AOP Wiki

NAMs Training Workshop

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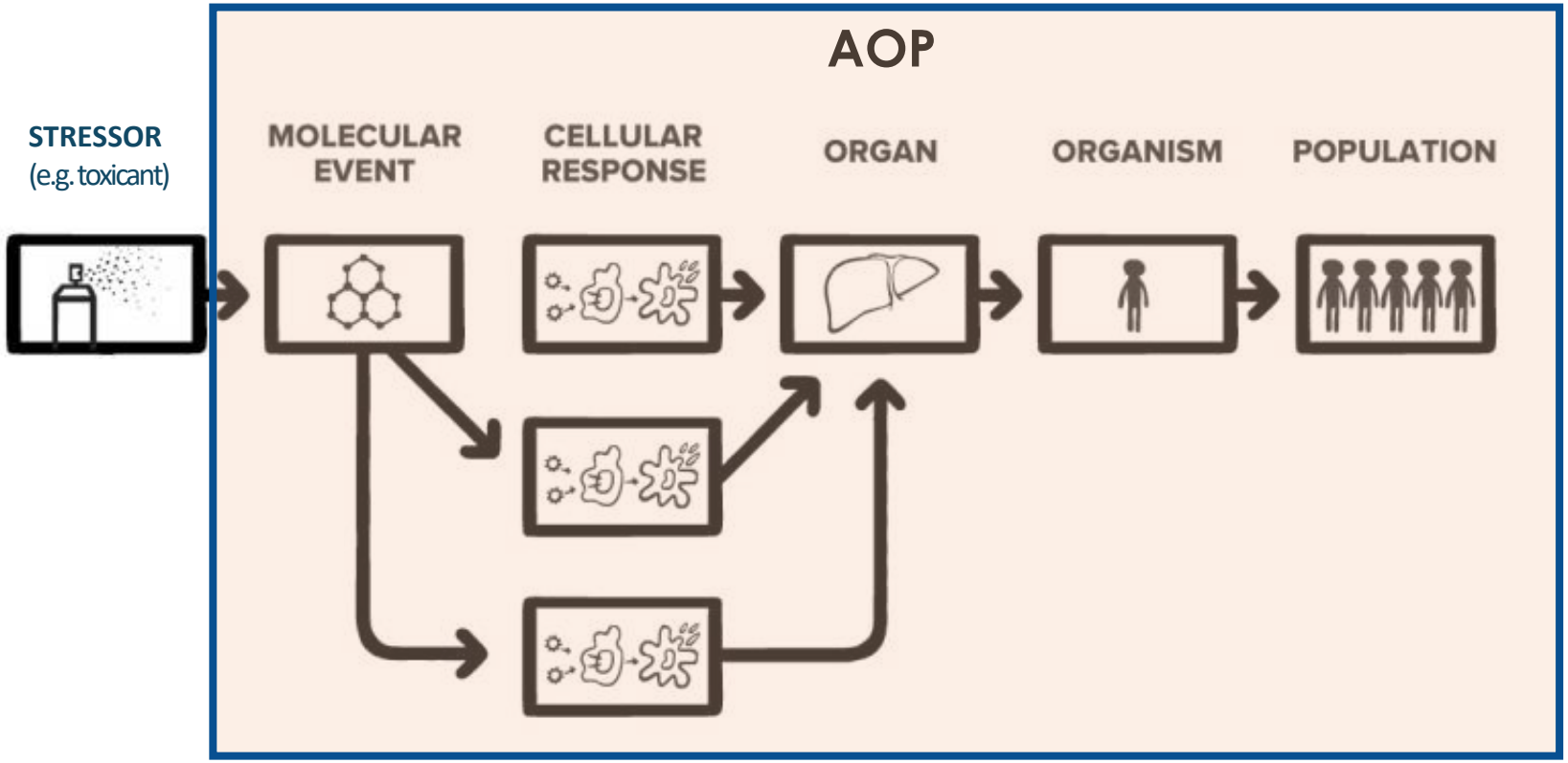
What are AOPs?

Adverse Outcome Pathways



An Adverse Outcome Pathway (AOP) is a conceptual framework that portrays existing knowledge concerning the linkage between a direct molecular initiating event and an adverse outcome, at a level of biological organization relevant to risk assessment.

(Ankley et al. 2010, Environ. Toxicol. Chem., 29(3): 730-741.)

Purpose of AOPs

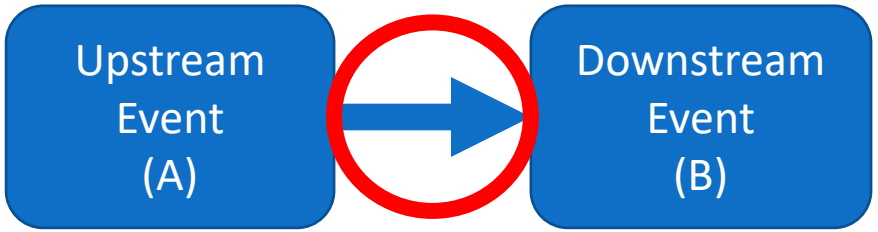
- Broad range of applications, but in the context of NAMs…
- ***NAMs****: any technology, methodology, approach, that can provide information on chemical hazard and risk assessment without the use of intact [protected life stages of vertebrate] animals, including in silico, in chemico, in vitro, and ex vivo approaches (ECHA, 2016b; EPA, 2018d).*
- Support the interpretation/translation of NAMs into associated hazards relevant to risk assessment and management

Building Blocks

Key Events

- Observable Δ biological state (measurable)
- Mark progression from initial perturbation toward the adverse outcome.
- Essential (but not necessarily sufficient)

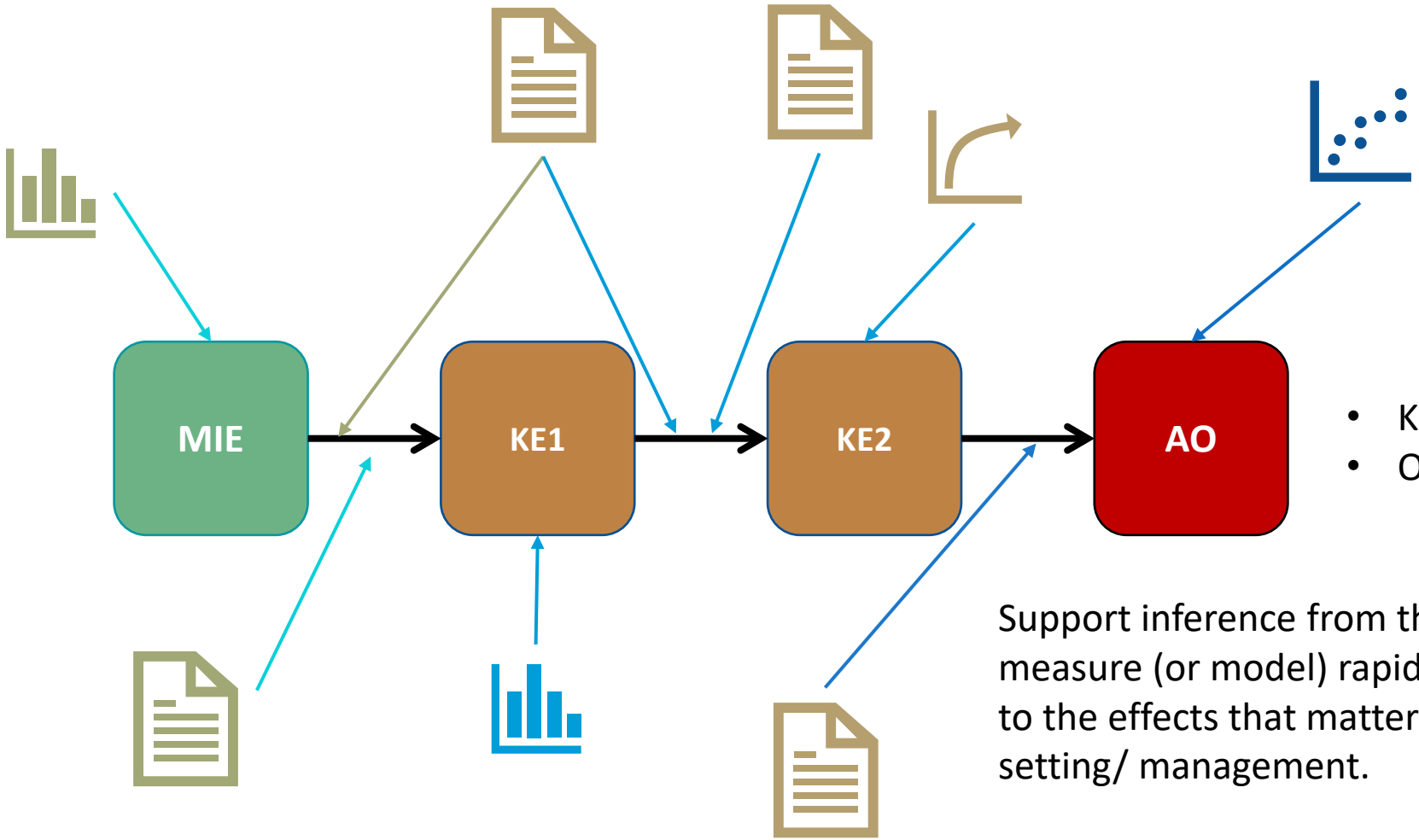
Relationships



- *Functional unit of inference/extrapolation*

- Defines a directed relationship (A causes B)
- Evidence for a causal relationship
- Conditions under which that causal relationship applies

Adverse Outcome Pathways (AOPs)



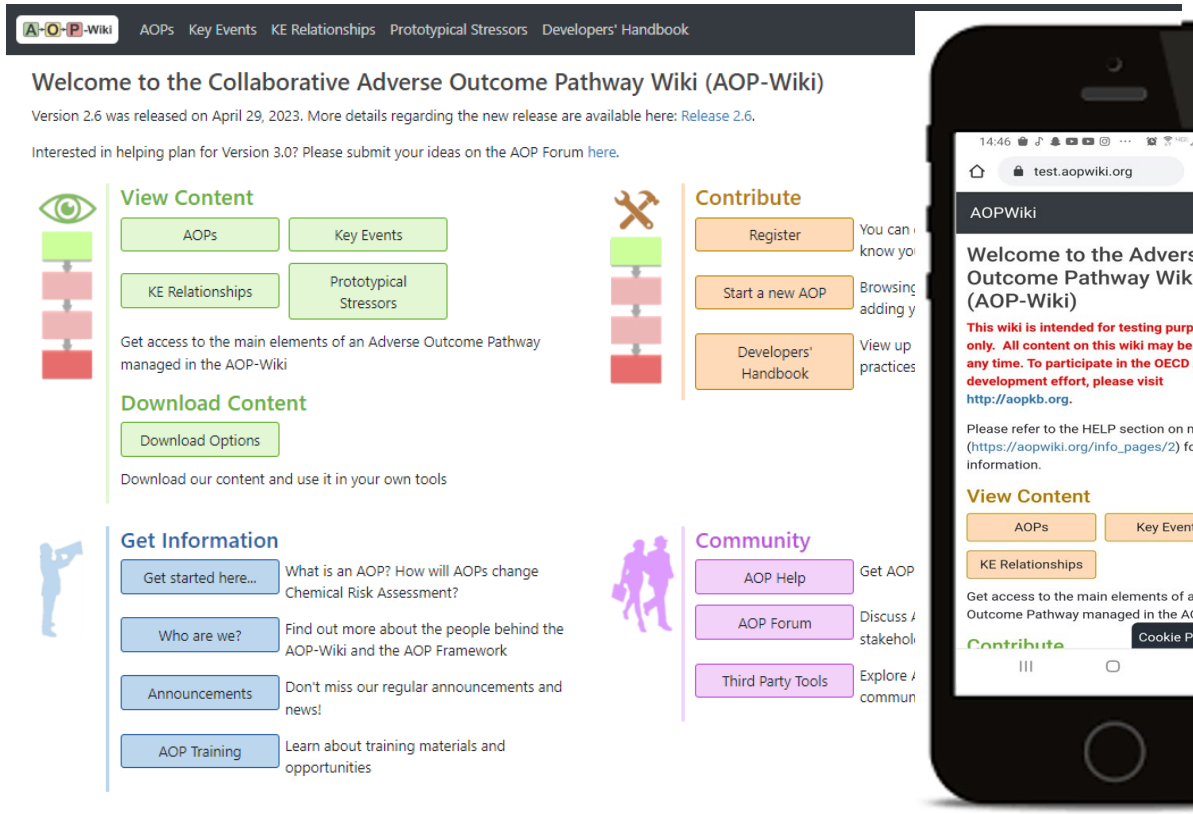
- Knowledge and evidence
- Organized a particular way

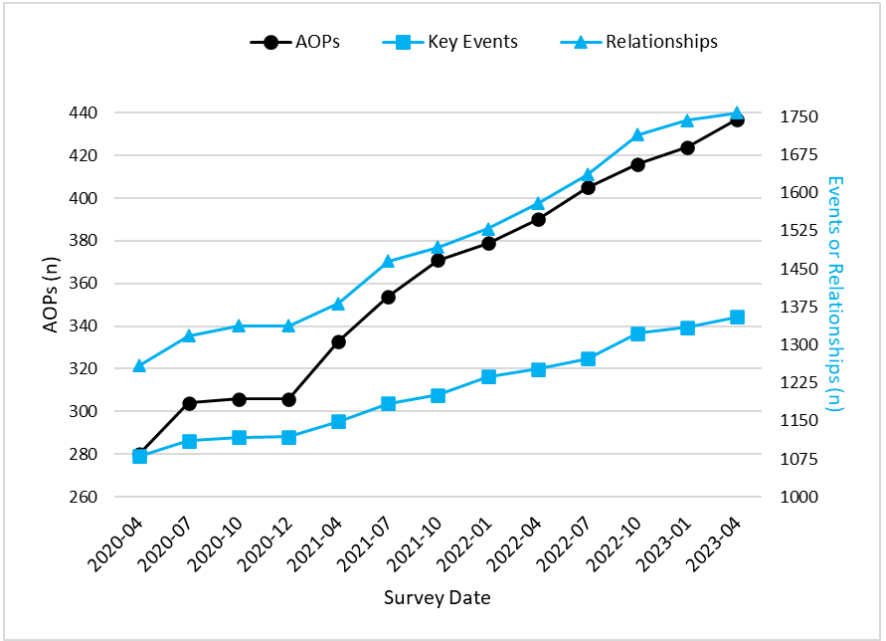
Support inference from the properties we can measure (or model) rapidly, cost-effectively, efficiently, to the effects that matter to decision-making/ policy-setting/ management.

Slide adapted from – Elizabeth Huliganga

AOPwiki.org

- Harmonized, globally accessible source of scientific information organized according to the AOP framework.
- Intended to support a wide range of NAMs-based decision-making





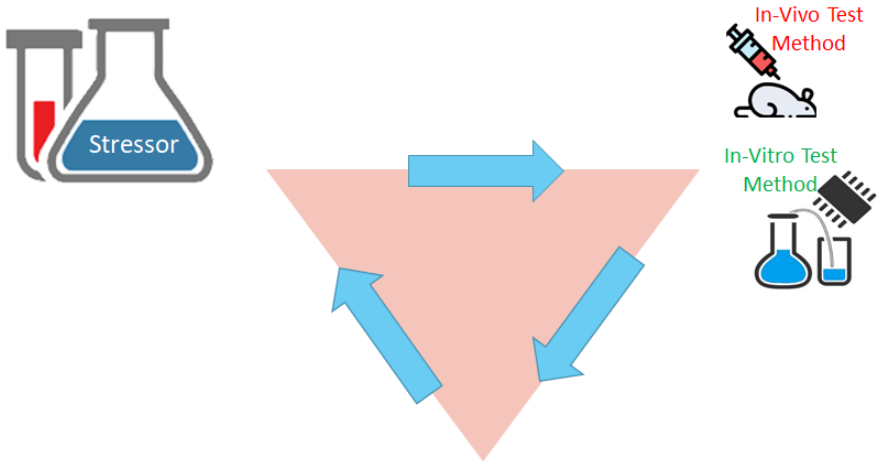
Searching the AOP-Wiki

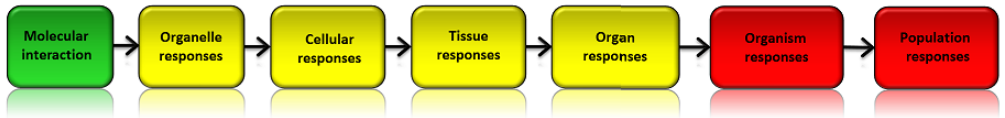
AOPs are stressor agnostic

In general, the entry point for searching the AOP-Wiki is a biological activity or biological effect.

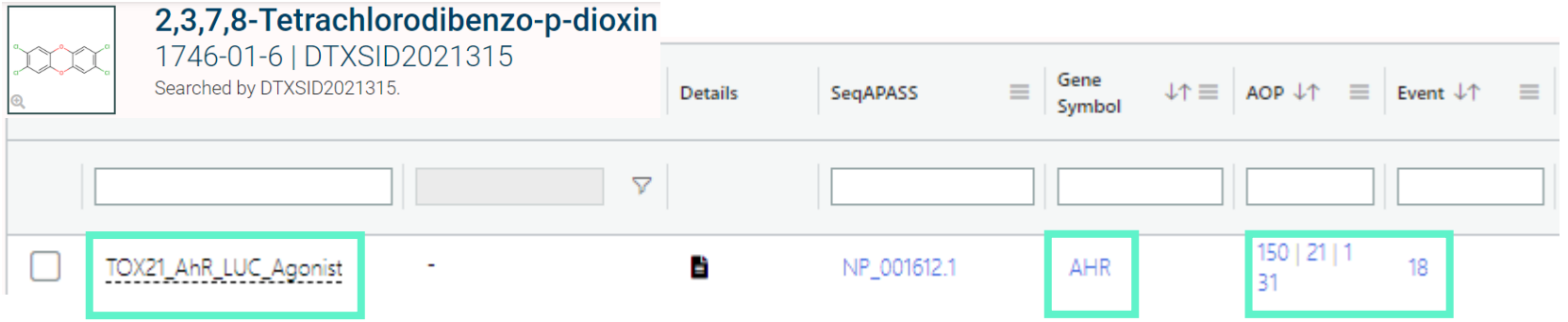
A test method or measurement is typically the connection between a stressor/substance tested and effect.

“Triangle of chemical safety”





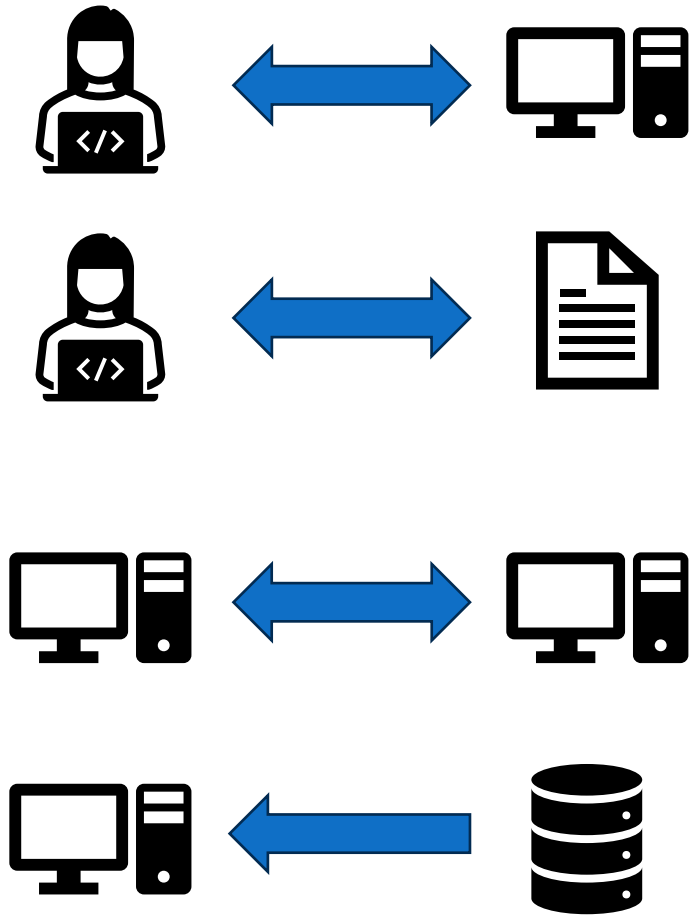
Adverse Outcome Pathways



Data Access

- Data is available via the web
  - https://aopwiki.org/aops/21
- Users can create snapshots in html and pdf formats
  - https://aopwiki.org/aops/21/snapshots

- Data is also available programmatically via a dynamic API
  - https://aopwiki.org/aops/21.json
- And via bulk downloads in XML format.
  - https://aopwiki.org/info_pages/5



Important considerations

- AOP-Wiki employs a crowd-sourced ethos
- Dependent on contributions from “the crowd”
  - Incentivizing AOP development has been challenging
- AOPs are not present for all biological effects, NAMs, or adverse outcomes of interest
- AOP-Wiki is growing steadily, but many AOPs are only partially developed – evidence assembly is often lacking
- To date, only around 10% of AOPs have been peer-reviewed and OECD endorsed.

Accessing AOP Wiki

- AOP Knowledge Base: Publicly accessible and searchable web-based resource of AOP information.
- AOP Wiki (https://aopwiki.org/): A globally accessible platform for developing and disseminating AOP descriptions in accordance with international guidance and templates.
- OECD-Endorsed AOPs: The Organisation for Economic Co-operation and Development provides guidance for development, scientific review, and OECD endorsement of AOPs.

Example of Tool Use

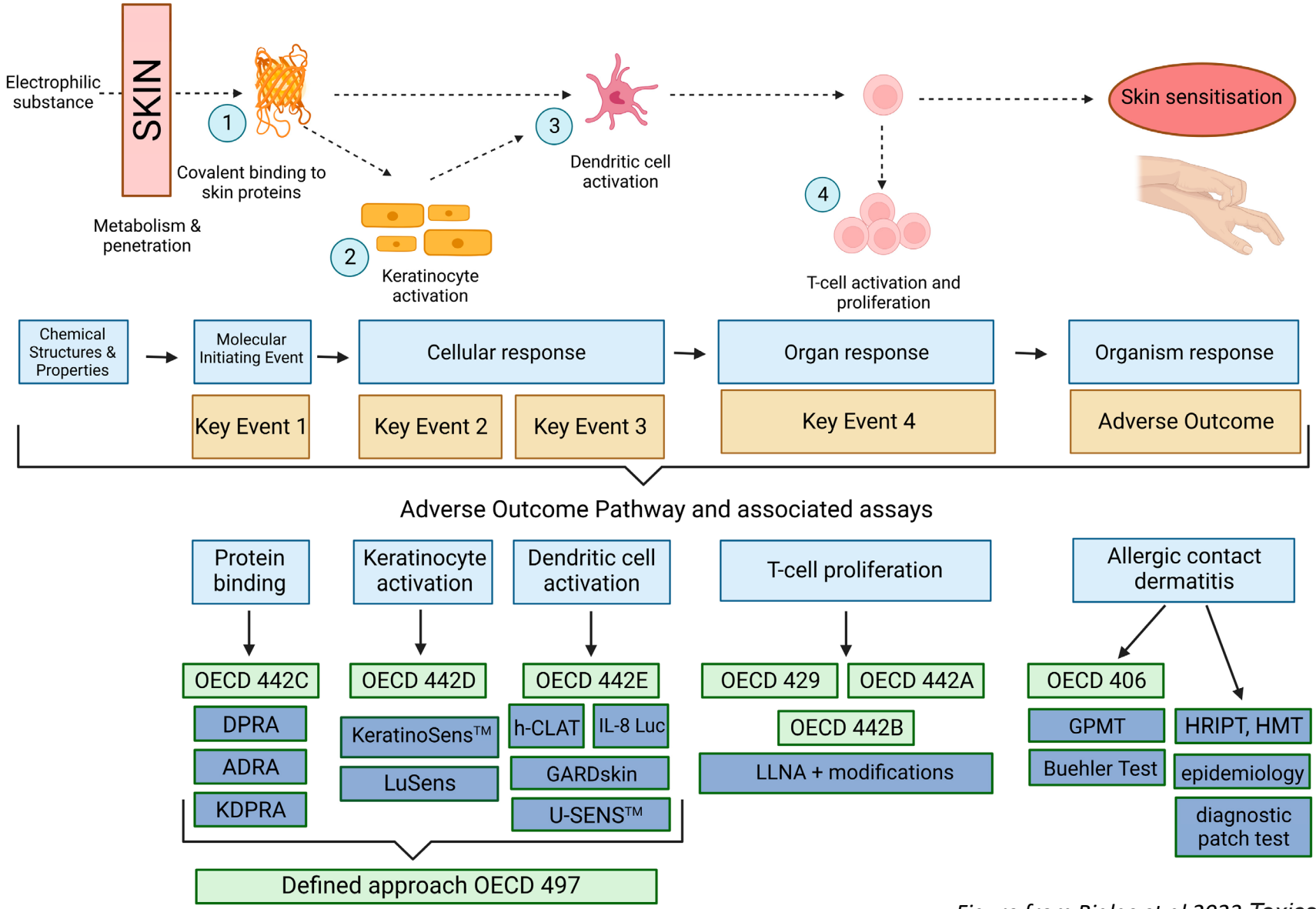


Figure from Bialas et al 2023 Toxics ***2023****, 11(4), 392;* https://doi.org/10.3390/toxics11040392

AOP: 40

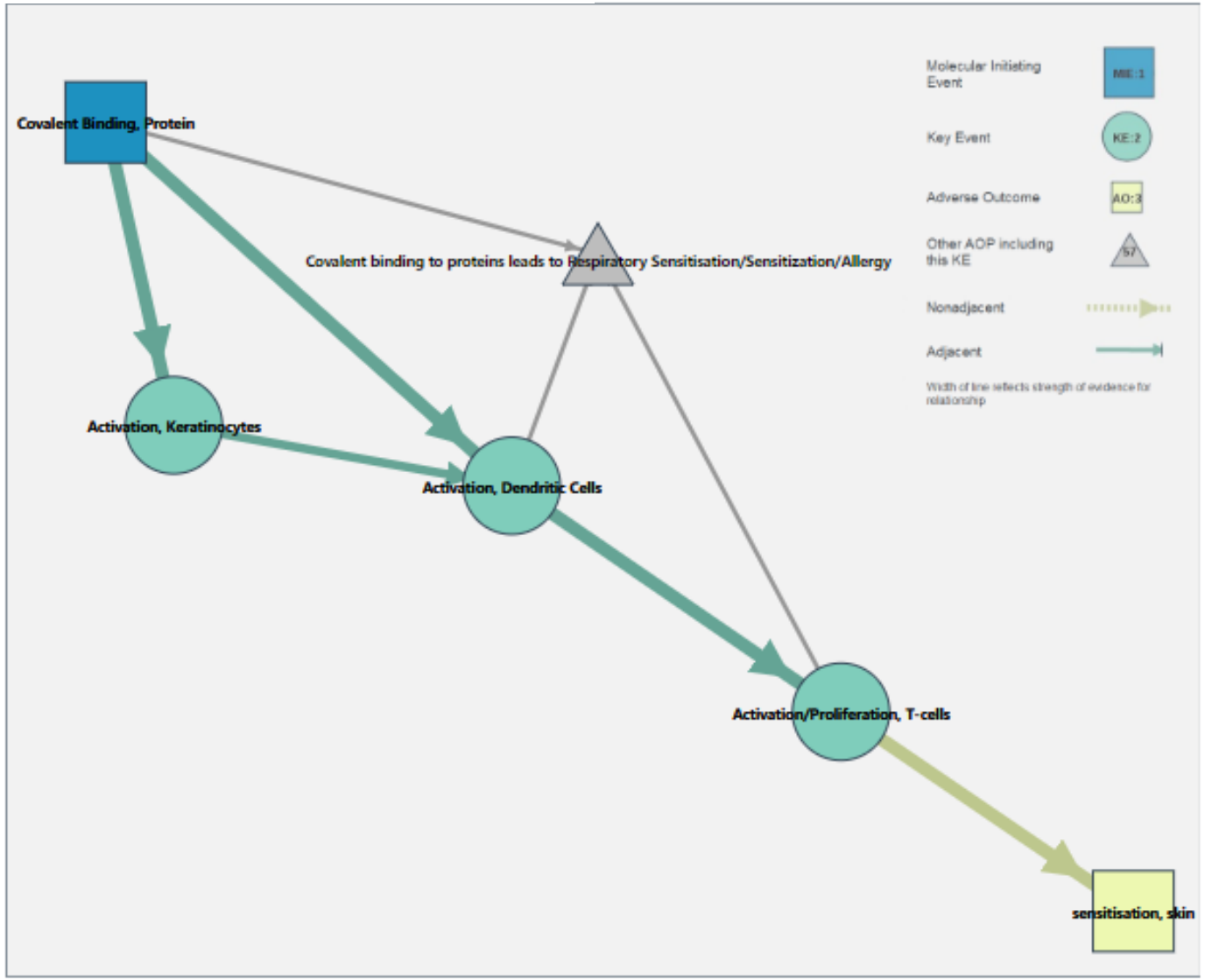
Title

Covalent Protein binding leading to Skin Sensitisation

Type	Event ID	Title
MIE	396	Covalent Binding, Protein
KE	826	Activation, Keratinocytes
KE	398	Activation, Dendritic Cells
KE	272	Activation/Proliferation, T-cells
AO	827	sensitisation, skin

Relationships Between Two Key Events (Including MIEs and AOs)

Title	Adjacency	Evidence
Covalent Binding, Protein leads to Activation, Keratinocytes	adjacent	High
Covalent Binding, Protein leads to Activation, Dendritic Cells	adjacent	High
Activation, Keratinocytes leads to Activation, Dendritic Cells	adjacent	Moderate
Activation, Dendritic Cells leads to Activation/Proliferation, T-cells	adjacent	High
Activation/Proliferation, T-cells leads to sensitisation, skin	adjacent	High



Aop:39 - Covalent binding to proteins leads to Respiratory Sensitisation/Sensitization/Allergy

Show IDS | Hide AOPs | Hide Nonadjacent | Reset Positions

AOP-Wiki Points of Contact

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