Introduction to the AOP-Wiki

- GLOBAL AOP NETWORK
  - >130 AOPS (USER DEFINED)
  - >750 KES
  - >1000 KERS
- ≈3500 EMERGENT
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, 16, 33, 38, 43, 58, 59, 60, 61, 68, 103, 104, 107, 124, 126, 150, 153, 163, 164, 175, 177, 187, 195, 200

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

- TPO inhibition
- TH synthesis, decreased
- Thyroxine (T4) in serum, decreased
- Thyroxine (T4) in tissues, decreased
- Triiodothyronine (T3) in tissues, decreased
- Amphibian metamorphosis, altered
Thyroxine and thyroxine synthesis

Thyroxine (T4) is a hormone-containing peptide or hormone that acts as the enzyme catalyst for thyroxine (TH) synthesis. TPO catalyzes several reactions in the thyroid gland, including the oxidation of iodide nonspecifically, the oxidation of tyrosyl residues of thyroglobulin (Tg), and the coupling of thyrosine to produce Tg-bound monokolathyrosine (MIT) and diolathyrosine (DIT) (D’Itri et al., 1987; Keating et al., 2000; Ruif et al., 2009; Tsunog et al., 1986). The outcome of TPO inhibition is decreased synthesis of thyroxine (T4) and triiodothyronine (T3), a decrease in release of these hormones from the gland into circulation, and a consequent decrease in systemic concentrations of T4 and possibly T3. The primary product of TPO-catalyzed TH synthesis is T4 (Tsunog et al., 1986; Zeller et al., 2007) that would be peripherally or centrally oxidized to T3.

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

Figure 1. Thyroperoxidase and thyroid hormone synthesis

<table>
<thead>
<tr>
<th>AOP Name</th>
<th>Role of event in AOP</th>
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<tbody>
<tr>
<td>TPO Inhibition and Altered Neurodevelopment</td>
<td>MolecularInitiatingEvent</td>
</tr>
<tr>
<td>Thyroid peroxidase- follicular adenoma/carcinoma</td>
<td>MolecularInitiatingEvent</td>
</tr>
<tr>
<td>TPO anterior swim bladder</td>
<td>MolecularInitiatingEvent</td>
</tr>
<tr>
<td>TPO inhib alters metamorphosis</td>
<td>MolecularInitiatingEvent</td>
</tr>
</tbody>
</table>
IYD inhibition

NIS inhibition

TPO inhibition

T4 in serum, decreased

T4 in tissue, decreased

T3 in tissue, decreased

TH in neural tissues, decreased

Hippocampal anatomy, altered

Hippocampal function, decreased

Cognitive function, decreased

Iodide in thyroid, decreased

Metamorphosis, impaired

Survival, reduced

TH synthesis, decreased

Anterior SB inflation, impaired

Hearing, reduced

y.o.y survival, reduced

Population trajectory, decreased

DIO1 inhibition

DIO2 inhibition

Hearing, reduced

Posterior SB inflation, impaired

Swimming performance, reduced
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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