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# Combination of Computational New Approach Methodologies for Enhancing Evidence of Biological Pathway Conservation Across Species

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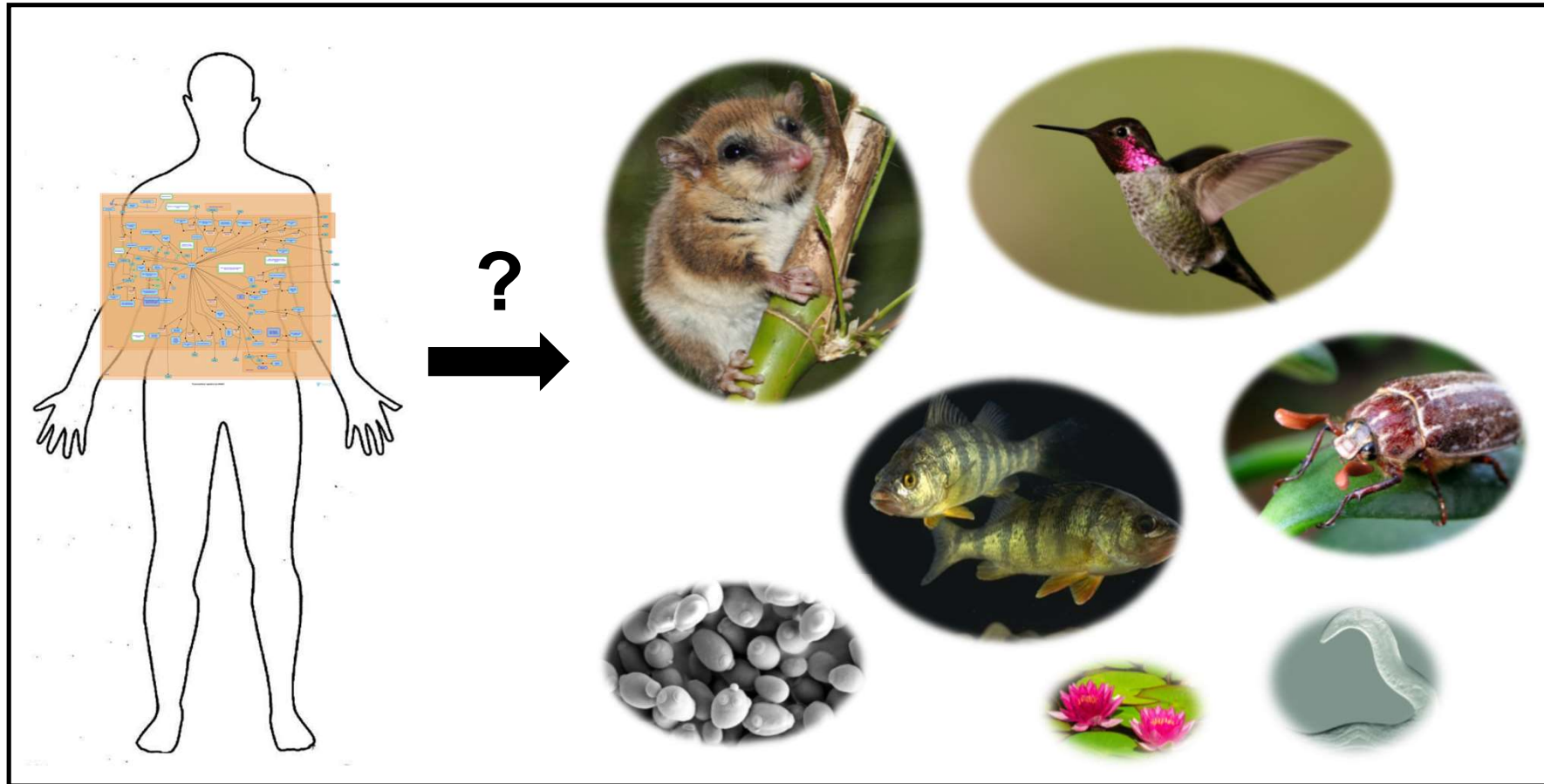
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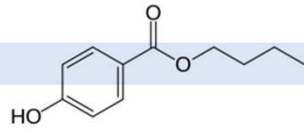


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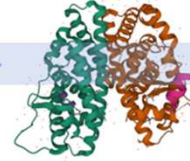


### Chemical of interest

### Molecular targets



**A** Review available data

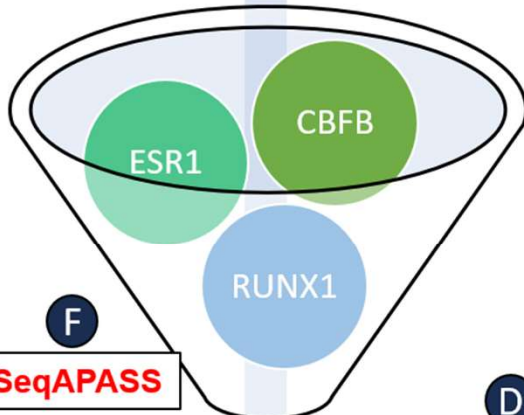


**B** G2P-SCAN

**Mapped pathways**  
+ Counts for pathway genes, proteins, protein families, entities and reactions

### Key pathway proteins

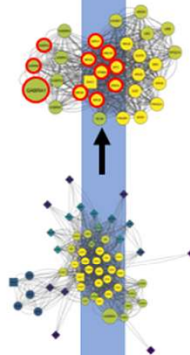
**E** Isoform selection



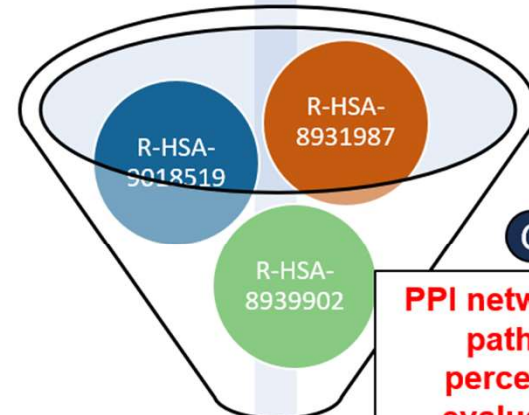
**F** SeqAPASS

### Susceptible Species

- Species where all key pathway proteins are conserved
- To be considered for expansion of tDOA for relevant AOPs



**D** Identify key pathway proteins



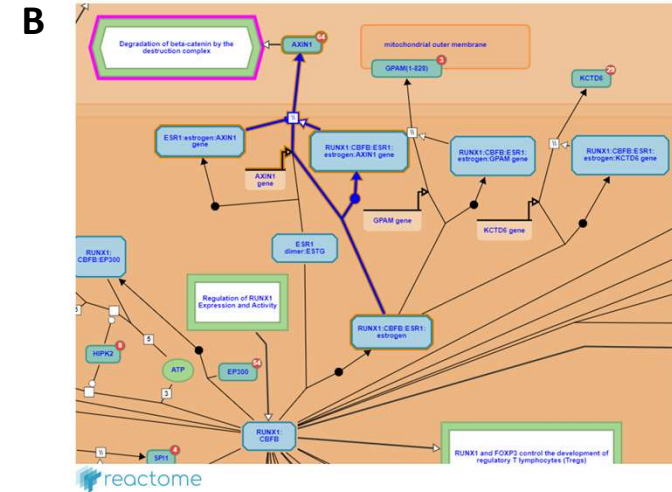
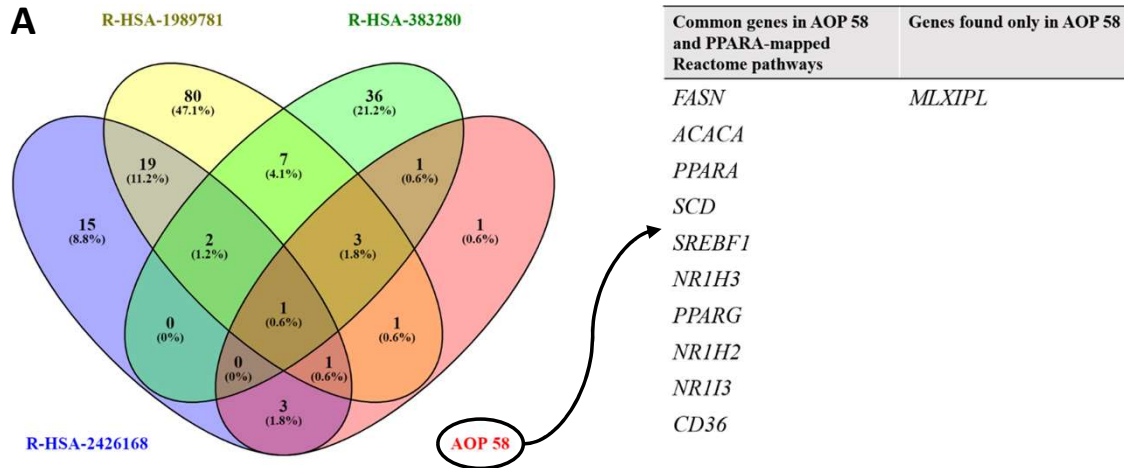
**C** PPI network and pathway percentage evaluations

### Priority Pathways

- Pathway coverage > 10%
- Molecular target found within highest scoring cluster

# Conclusions and Next Steps

- ▶ **(A)** Gene identity and **(B)** functional overlaps mapped biological pathways and related Adverse Outcome Pathways



- ▶ In combination, it was demonstrated that these tools can be used to:
  - Expand the prediction of biological pathway conservation across species (several additional lines of evidence are generated through the use of G2P-SCAN)
  - Aid in the prediction of cross-species chemical susceptibility (approaching a systems perspective)
  - Potentially extend the biologically plausible tDOA of relevant AOPs
  - Provide additional biological information to help further characterize certain KEs and KERs
- ▶ Areas of improvement:
  - Additional factors such as life stage, life history, biological sex, and toxicokinetic factors like absorption, distribution, metabolism, excretion (ADME) may be incorporated to yield a more complete understanding of the chemical exposure and resulting biological impacts
  - Incorporation of quantitative pathway information through the use of (high-throughput) transcriptomics or proteomics would allow for pathway topology evaluations for molecular target and pathway prioritizations