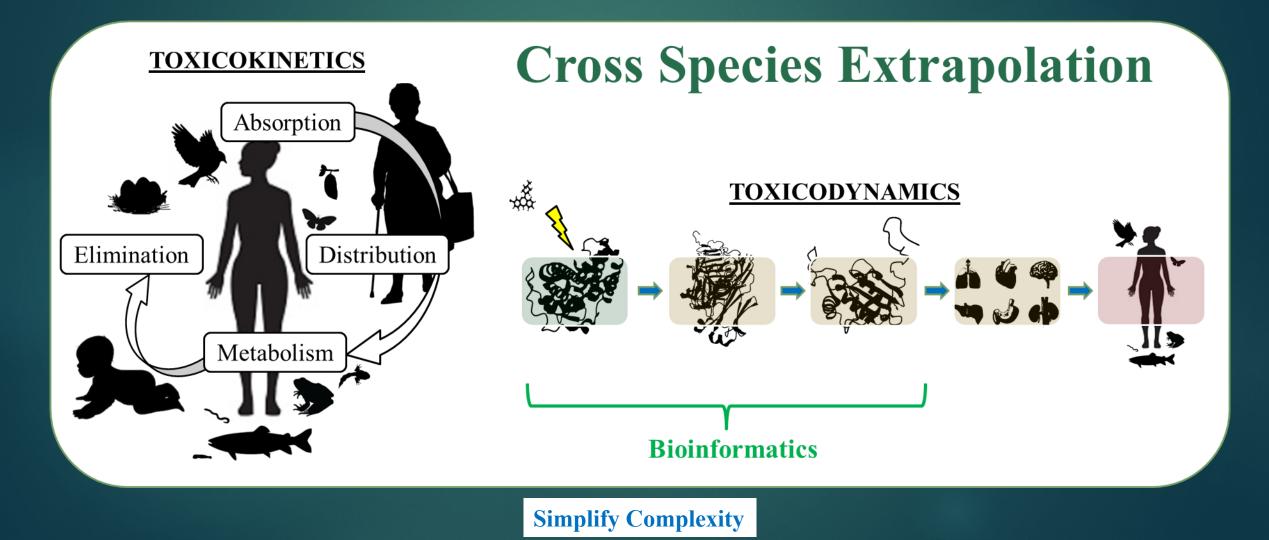




requires least space and time-consuming care

ability to control diet and surroundings

Sensitivity to Chemical Perturbation



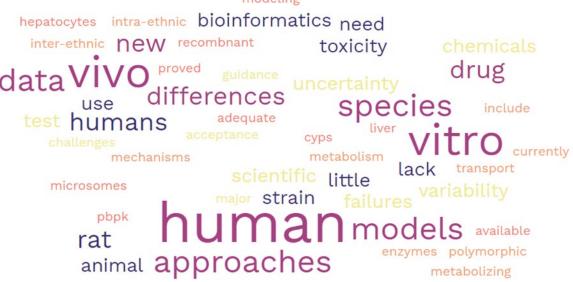


Bioinformatics

- Combines mathematics, information science, and biology to <u>answer biological questions</u>
- Developing methodology and analysis tools to <u>explore</u> <u>hrpe volumes of biological data</u>
 - Query, extract, store, organize, systematize, annotate, visualize, mine, and interpret complex data
 - Usually pertains to DNA and amino acid sequences

Let the computers do the work

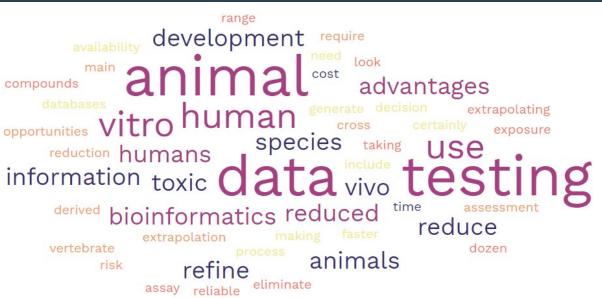
In your view what are the main challenges/roadblocks in regulatory science for which crossspecies extrapolation (with a focus on bioinformatics) modeling approaches can hepatocytes intra-ethnic bioinformatics need inter-ethnic **NeW** recombnant data V help? differences use



In your view what are the (potential) barriers for acceptance of cross-species extrapolation (with a focus on bioinformatics) in regulatory science/ decision-making?



In your view what are the main opportunities/advantages in regulatory science/ decision making for cross-species extrapolation (with a focus on compounds bioinformatics) reduction humans approaches?



Which approaches in cross-species extrapolation (with a focus on bioinformatics) do you believe offer the best opportunities/advantages for helping address/provide solutions to the challenges of a future regulatory landscape (i.e. focused on non-animal testing). Please provide some explanation of the approach (es).

What are the challenges/roadblocks for using bioinformatics approaches in species extrapolation for regulatory decision making?



What are the criteria necessary for integration of bioinformatics approaches for cross species extrapolation in regulatory decision making for toxicokinetics pharmacokinetics disposition infection chemical accompanied variables concept altererd risk cancer data published addition making ^{liver} major chemicals safety? clinical decision

transport dt pharmacogenetics dm depends drug inter-individual differences information individual approach regulatory mechanisms metabolism therefore expression proof-of safety role organ

determining

altered

changes

Which tools/databases/approaches are currently appropriate and ready for use in research, and which are appropriate and ready for regulatory decision-making (timescale: current or ready in the next bioinforomatic pathways metabolism 12-18 months)? VIVO accurate



Application of these bioinformatics approaches for cross species extrapolation to which regulatory challenge(s) would be most convincing of their regulatory opportunity mixtures matrix information sure applicability? data clinical ingestion valuable

soil risk gulf VIVO start along understand think pbpk genotoxicity approaches together modeling bioinformatic comment drug water estimating question generally oral available dermal deal food inhalation

Government

Industry

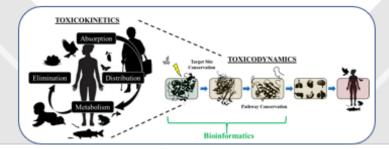
NGO

Consortium to Advance Cross Species Extrapolation in Regulation

<u>Steering Committee:</u> Carlie LaLone (US EPA) Geoff Hodges (Unilever) Nil Basu (McGill U) Steve Edwards (RTI) Fiona Sewell (NC3Rs) Michelle Embry (HESI)

- 1. Define the taxonomic domain of applicability
- 2. Define the global regulatory landscape/need
- 3. Develop a bioinformatics toolbox
- 4. Communicate a shared scientific vision

Interested in Learning more or Joining: Contact LaLone.Carlie@epa.gov or Geoff.Hodges@unilever.com



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