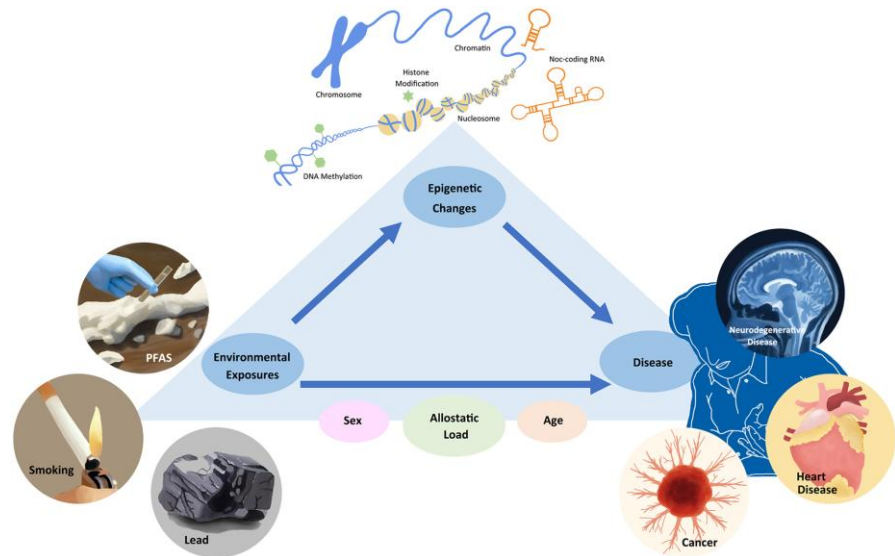


A zebrafish platform for assessing whole-body epigenetic toxicity of environmental toxicants at single cell resolution

Yijie Geng, PhD
Assistant Professor, DEOHS

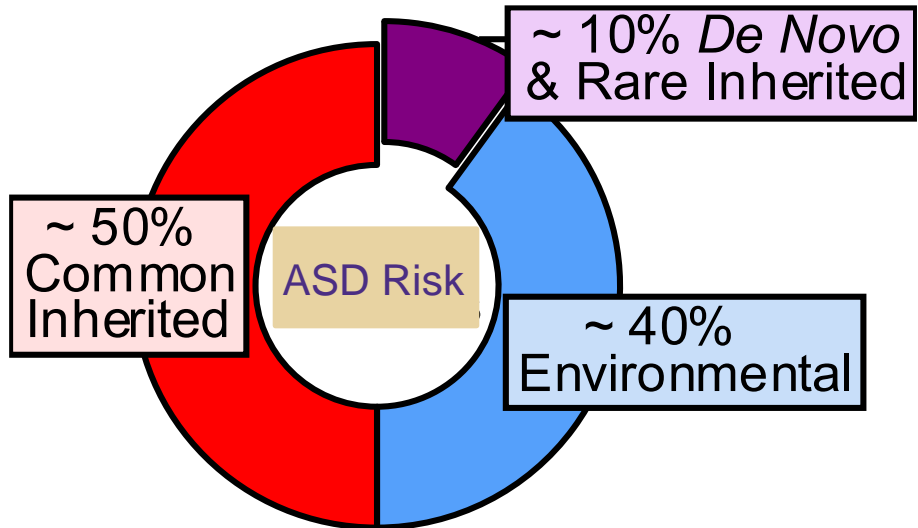
DOHaD and Toxicoepiggenetics

- > DOHaD: Developmental Origins of Health and Disease
- > Toxicoepiggenetics: how environmental exposures alter the genome without mutating the DNA

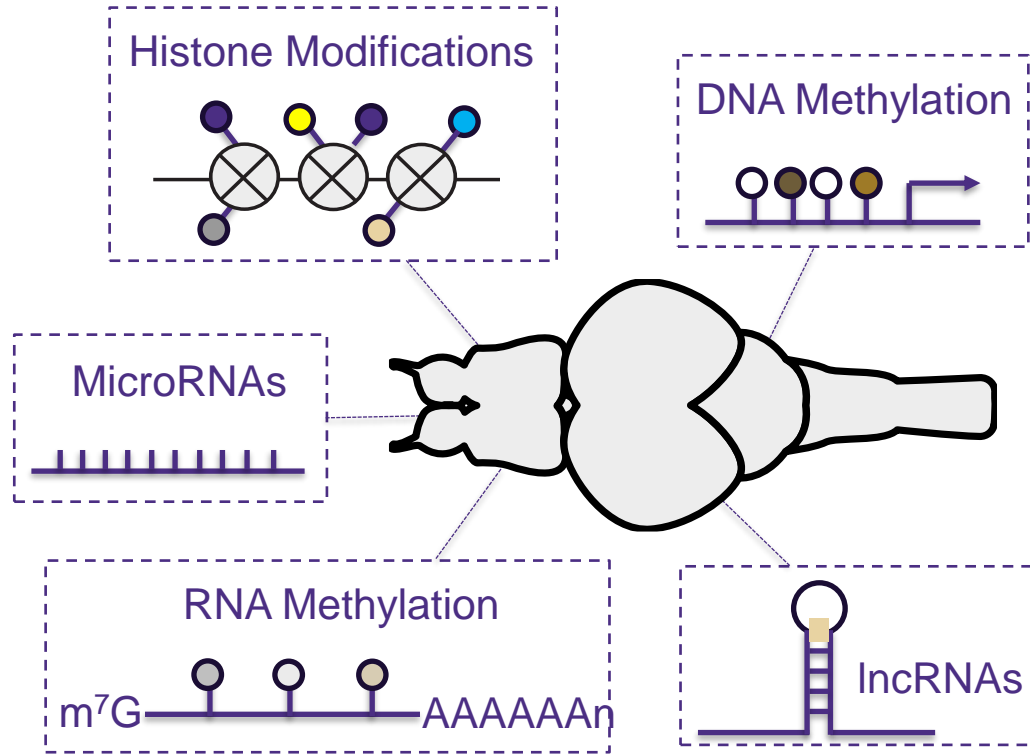


Env-EpiTox Pathways We Found for ASD

- > Hypothesis: environmental chemicals regulate social behavioral development & ASD risk primarily through epigenetic mechanisms.
- > 1. Top2a inhibitors / Top2a-PRC2-H3K27me3 pathway (*Geng 2022 Sci Adv; He 2026 bioRxiv; Johnson, 2026, bioRxiv*)
- > 2. Organophosphate pesticides / OP-microbiome-NO-HDAC pathway (*Diaz, 2026, eLife*)
- > 3. PFAS / PFAS-folate-DNAme pathway (*Kong, 2024, bioRxiv; Kong, 2026, J Hazard Mater*)
- > 4. Monoterpenes / Monoterpenes-KDM5-H3K4me pathway (*He, in review*)

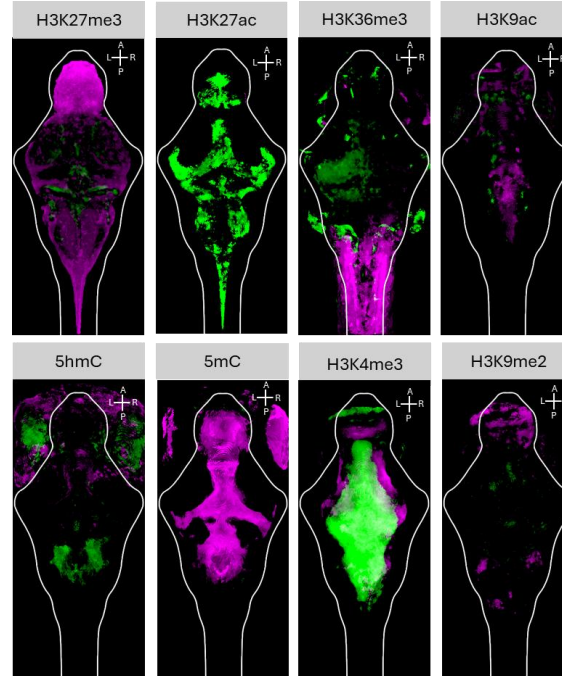
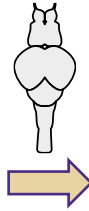
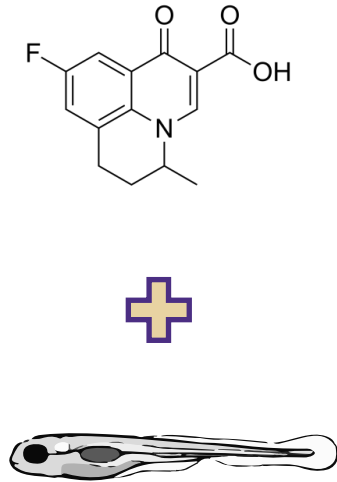


Env Toxicants → Brain's Epigenetic State?



Brain's Epigenetic State

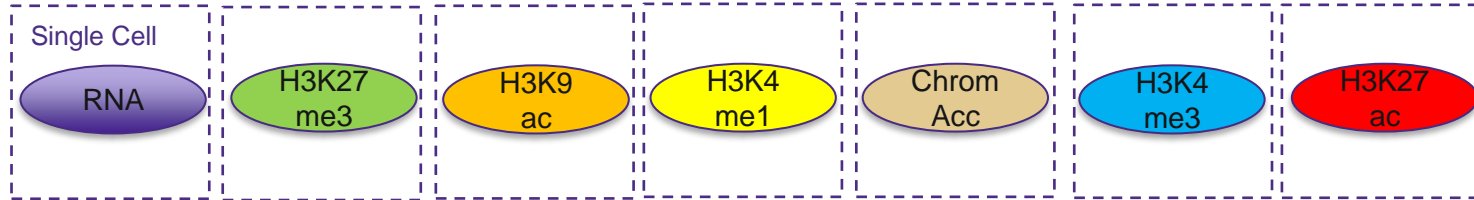
EpiBrain Detects Whole-Brain Epi Changes



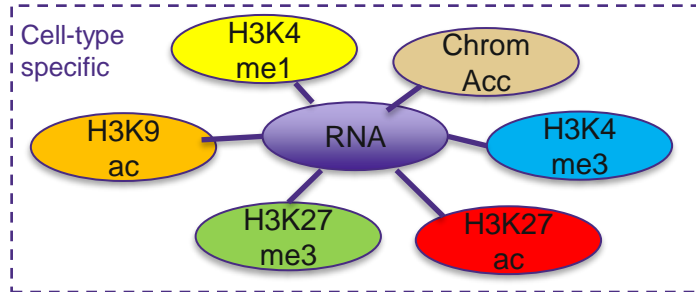
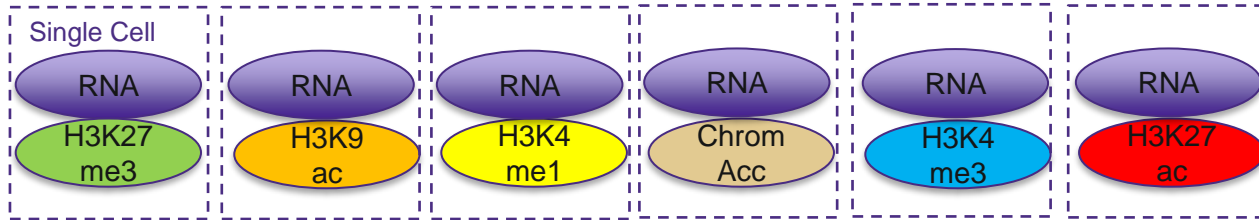
Which cell types?
Which genes?

Epigenetics at Single-Cell Resolution

> Traditional:



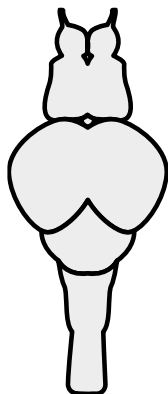
> Paired-Tag:



Design

Larval zebrafish brain

Tissue collection



Treatment conditions:

- Vehicle
- Toxicant

Single cell profiles

Paired-tag

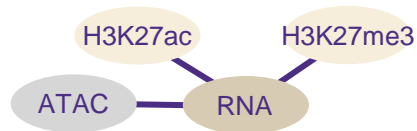
RNA — H3K27ac

RNA — H3K27me3

10x Multiome

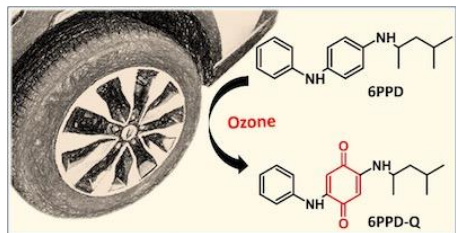
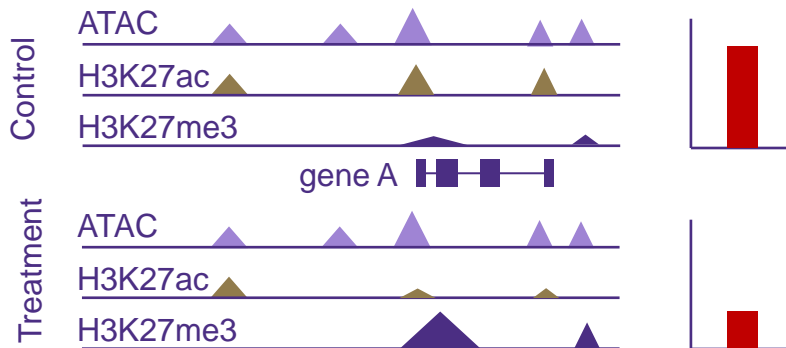
RNA — ATAC

Integrative analysis

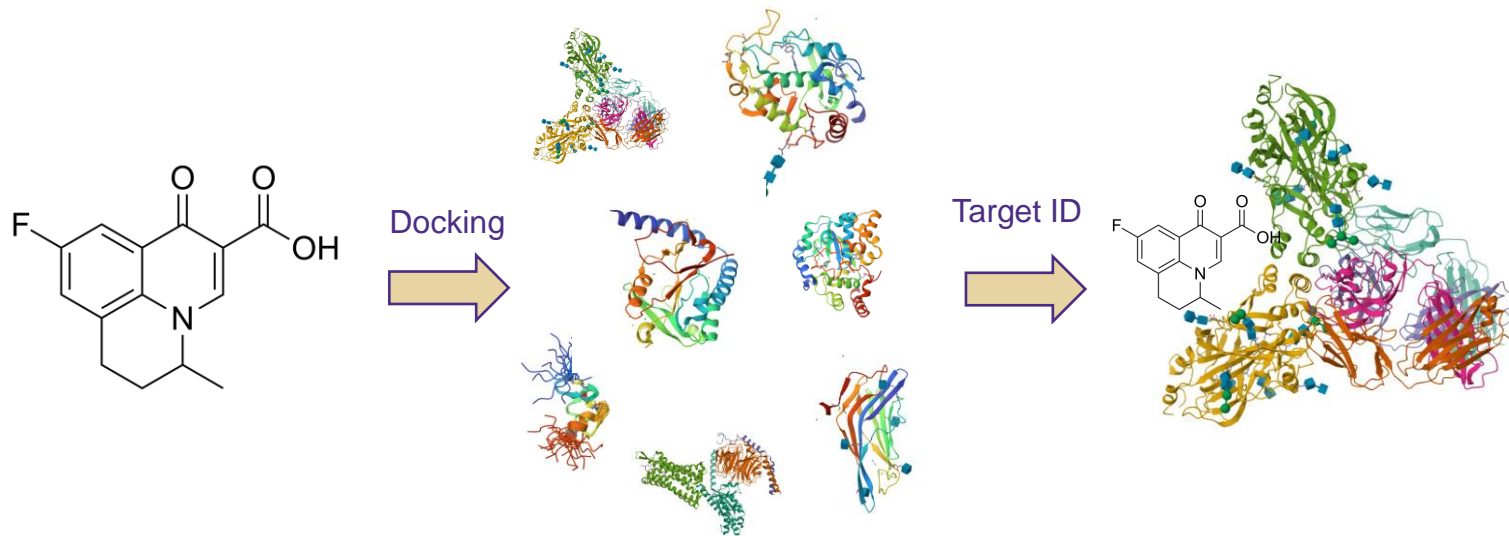


Epigenetic landscapes

Gene expression

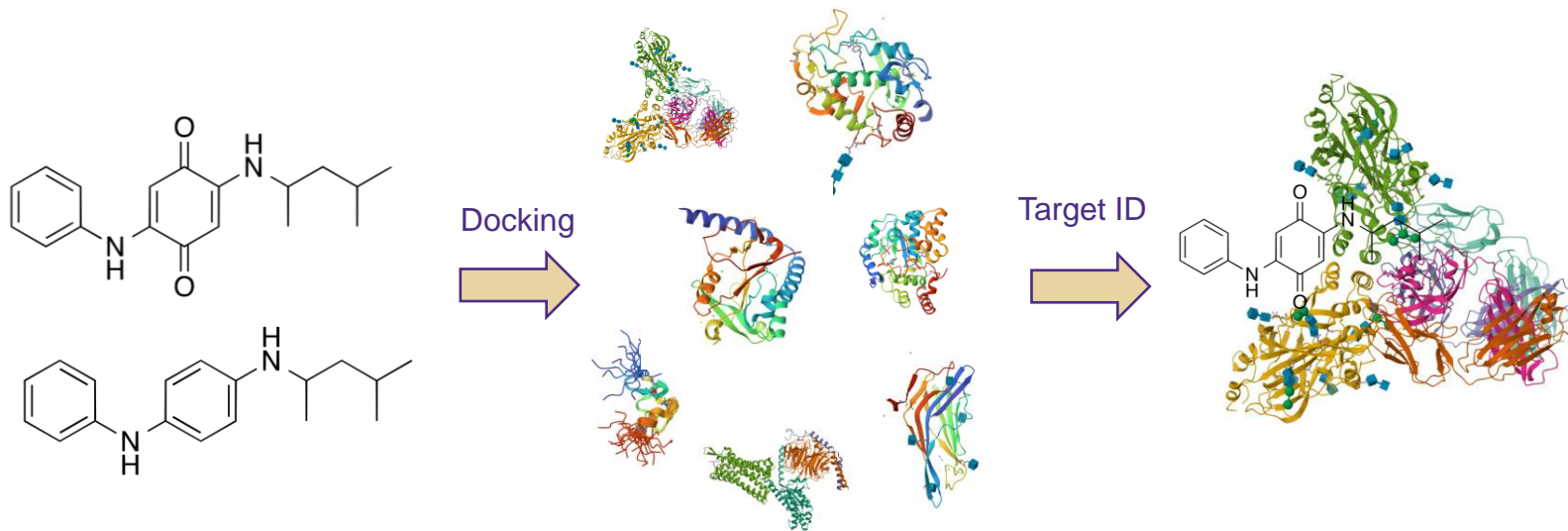


Integration (MIE): Proteome-Wide Docking

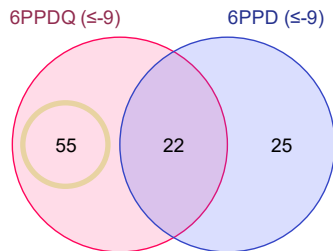


Kong et al., bioRxiv, 2024
Kong et al., J Hazard Mater, 2026
He et al., in review

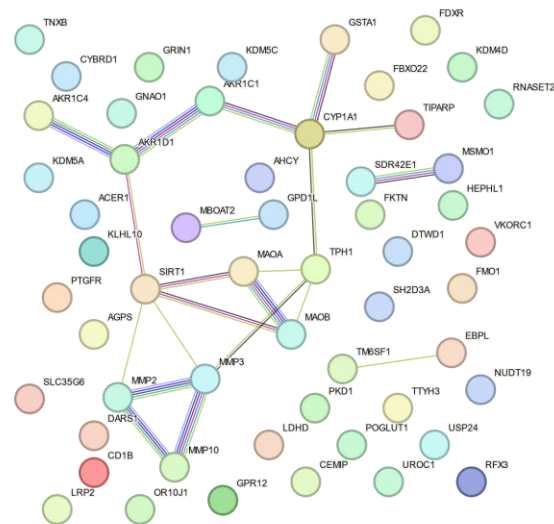
Integration (MIE): Proteome-Wide Docking



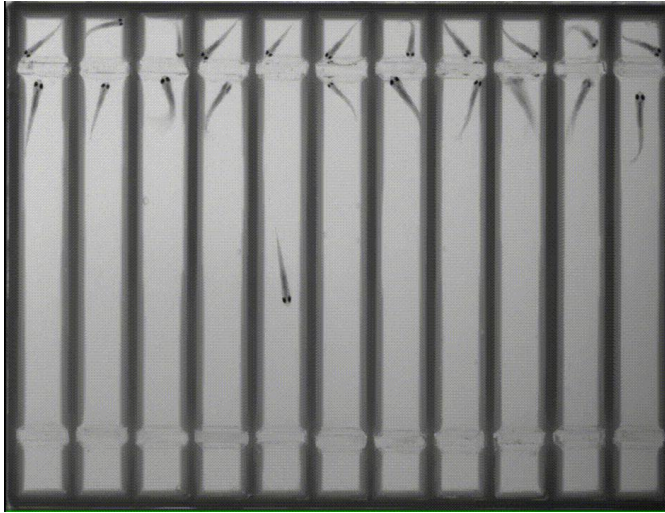
Integration (MIE): Proteome-Wide Docking



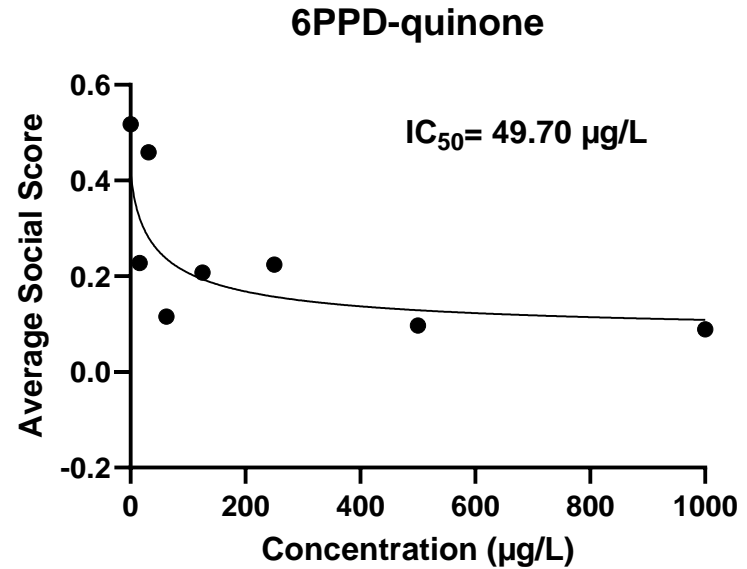
Biological Process (Gene Ontology)					
GO-term	description	count in network	strength	signal	false discovery rate
GO:0008202	Steroid metabolic process	10 of 258	1.14	1.19	1.46e-05
GO:1901615	Organic hydroxy compound metabolic process	13 of 478	0.99	1.12	5.18e-06
GO:0006805	Xenobiotic metabolic process	6 of 115	1.27	0.84	0.0015
GO:0006694	Steroid biosynthetic process	6 of 116	1.27	0.83	0.0015
GO:0006629	Lipid metabolic process	17 of 1210	0.7	0.74	6.14e-05
(more ...)					
Molecular Function (Gene Ontology)					
GO-term	description	count in network	strength	signal	false discovery rate
GO:0016491	Oxidoreductase activity	21 of 731	1.01	1.75	1.45e-12
GO:0016705	Oxidoreductase activity, acting on paired donors, with incorporation o...	10 of 177	1.31	1.7	1.51e-07
GO:0004497	Monoxygenase activity	7 of 103	1.39	1.3	2.75e-05
GO:0016709	Oxidoreductase activity, acting on paired donors, with incorporation o...	5 of 40	1.65	1.21	0.00015
GO:0047086	Ketosteroid monoxygenase activity	3 of 5	2.33	1.04	0.00093



Integration (AO): Behavior (Fishbook)



1 cm

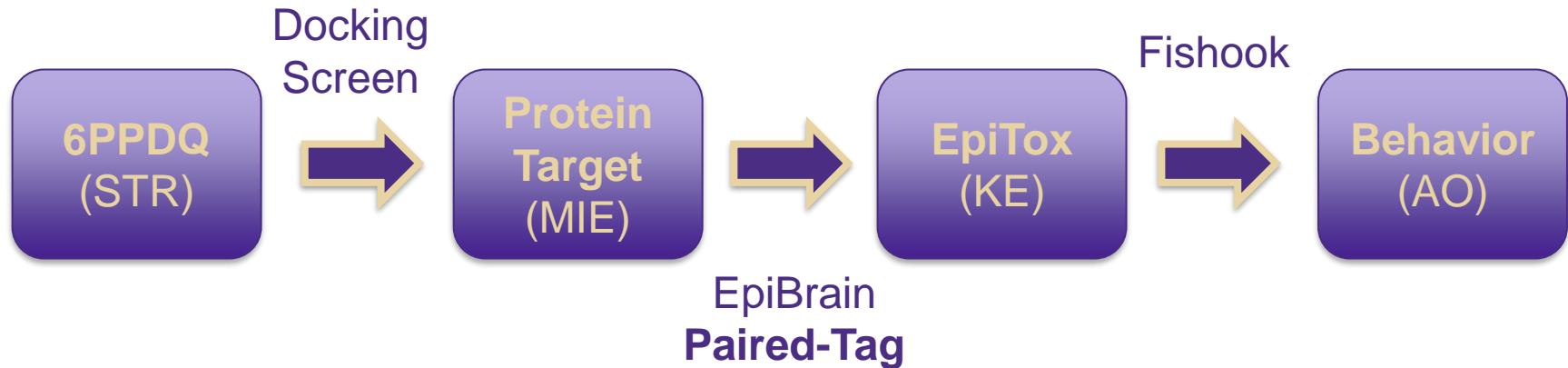


Geng et al., *Sci. Adv.*, 2022

Kong et al., *J Hazard Mater*, 2026

Diaz et al., *eLife*, 2026

Integration: AOP



Acknowledgement

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- Leo Diaz

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- Theo Bammler, PhD
- James MacDonald

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Sheldon D. Murphy Endowed Chair in Toxicology and
Environmental Health

