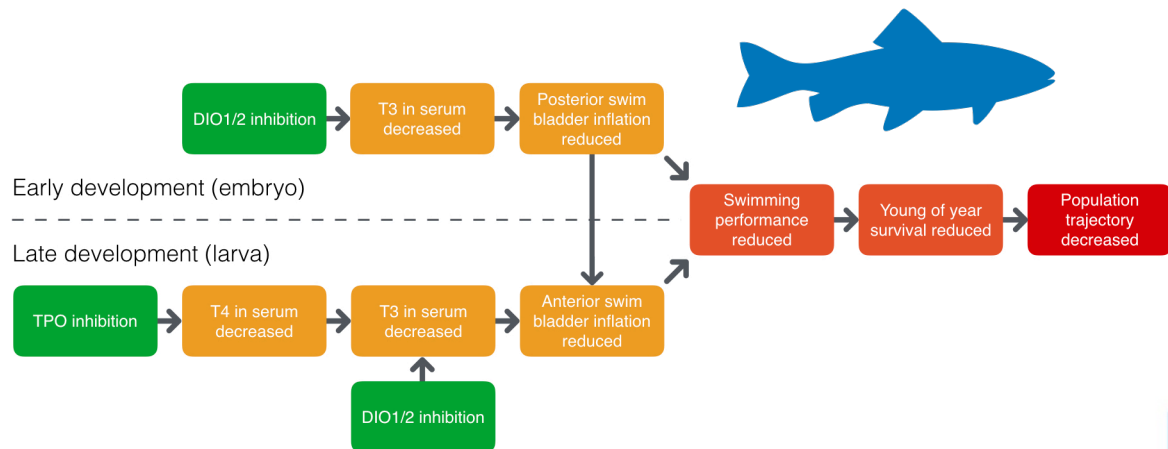# Evaluation of an Adverse Outcome Pathway Network for Thyroid Hormone System Disruption Across Taxonomic Groups
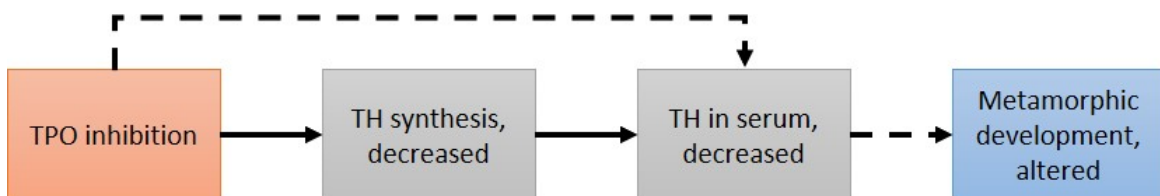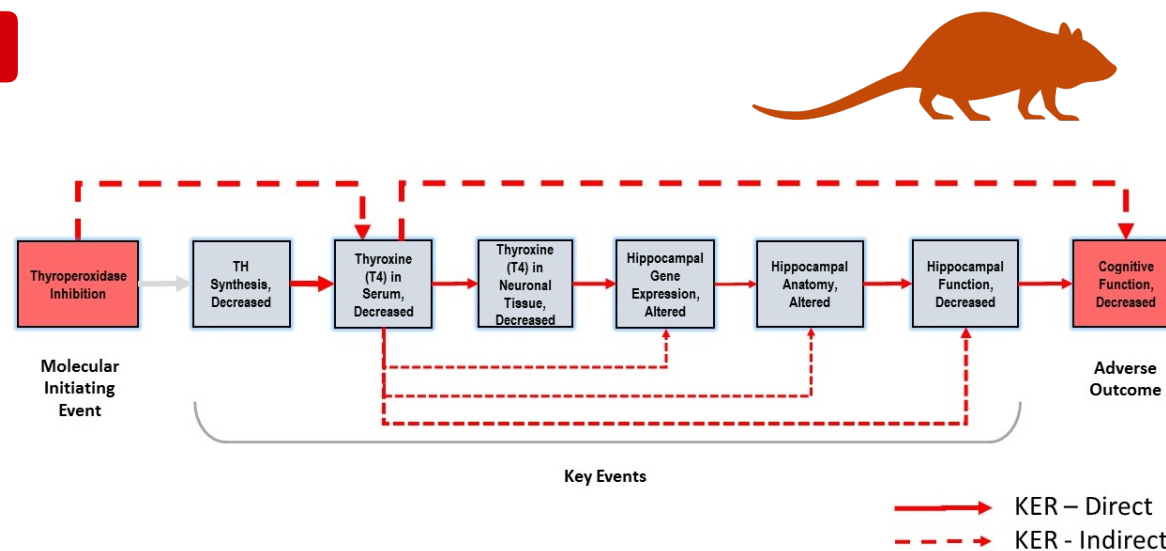
Lucia Vergauwen, Jason M. O'Brien, Carlie A. LaLone, Daniel L. Villeneuve, Dries Knapen

SETAC PORTLAND, 2021

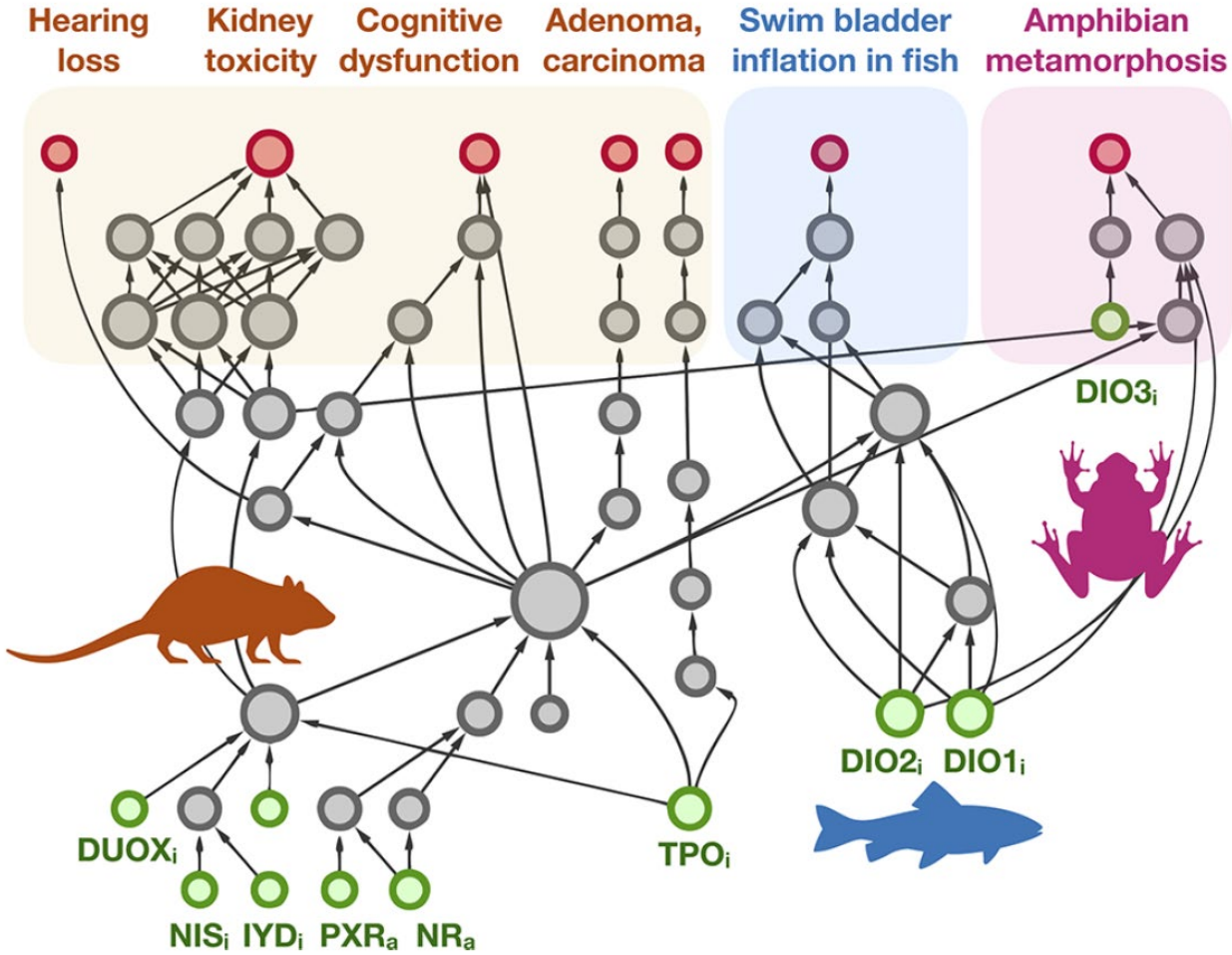# AOPs describing thyroid hormone system disruption

AOPs 155-159, OECD review process almost finished

AOP 175 under development

Break down the wall between ecotoxicology & human toxicology

Horizon2020, part of EURION cluster

Workflow

- **Initial evaluation**
  - Starting point, Oct 2020
  - Information on tax DOA is often missing
  - AOPs mostly focus on one taxonomic group
- **Curation in collaboration with Wiki authors**
  - Add taxonomic domain of applicability
  - Remove redundant KEs to increase connections
  - Version after curation, Oct 2021
- **Taxonomic filtering and evaluation**
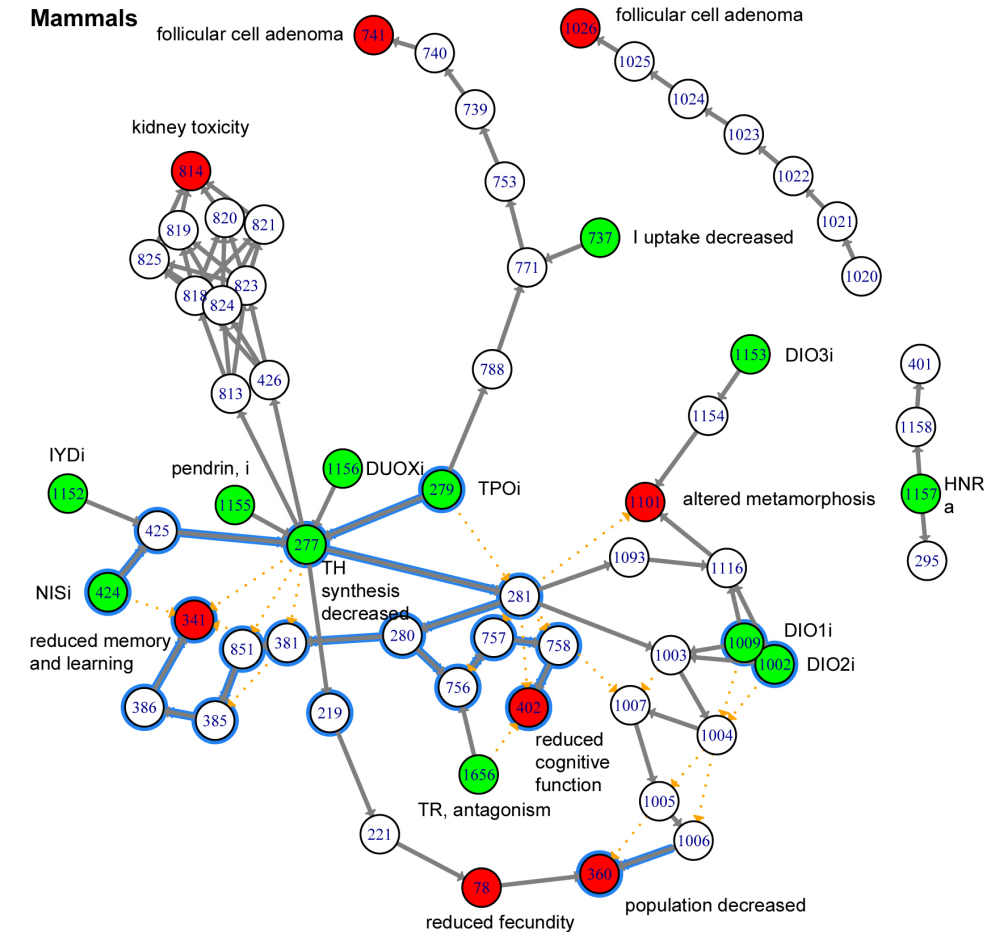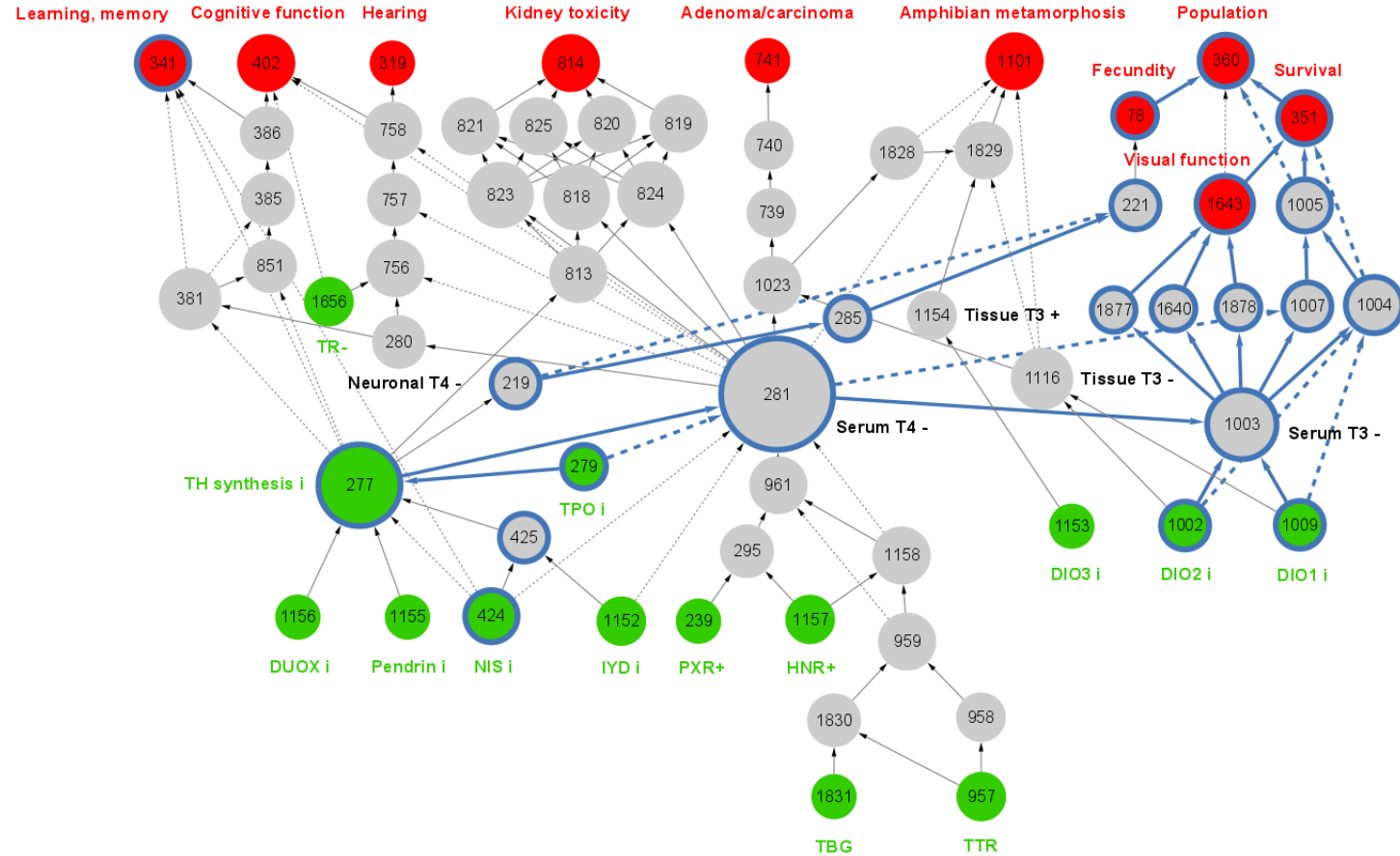

Oct 2020

Mammalian AOP network

- **Focus is mainly on DNT**
- **More AOs could be explored: reproduction, visual function**
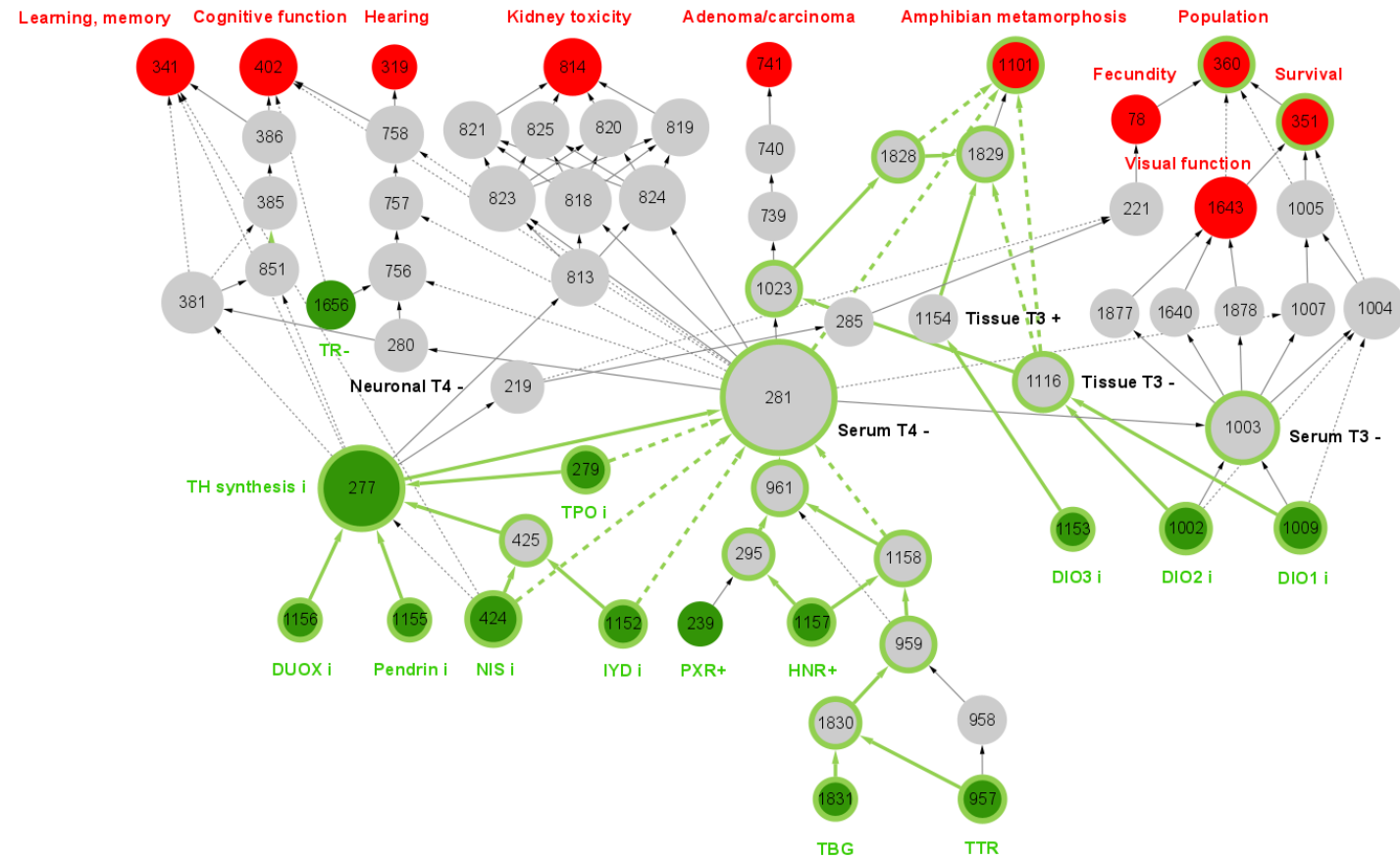- **MIEs could be expanded**
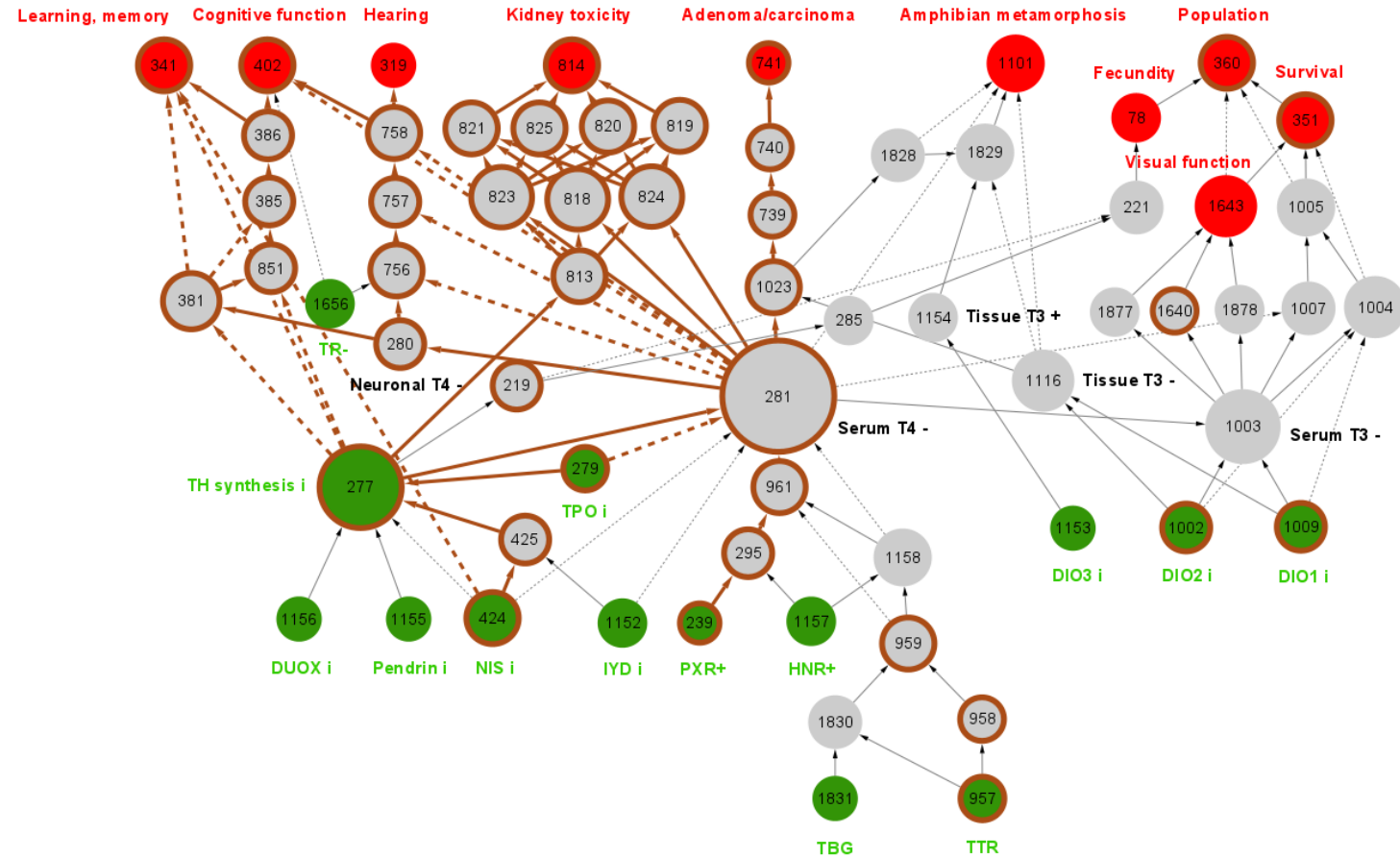
Fish AOP network

- **Taxon-specific: impaired swim bladder inflation**
- **More AOs could be explored: DNT, kidney toxicity, …**
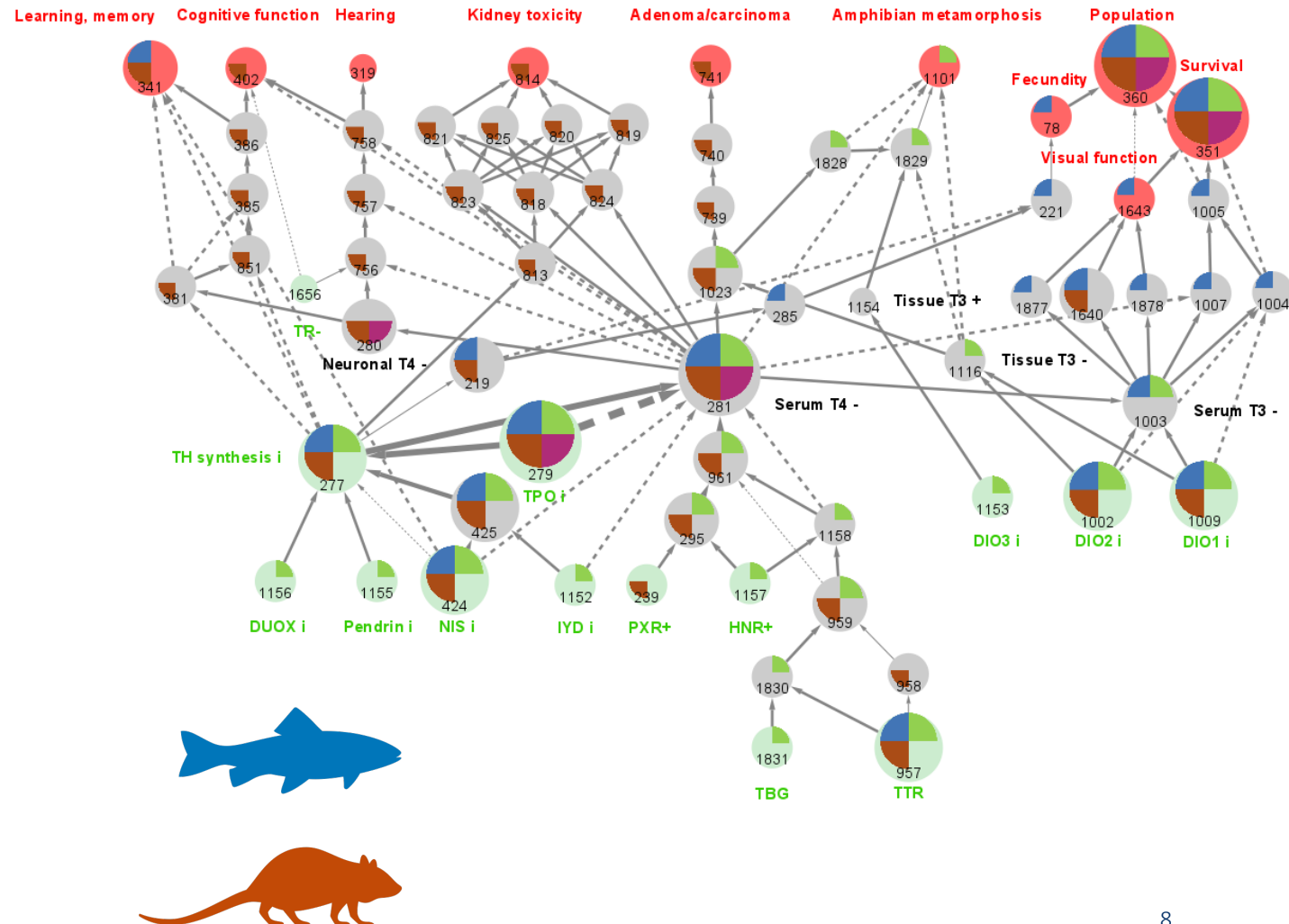- **MIEs could be expanded**

Amphibian AOP network

- **Limited to taxon-specific AO: altered amphibian metamorphosis**

- **More AOs could be explored: DNT, kidney toxicity, …**

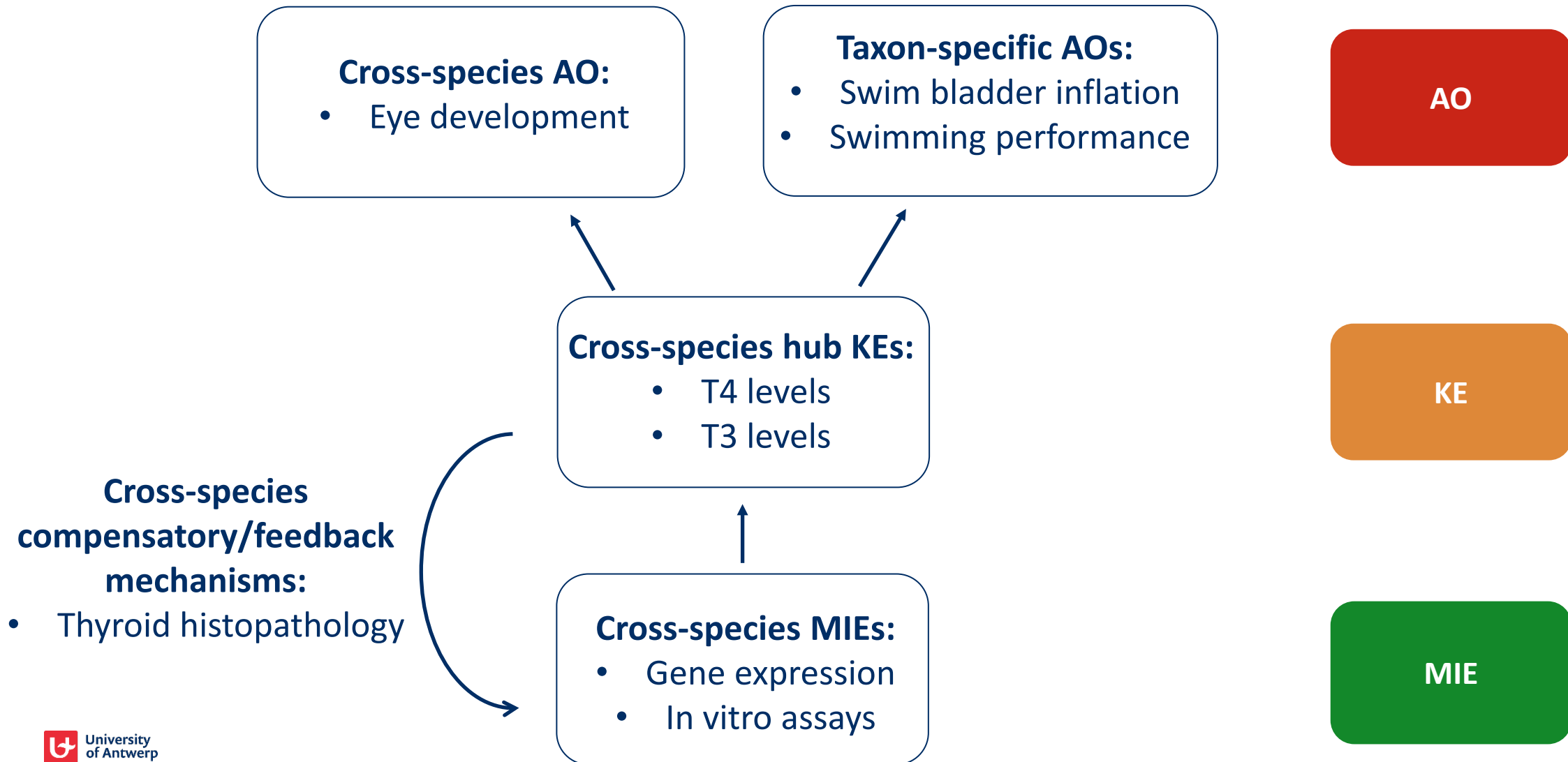- **Highest MIE coverage currently**

Knowledge gaps & priorities for cross-species AOP development

- **MIEs broadly applicable across vertebrates with some exceptions**
- **Potential for cross-species AOs**
  - Altered visual function
  - DNT
- **Taxon-specific AOs**
- **Cross-species hub KEs**
- **No AOPs defined yet for birds and reptiles**

Identification of KEs/assays in fish and amphibians

Cross-species AO:
- Eye development

Taxon-specific AOs:
- Swim bladder inflation
- Swimming performance

Cross-species hub KEs:
- T4 levels
- T3 levels

Cross-species compensatory/feedback mechanisms:
- Thyroid histopathology

Cross-species MIEs:
- Gene expression
- In vitro assays

AO

KE

MIE

University of Antwerp

Outlook on improving AOPN-based cross-species extrapolation

- **Increase awareness of importance of tax DOA**

- **Apply computational approaches to define tax DOA**
  - Phylogenetic distance (low WoE)
  - SeqAPASS (moderate WoE)
  - Experimental data (high WoE)

- **Apply automatic filtering based on tax DOA**

Acknowledgements