

# Interaction of thyroid hormones and eye development in fish: An adverse outcome pathway approach

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## Background

- Some Endocrine Disruptors can affect the **thyroid hormone (TH)** system, which is involved in the regulation of many important physiological and developmental processes, including the **development of eyes in vertebrates**.
- A chemical-induced impairment of the visual system can have **severe consequences for the survival rate in wildlife**, especially for developing fish larvae, which are thought to be very sensitive to **thyroid disrupting chemicals (TDCs)**
- The direct interaction between THs and eye development in fish is not fully understood yet**, especially with regard to the environmental consequences of impaired eye development. It is important to understand the **full chain of events** from molecular interaction with the TH system, over morphological and physiological changes up to the adverse outcome at individual and population level.
- A literature study forms the basis for **AOP development** and selection of AOP-based assays for addition to test guidelines.

## Methods

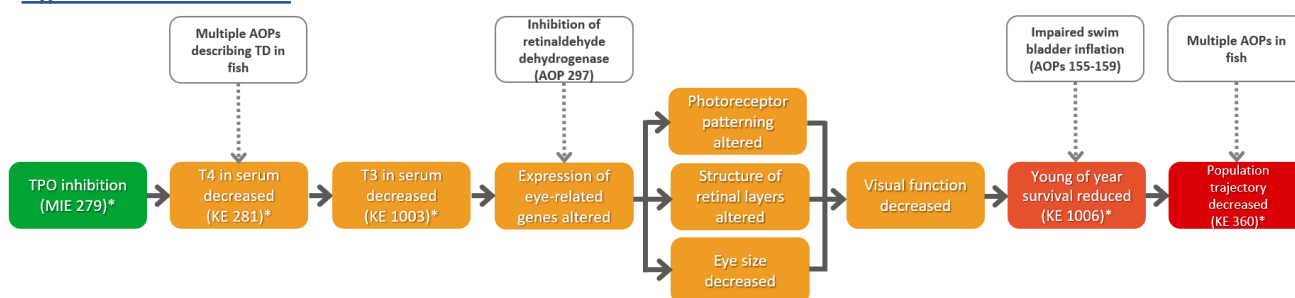
- Objective:** Develop an Adverse Outcome Pathway (AOP) linking TH disruption to eye development and function based on published scientific findings.
- Data analysis:** Screening of 89 papers which investigated the eye development of different fish species and at different life stages (not always TH-related)
  - Papers were published between 1994 and 2019
  - Mostly on zebrafish (*Danio rerio*) → 84,3%
  - Variety of different techniques for TH disruption, including TDCs, transgenic or mutant fish, microinjection, morpholino oligonucleotides, thyroid ablation, etc.
  - Endpoints range from gene and hormone levels to physiological and behavioral changes

## Results

### New Key events (KE):

Level	KE title	AOP-based assays	Brief description/ Example
Molecular	Expression of eye-related genes altered	Gene expression	Opsins and other genes related to eye function; genes related to eye development
Tissue	Photoreceptor patterning altered	Staining to determine photoreceptor counts	Altered numbers and ratio of photoreceptor subtypes
Tissue/organ	Structure of retinal layers altered	Histological analysis of retinal layers	Altered retinal structure, altered thickness of retinal layers, proliferation of retinal layers, looseness of tissue, malformations, characteristics of the pigment layer
Organ	Eye size decreased	Morphometric analysis	Reduced eye diameter
Organism	Visual function decreased	Physiological and behavioral changes	Altered optomotor response, optokinetic response, light-dark response

### Hypothesized AOP network :



**Hypothesized AOP network 'Thyropoxidase (TPO) inhibition leading to impaired visual function in fish'**  
\* existing KE in AOP-Wiki; Grey boxes show relation between existing AOP and new AOP network

## Conclusions

- This AOP network will lay the foundation for further research on the consequences of thyroid disruption in fish, an area of research where there are many gaps in knowledge.
- The AOP network will be used for selecting assays to include in existing test guidelines.
- In a next step, the literature study will include other model species (amphibians, mammals) in order to expand the taxonomic applicability of the AOP network.
- This AOP network links to several AOPs in fish that are currently in the AOP-Wiki and is specifically related to AOP 297: « *Inhibition of retinaldehyde dehydrogenase leads to population decline through impaired visual function* »