

Mechanism of action (MOA): EE2 in quail



BACKGROUND INFORMATION

Ethinylestradiol (EE2) is widely used in birth control pills. The chemical is regularly found in waterways, largely because it is not fully captured by wastewater treatment plants. Ecological studies have demonstrated that EE2 can have deleterious effects on aquatic organisms.

OBJECTIVE

To characterize the molecular mechanisms of action of ethinylestradiol (EE2) in exposed Japanese quail (JQ) embryos using the Version 1 (V1) JQ EcoToxChip and EcoToxXplorer.

METHODS & RESULTS

Fertilized JQ eggs were injected on embryonic day 0 with 54 ug/g EE2 (in DMSO). At embryonic day 9, the liver was excised and immediately flash frozen. RNA was extracted, cDNA run on the V1 JQ EcoToxChip. The data were analyzed with [EcoToxXplorer.ca](https://ecotoxexplorer.ca) with key findings noted below.

1. Top differentially expressed genes¹

	Fold Change
APOV1	404
VTG2	144
CYP2H1	42
ZPSP2	39
SPATA1	22

2. OECD adverse outcome pathways (AOPs) flagged¹

- PPAR Antagonism (AOP6)
- CAR Activation (AOP107)
- Aromatase Reduction (AOP7)
- ER Antagonism (AOP30)
- Aromatase Inhibition (AOP25)
- Androgen Agonism (AOP23)
- AhR Activation (AOP21)

3. EcoTox processes and EcoTox modules flagged²



TAKEAWAYS

Using the EcoToxChip, we flag these samples as “YELLOW”. We conclude that the main biological pathways affected by this exposure were those related to metabolism and cellular signaling. Notable genes are expressed (e.g., vitellogenin), and several AOPs are flagged. In general, these are responses that would be expected by EE2.

Notes

Farhat, A., Crump, D., Bidinosti, L., Boulanger, E., Basu, N., Hecker, M., Head, J.A. 2019. An Early life Stage Alternative Testing Strategy for Assessing the Impacts of Environmental Chemicals in Birds. Environ Toxicol Chem. doi: 10.1002/etc.4582.

¹ p<0.05; ² EcoToxXplorer V1 settings were 1.2 for yellow and 1.5 for red