Introduction to the AOP-Wiki

- GLOBAL AOP NETWORK
  - >130 AOPS (USER DEFINED)
  - >750 KES
  - >1000 KERS

- ≈3500 EMERGENT
Welcome to the Collaborative Adverse Outcome Pathway Wiki (AOP-Wiki)

This wiki represents a joint effort between the European Commission - DG Joint Research Centre (JRC) and U.S. Environmental Protection Agency (EPA). This serves as one component of a larger OECD-sponsored AOP Knowledgebase (AOP-KB) effort and represents the central repository for all AOPs developed as part of the OECD AOP Development Effort by the Extended Advisory Group on Molecular Screening and Toxicogenomics. The other major components of this Knowledgebase are EffecToxpedia, produced by the Organization for Economic Co-operation and Development (OECD), the AOP Xplorer, produced by the US Army Corps of Engineers - Engineering Research and Development Center, and the Intermediate Effects DB produced by the JRC. All AOPs from the AOP Knowledgebase are available via the a AOPPortal, which is the primary entry point for the AOP-KB.

This wiki is based on the Chemical Mode of Action wiki developed by the EPA under the auspices of the WHO International Programme on Chemical Safety (IPCS) Mode of Action Steering Group.

Disclaimer
The content of this wiki is the sole responsibility of the individual contributors and does not necessarily represent the views of the authors' organizations nor the organizations responsible for development of the AOP-Wiki or the AOP-KB. Mention of trade names or commercial products does not constitute endorsement by any of these organizations.

Aopwiki.org
https://training.aopwiki.org
State of the AOP-Wiki

• GLOBAL AOP NETWORK
  • >130 AOPS (USER DEFINED)
  • >750 KES
  • >1000 KERS

• ≈3500 EMERGENT PATHS
No genotoxicity findings reported

- Reproductive Toxicology
  - 1 Reproductive toxicity PODs available

- Chronic Toxicology
  - 36 Chronic toxicity PODs available

- Subchronic Toxicology
  - No subchronic toxicity data available.

- Developmental Toxicology
  - 4 Developmental toxicity PODs available

- Acute Toxicology
  - 3 Acute toxicity PODs available

- Subacute Toxicology
  - No subacute toxicity data available.

- Neurotoxicology
  - No neurotoxicology data available.

- Endocrine System
  - Endocrine Disruption Potential. Significant Estrogen Receptor activity seen. Chemical was positive in 9 ER assays (out of 17) and was positive in 1 AR assays (tested in 9).

- ADME
  - No HTTK data

- Fate and Transport
  - No bioaccumulation concern.
  - No volatility concern.
  - Biodegradation predictions are available
  - BCF predictions are available
  - Vapor Pressure predictions are available

- Exposure
  - Exposure Estimates have been predicted using the SEEM modeling methodology

- AOP Information
  - AOP Links: 13, 19, 33, 36, 43, 58, 59, 60, 61, 66, 103, 104, 107, 124, 126, 150, 153, 163, 164, 175, 177, 187, 195, 209

- Other Notes
  - No water quality values available.
  - No air quality values available.
  - No occupational exposure values available.
A Hazard Narrative, Supported by Evidence

Aop: 175
AOP Title

Thyroperoxidase inhibition leading to altered amphibian metamorphosis
Event: 279

Key Event Title

Thyroperoxidase, Inhibition

AOPs Including This Key Event

<table>
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<tr>
<th>AOP Name</th>
<th>Role of event in AOP</th>
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<td>TPO Inhibition and Altered Neurodevelopment</td>
<td>MolecularInitiatingEvent</td>
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<tr>
<td>Thyroid peroxidase- follicular adenoma/carcinoma</td>
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<td>TPOi anterior swim bladder</td>
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<tr>
<td>TPO inhibit alters metamorphosis</td>
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Thyroperoxidase (TPO) is a heme-containing apical membrane protein within the follicular lumen of thyrocytes that acts as the enzymatic catalyst for thyroid hormone (TH) synthesis. TPO catalyzes several reactions in the thyroid gland, including: the oxidation of iodide, nonspecific iodination of tyrosyl residues of thyroglobulin (Tg); and, the coupling of iodothyronines to produce Tg-bound monoiodothyronine (MIT) and diiodothyronine (DIT) (Divi et al., 1997; Kessler et al., 2006; Ruf et al., 2006; Tauer et al., 1996). The outcome of TPO inhibition is decreased synthesis of thyroxin (T4) and triiodothyronin (T3), a decrease in release of these hormones from the gland into circulation, and unless compensated, a consequent decrease in systemic concentrations of T4, and possibly T3. The primary product of TPO-catalyzed TH synthesis is T4 (Tauer et al., 1996; Zoeller et al., 2007) that would be peripherally or centrally deiodinated to T3.

The figure below illustrates the enzymatic and nonenzymatic reactions mediated by TPO.
TPO inhibition

TH synthesis, decreased

T4 in serum, decreased

T4 in tissue, decreased

T3 in tissue, decreased

TH in neural tissues, decreased

Iodide in thyroid, decreased

IYD inhibition

NIS inhibition

TPO inhibition

DIO1 inhibition

DIO2 inhibition

Hippocampal anatomy, altered

Hippocampal function, decreased

Cognitive function, decreased

Metamorphosis, impaired

Survival, reduced

Anterior SB inflation, impaired

Hearing, reduced

Posterior SB inflation, impaired

Swimming performance, reduced

y.o.y survival, reduced

Population trajectory, decreased

Hearing, reduced

Survival, reduced

Population trajectory, decreased
Predicted taxa-specific hazards

Conserved biology that readily extrapolates across taxa
So, you’d like to be an AOP Developer......

Part 2.

• Objective: Gain hands on experience searching the AOP-Wiki and creating a new AOP (including linking to existing KEs, KERs, where relevant).

Follow along as we demonstrate the entry of the AOP defined in exercise 1 into the AOP-Wiki.

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https://aopwiki.org/wiki/index.php/Main_Page

- **Read access**
  - Open to anyone, no account required

- **Commenting**
  - Create account, no approvals required

- **Development/write access**
  - Create account
  - Submit brief developer application for approval
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