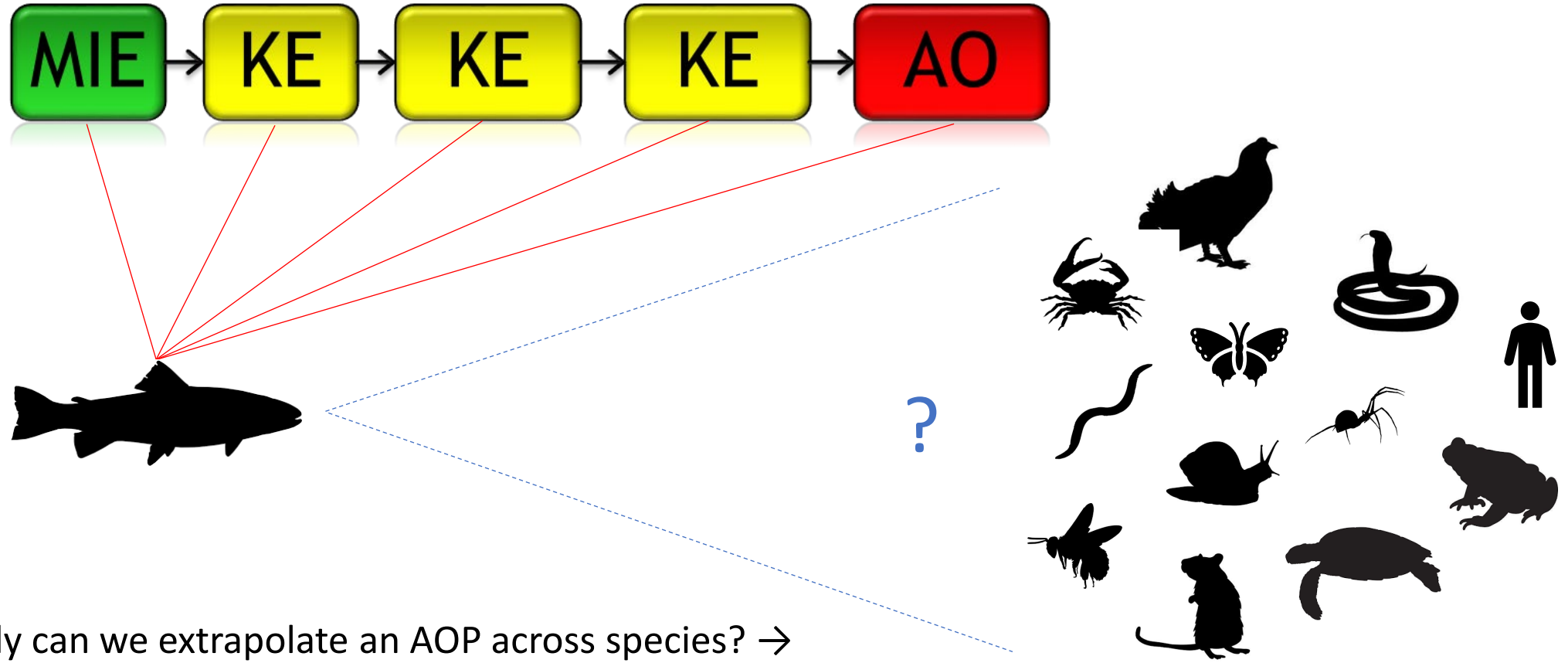
Marissa Jensen

Extrapolating Biological Pathway Knowledge

Adverse Outcome Pathway

Organizes existing biological pathway knowledge



How broadly can we extrapolate an AOP across species? →
Taxonomic Domain of Applicability of AOP

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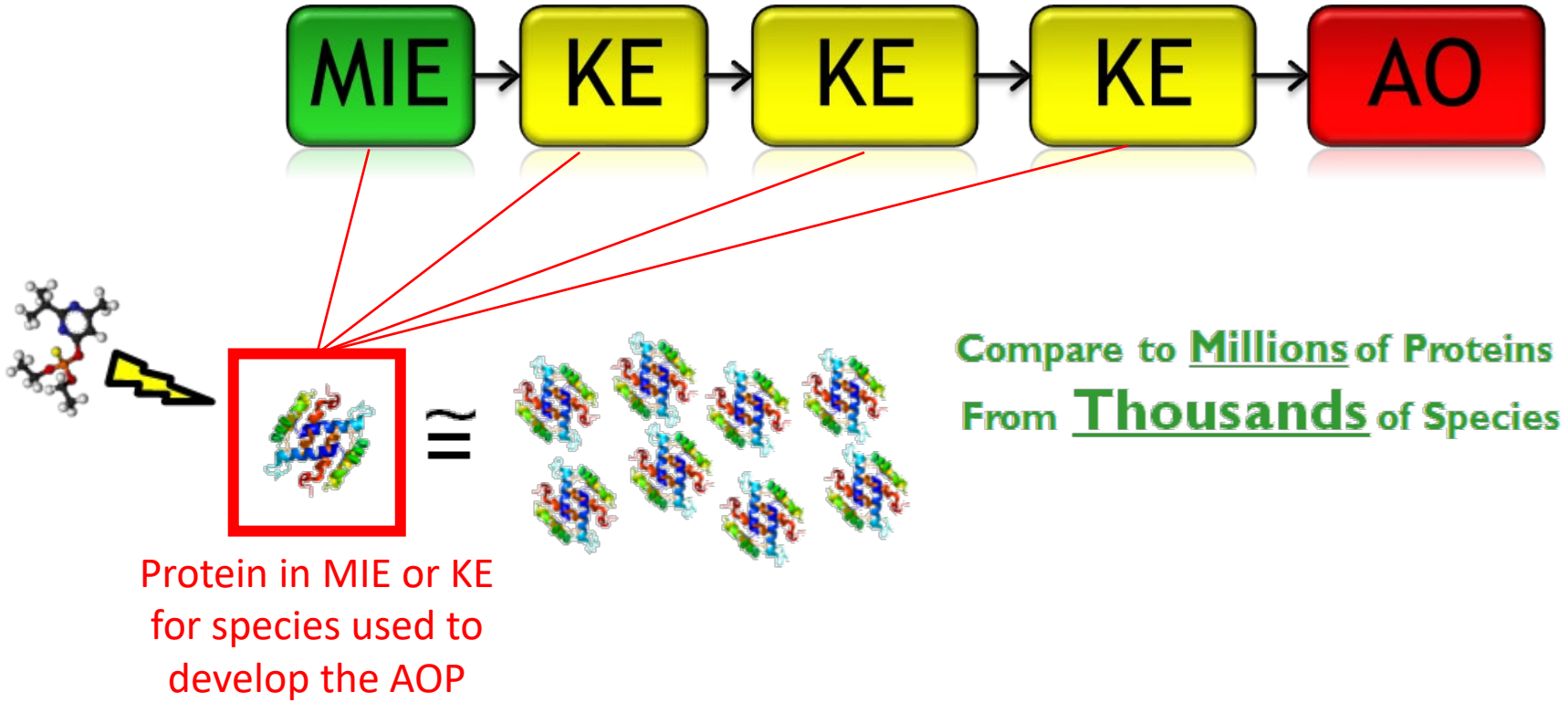
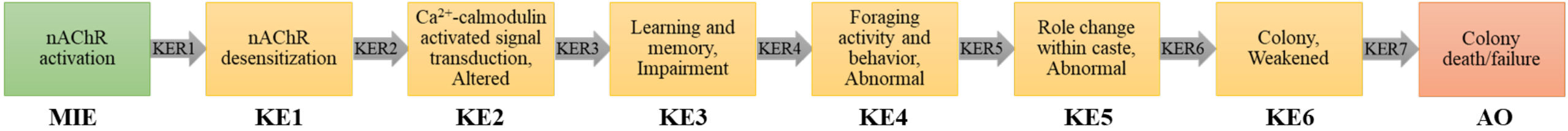
Evaluation of Protein Conservation Across Species Using SeqAPASS

Sequence Alignment to Predict Across Species Susceptibility (SeqAPASS)
assesses protein sequence and structure similarity across species

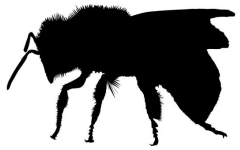


Provides lines of evidence of structural conservation for extrapolation across species

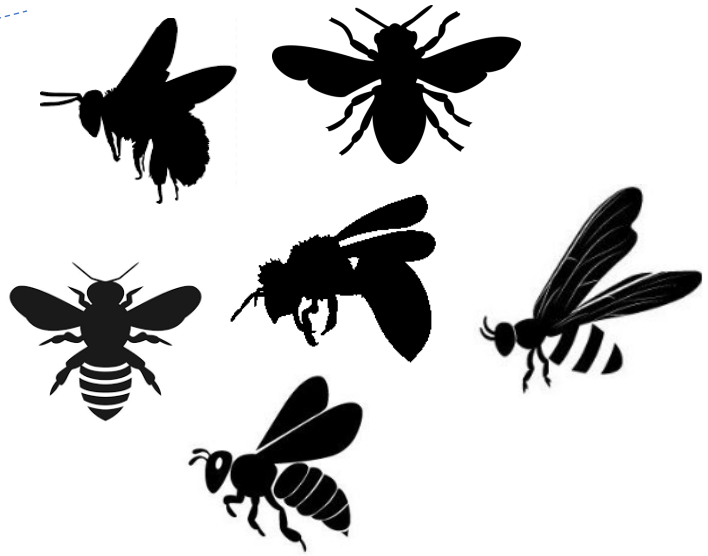
Defining the Taxonomic Domain of Applicability: Case Study



Case Example



?



- SeqAPASS evaluations revealed conservation across *Apis* and non-*Apis* bees at early KEs
- Downstream KEs are expected to differ across bee species depending on species-specific factors (i.e., colony structure, foraging strategies)
- As sequence information continues to expand, it is expected that the use of bioinformatics will continue to enhance tDOA descriptions

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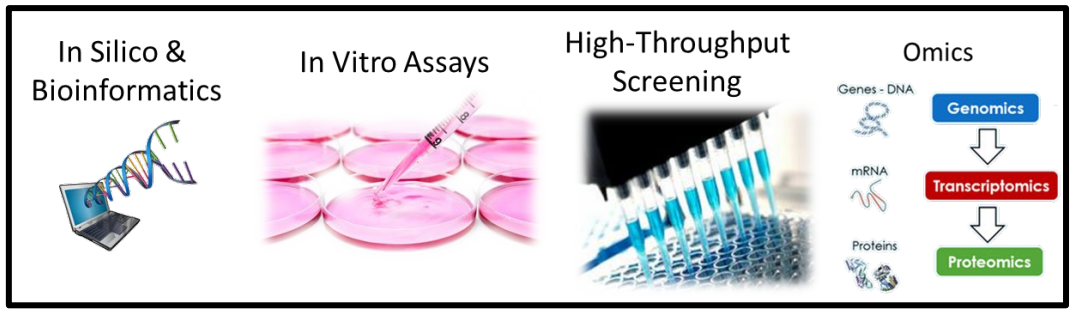
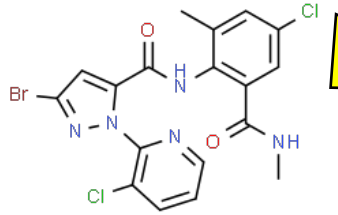
Transformation of Toxicity Testing

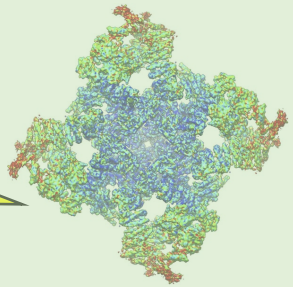


- Use SeqAPASS to address species extrapolation
- Building confidence in predictive approaches
- Combine with existing and new knowledge to learn more about a pathway cross species

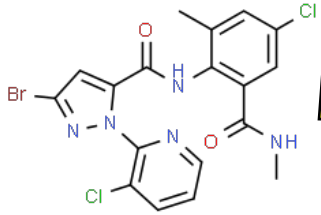
- Simple question to address: is the known chemical target available in a species for a chemical to act upon?



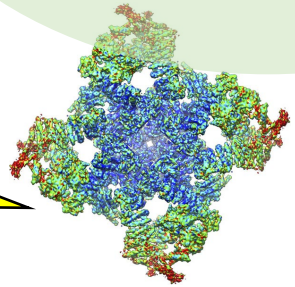
Chlorantraniliprole



Susceptible ☑ Yes



Chlorantraniliprole



Not Susceptible ☐ No