



Introduction

Adverse outcome pathways (AOPs) represent a formalised knowledge framework for capturing mechanisms leading to toxicity.^[1] AOPs are a key tool in the development of integrated approaches to testing and assessment (IATA) and AOP-Wiki is the main public repository of this knowledge.[2] The data available from this resource can be viewed as single linear AOPs and, while this representation is valuable, new emergent pathways and previously unknown relationships can be discovered if the AOPs are viewed as a network.[3] Kaptis is an application developed by Lhasa which allows users to store, search and edit AOP knowledge. A key feature is the functionality to visualise AOPs as AOP networks from a selected Key Event (KE).

Objective

The aim of this collaboration was:

- Allow knowledge from AOP-Wiki to be visualised and interrogated as a network of KEs and Key Event Relationships (KERs) within a software application
- Allow users to view emergent pathways, contained within AOP-Wiki knowledge, which were not specifically encoded by the AOP curators



Kaptis	Search AOP Wiki Q type to search	Search AOP Wiki Key Events all key events	Reduction, 17beta-estradiol synthesis by ovarian	granulosa cells
		Agonism, Androgen receptor	Reduction, Gonadotropins, circulating concentrations	Reduction, Testoster
€ Q	modulation, Unknown	Increased, HIF-1 alpha transcription	Increased, HIF-1 heterodimer	reduction in ovarian g
Activation, AhR	dimerization, AHR/ARNT	Inhibition, Prolyl hydroxylases	Increase, hypermethylation of the promotor region of gonadotropin releasing hormone receptor	Decrease, expression of get
				Inh

Figure 3: A network generated from the KE "Reduction, Plasma 17beta-estradiol concentrations". 6 user generated AOPs [AOP7; AOP23; AOP23; AOP122; AOP123; AOP123; AOP310] lead to a reduction in of this key enzyme.

Mapping AOP-Wiki knowledge to Kaptis

The AOP-Wiki XML was parsed and converted into Java objects which were then mapped to the Kaptis data model. There were some concepts which were shared between the two AOP knowledge formats, as shown in Figure 1.



- Figure 1: Mapping AOP-Wiki data to Kaptis data model. POAC: Process, Object, Action, Context; WoE: Weight of Evidence
- Other concepts required conversion to match the new data format. Examples include Applicability where **HIGH** was mapped to **Strongly for**, **Moderate** to **Moderately for** etc.
- Finally, stressors was the only concept which was not mapped to a concept in Kaptis.



Interrogating AOP-Wiki Knowledge As A Network

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AOP Wiki Database Snapshot: 1 Jan 2022 Reduction, Vitellogenin accumulation into oocytes and oocyte growth/developme

We have demonstrated a tool which will allow users to view and interact with the knowledge from the AOP-Wiki as a network. The Wiki Kaptis application is accessible here [5] and should soon be accessible directly through the AOP-Wiki site using a "Third party tool" launcher. Potential future work may involve (i) improvements to data pipeline processes as AOP-Wiki is updated and (ii) generate domain specific networks based on the available metadata e.g. taxon or lifestage specific filters on the KE networks.

- **References:**

- <u>nttp://aopwiki.org.</u>

by Lhasa Limited

Kaptis

https://wikikaptis.lhasacloud.org/

Conclusions and future work

WIKI

Ankley et al, Environ Toxicol Chem., 2010, 28, 730-741. doi: 10.1002/etc.34 [2] Tollefsen et al, Regul Toxicol Pharmacol., 2014, 70, 629-640. doi: 10.1016/j.yrtph.2014.09.009 [3] Knapen et al, Environ Toxicol Chem., 2018, 37, 1723-1733doi: 10.1002/etc.4125 4] Society for Advancement of AOPs. [2022]. AOP-Wiki. [2022-01-01]. Available from

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