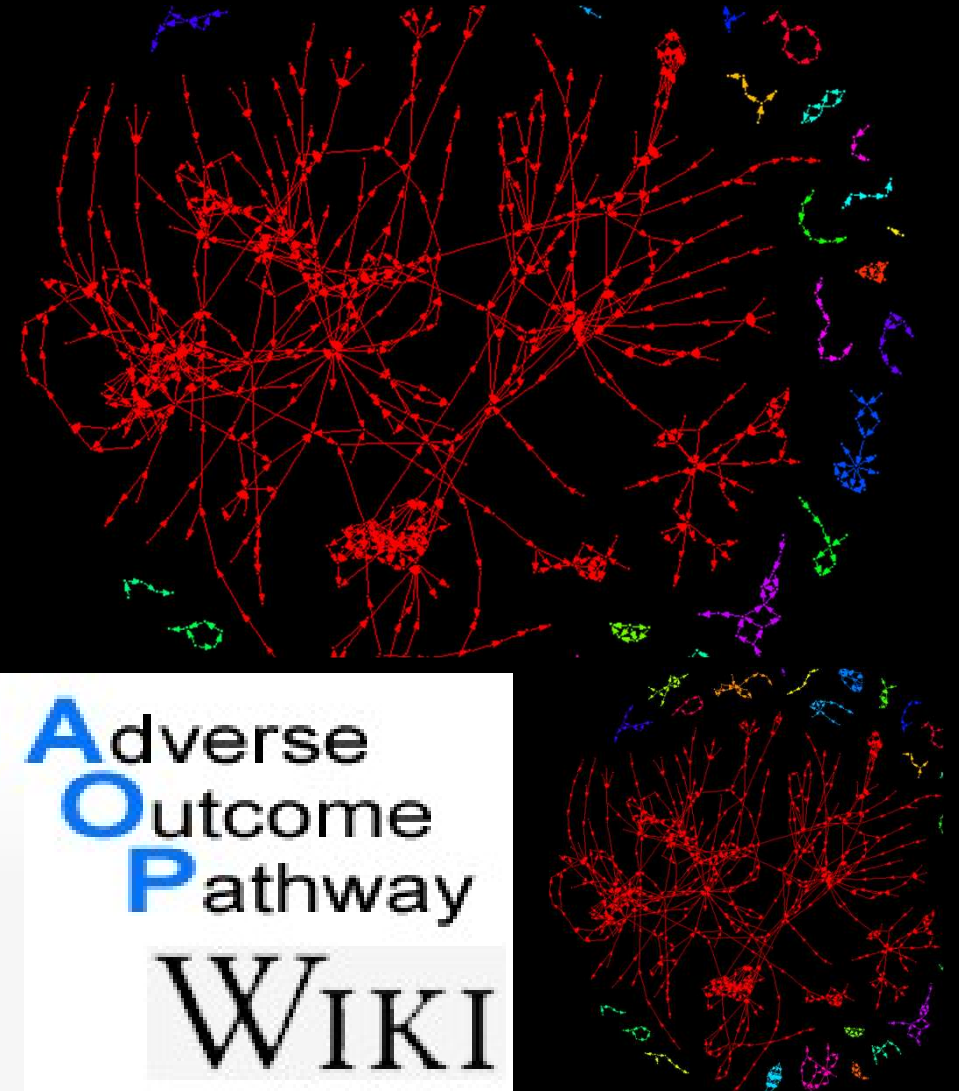


Introduction to the AOP-Wiki


- GLOBAL AOP NETWORK
 - >130 AOPS (USER DEFINED)
 - >750 KES
 - >1000 KERS
- ≈3500 EMERGENT



Secure | <https://aopwiki.org>

AOPWiki AOPs Key Events KE Relationships Stressors

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 Effectopedia, produced by the Organisation 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 e.AOP.Portal, which is the primary entry point for the AOP-KB.

This wiki is based upon 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.

AOP Page



The screenshot shows an 'AOP Page' with a flowchart at the top representing the Adverse Outcome Pathway. Below the flowchart are three tables: 'Molecular Initiating Events', 'Key Events', and 'Adverse Outcomes'. Each table has columns for 'Title', 'Description', 'Evidence', and 'References'. The 'Key Events' table is highlighted with a dashed green line pointing to the 'KE Pages' box. The 'Adverse Outcomes' table is highlighted with a dashed green line pointing to the 'KER Pages' box.

- ### KE Pages
- Description
 - Measurement/ detection
 - Domain of applicability

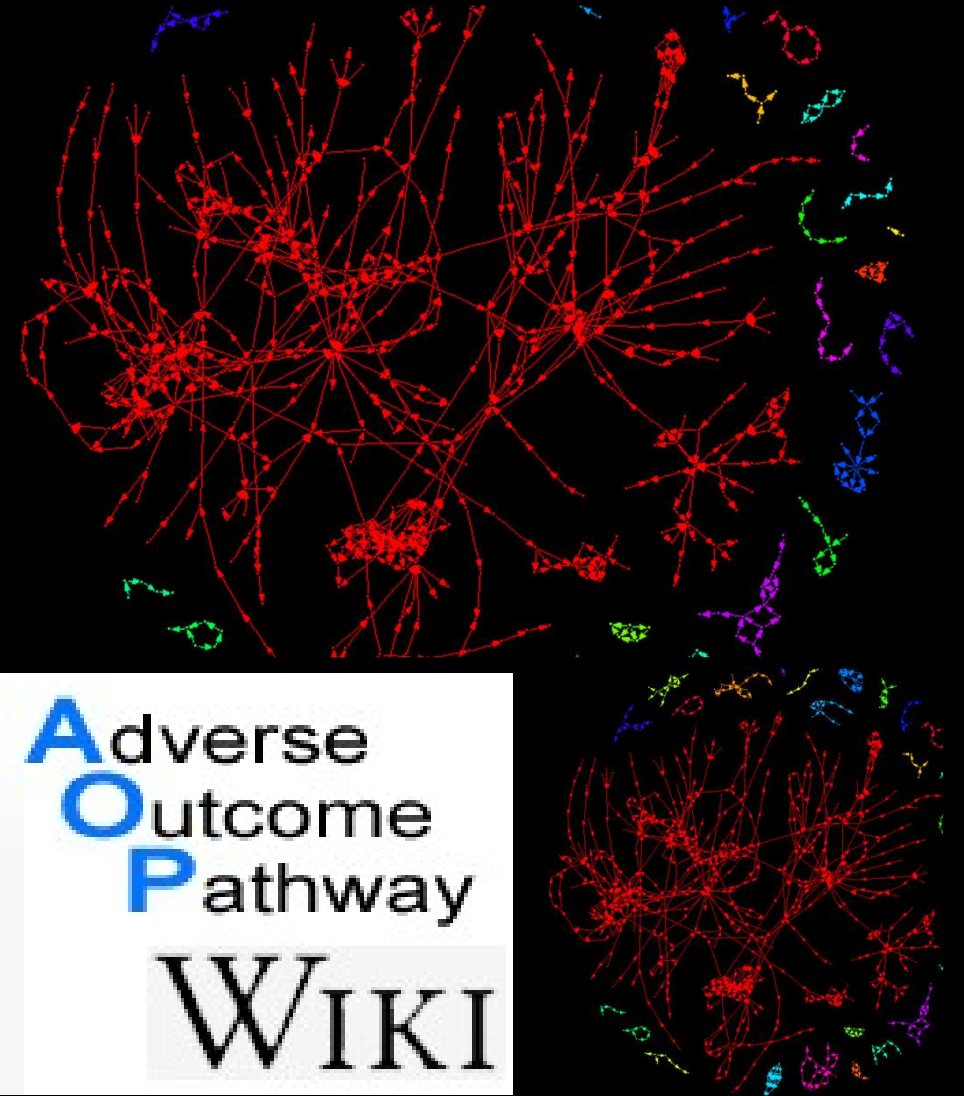
- ### KER Pages
- Title
 - Description
 - Biological plausibility
 - Empirical support
 - Inconsistencies and uncertainties
 - Quantitative understanding

Aopwiki.org

<https://training.aopwiki.org>

State of the AOP-Wiki

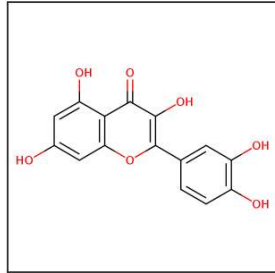
- GLOBAL AOP NETWORK
 - >130 AOPS (USER DEFINED)
 - >750 KES
 - >1000 KERS
- ≈3500 EMERGENT PATHS



Chemistry Dashboard

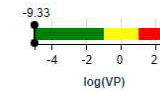
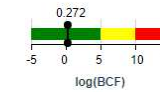
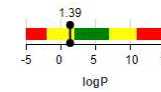
117-39-5 | DTXSID4021218

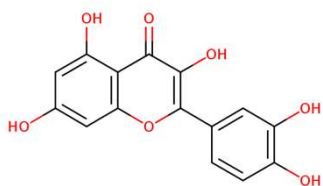
Searched by Approved Name: Found 1 result for 'Quercetin'.



- ✘ 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, 36, 43, 58, 59, 60, 61, 66, 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.

PhysChem Parameters





Quercetin

Chemistry Dashboard

Submit Comment

Copy ▾

Aa ▾

Aa

Aa ▾

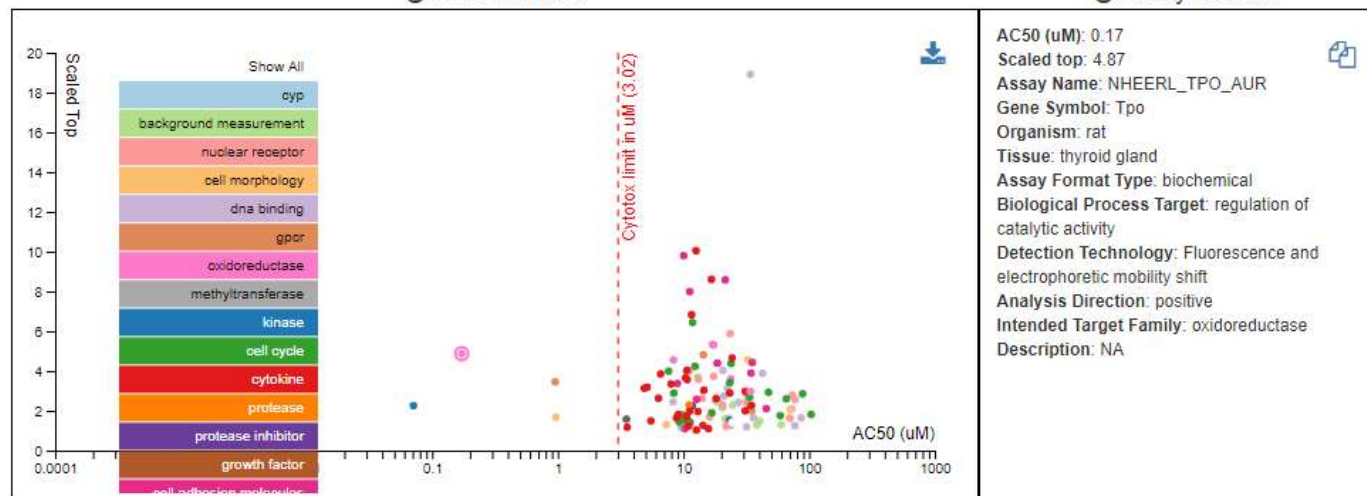
ToxCast: Summary

PubChem

Chemical Activity Summary ⓘ

ⓘ ToxCast Data

ⓘ Assay Details



AC50 (uM): 0.17
 Scaled top: 4.87
 Assay Name: NHEERL_TPO_AUR
 Gene Symbol: Tpo
 Organism: rat
 Tissue: thyroid gland
 Assay Format Type: biochemical
 Biological Process Target: regulation of catalytic activity
 Detection Technology: Fluorescence and electrophoretic mobility shift
 Analysis Direction: positive
 Intended Target Family: oxidoreductase
 Description: NA

Download as: TSV Excel Show: Inactive Background

Assay Name Assa... ⓘ SeqA... **AOP Link AOP Ev...** ⓘ Hit Call ⓘ ... Scale... ⓘ ... log ... ⓘ Target Family

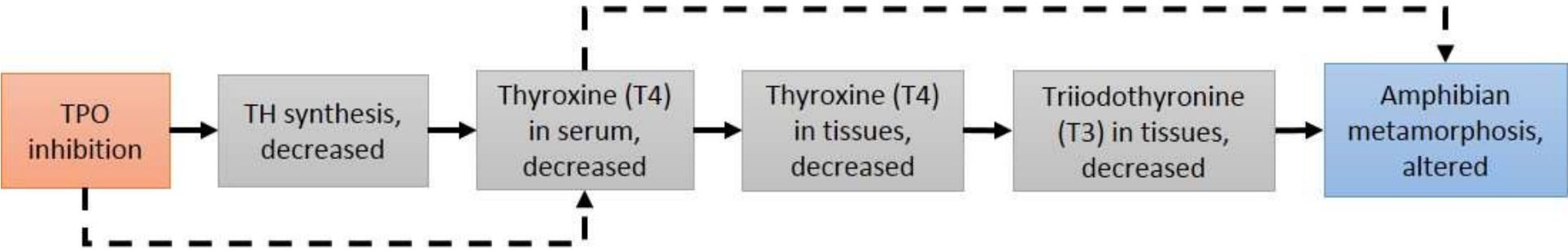
ⓘ NVS_ENZ_hGSK3b	-	NP_001139628.1 	-	ACTIVE	45.0	2.25	0.0710	-1.15	kinase
ⓘ NCCT_TPO_AUR_dn	-	P14650 175	279	ACTIVE	97.4	4.87	0.172	-0.764	oxidoreductase
ⓘ NVS_GPCR_bAdoR_No nSelective	-	NP_776922.2 	-	ACTIVE	71.3	3.45	0.955	-0.0202	gpcr
ⓘ TOX21_MMP_ratio_dow n	-	-	-	ACTIVE	103	1.67	0.965	-0.0154	cell morphology

A Hazard Narrative, Supported by Evidence

Aop: 175

AOP Title ?

Thyropoxidase inhibition leading to altered amphibian metamorphosis



Event: 279

Key Event Title ?

Thyroperoxidase, Inhibition

AOPs Including This Key Event ?

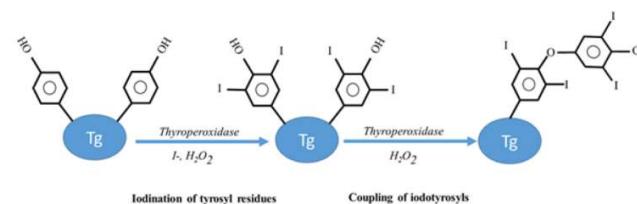
AOP Name	Role of event in AOP
TPO Inhibition and Altered Neurodevelopment	MolecularInitiatingEvent
Thyroid peroxidase- follicular adenoma/carcinoma	MolecularInitiatingEvent
TPOi anterior swim bladder	MolecularInitiatingEvent
TPO inhib alters metamorphosis	MolecularInitiatingEvent

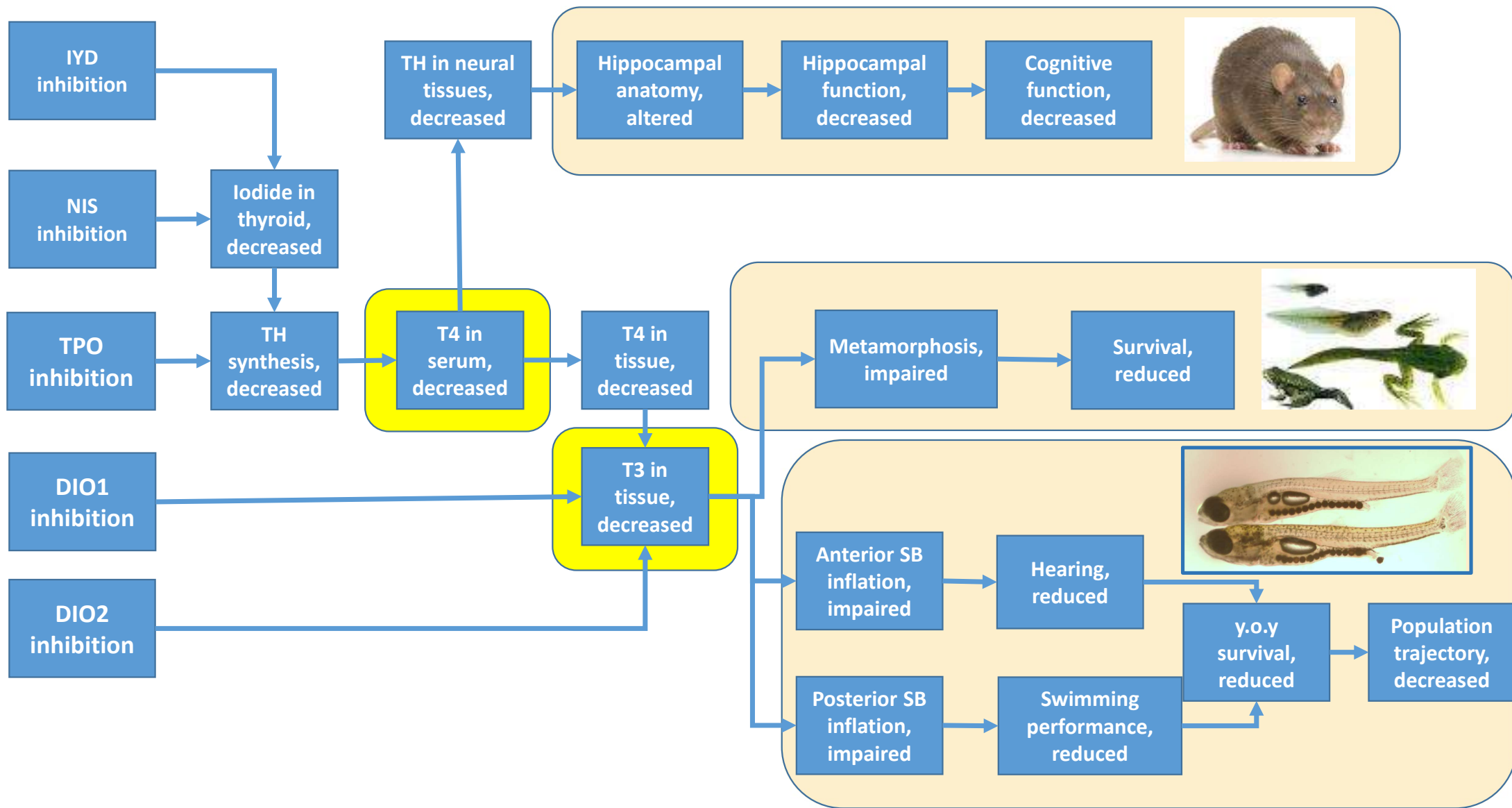
Key Event Description ?

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 iodotyrosyls to produce Tg-bound moniodotyrosine (MIT) and diiodotyrosine (DIT) (Divi et al., 1997; Kessler et al., 2008; Ruf et al., 2006; Taurog et al., 1996). 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 unless compensated, a consequent decrease in systemic concentrations of T4, and possibly T3. The primary product of TPO-catalyzed TH synthesis is T4 (Taurog 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.

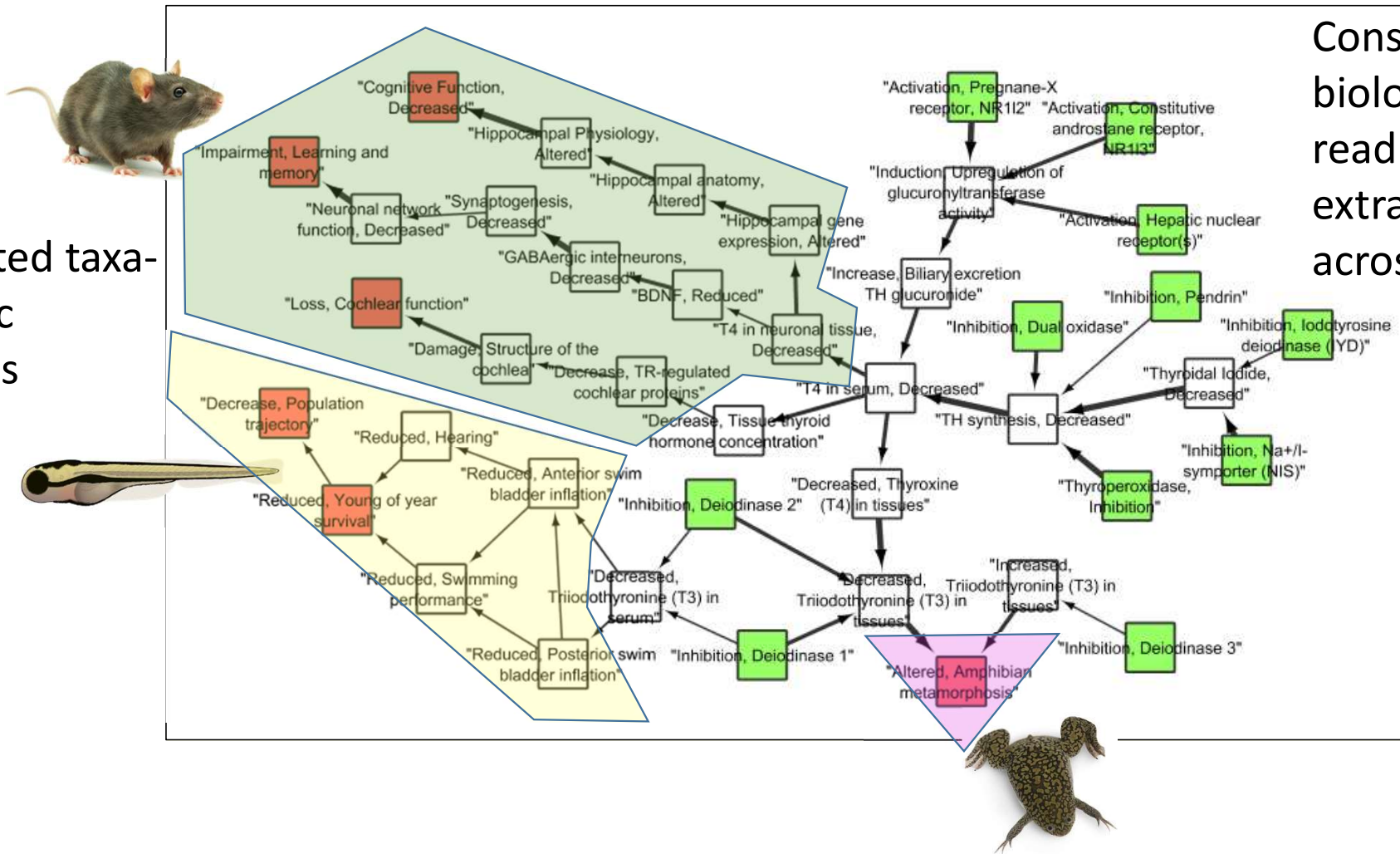
Figure 1. Thyroperoxidase and thyroid hormone synthesis





Predicted tax-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.

<https://training.aopwiki.org>

User name: author@epa.gov

Password: AOPtraining4@!!

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
- <http://www.saaop.org/AccessPage.html>.

<https://training.aopwiki.org>

User name: author@epa.gov

Password: AOPtraining4@!!