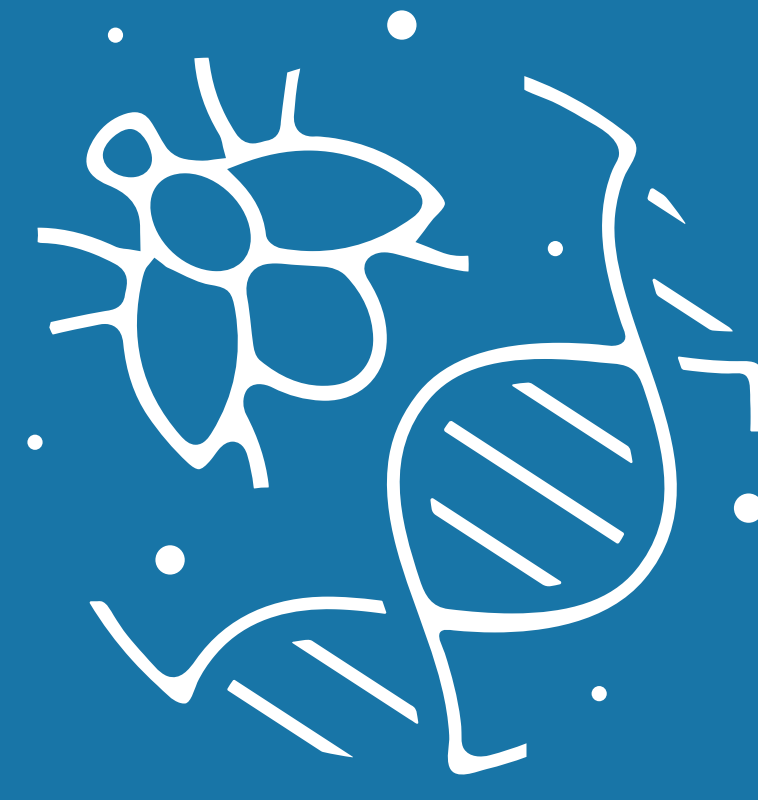


Ecdysone Receptor Agonism Adverse Outcome Pathway Validation for Insect - Specific In Vitro Assay Development

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INTRODUCTION

BACKGROUND

- **Next Generation Risk Assessment (NGRA)** is an exposure-led, hypothesis-driven risk assessment approach that integrates *in silico*, *in chemico* and *in vitro* data.¹
- **Ecdysone receptor agonism** - incomplete ecdysis associated mortality following a conserved pathway.²
- **Ecdysone (20E)** - insect hormone for moulting and metamorphosis.
- **S2 cells** - *D. melanogaster* embryonic cell line.

OBJECTIVE

- To provide empirical data supporting the key events of the **EcR Agonism AOP** and a proof of concept.
- Development of an *in vitro* assay.

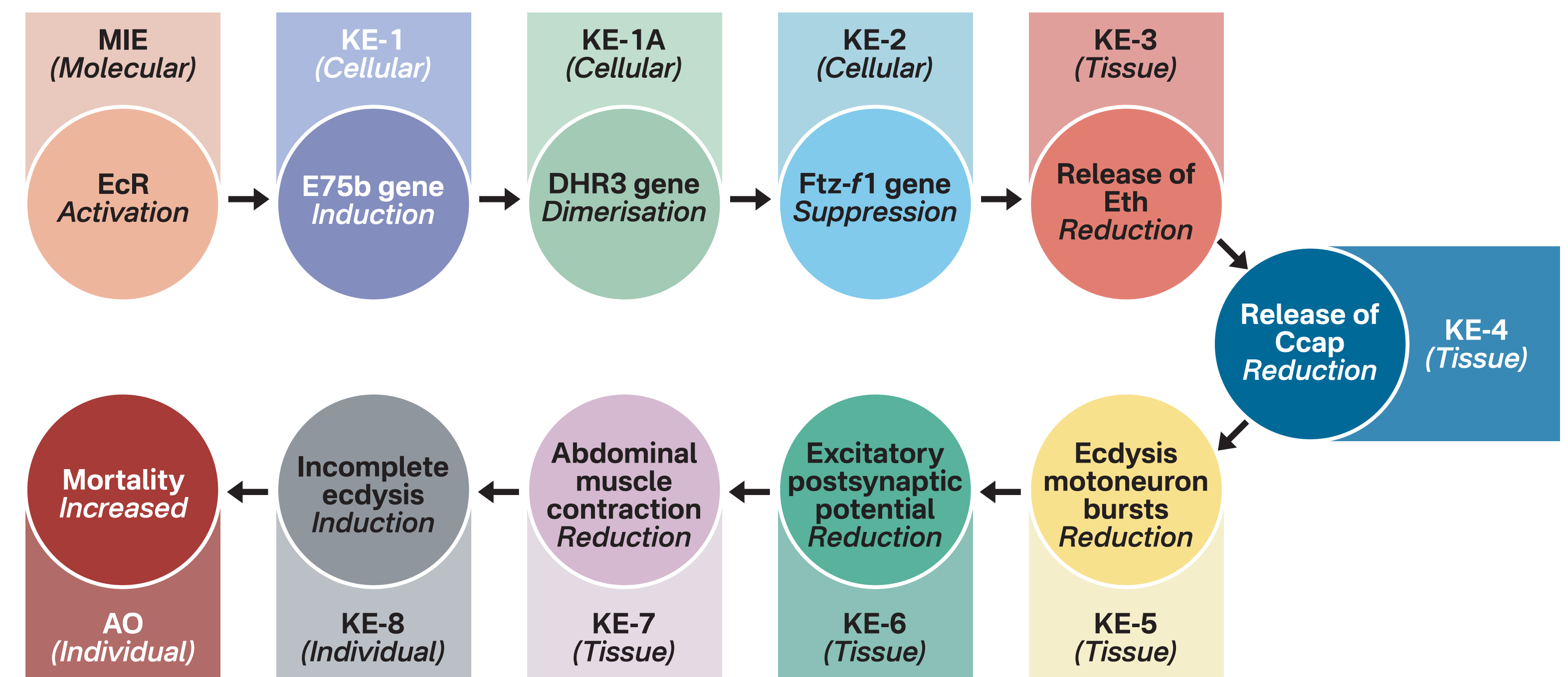
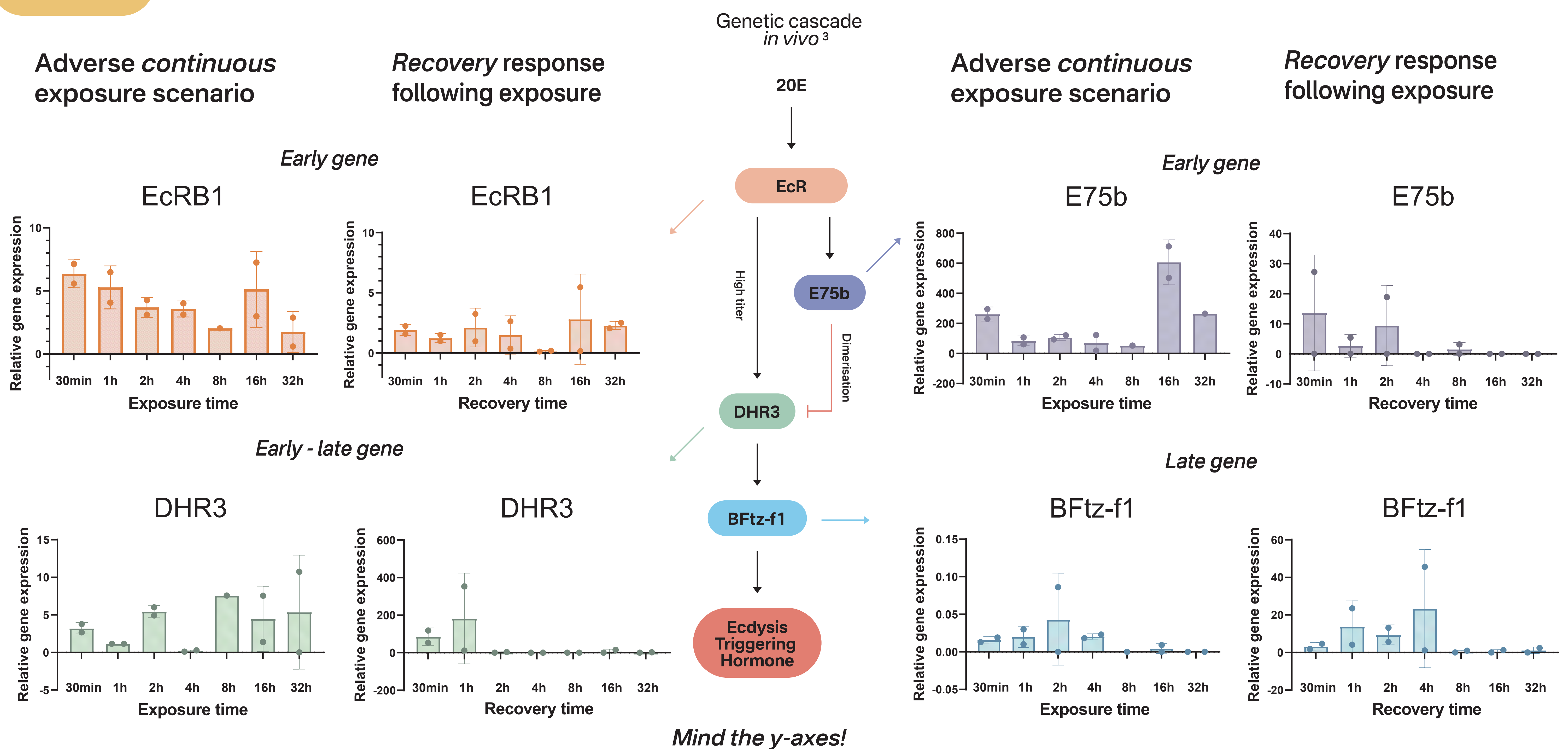


Figure 1 Graphical representation of Ecdysone receptor agonism Adverse Outcome Pathway (AOP) based on Song et al (2017)

Can the S2 cell based assay show the initial KEs potentially leading to adverse outcome?

RESULTS



CONCLUSION

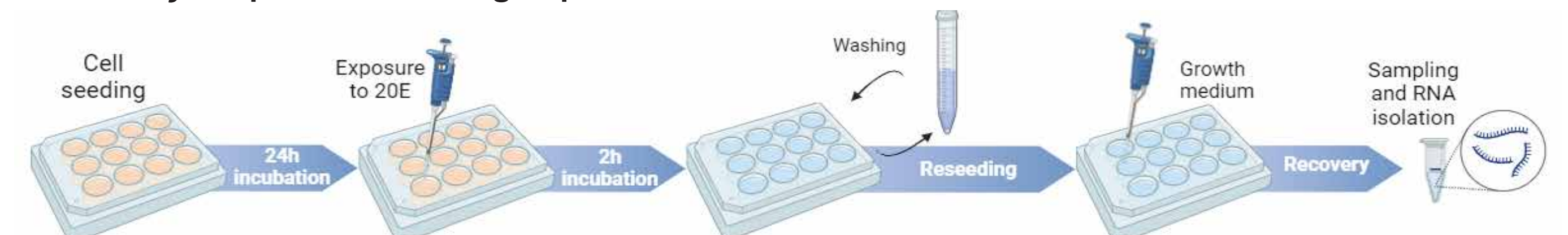
S2 cell line mimics the ecdysone response cascade observed *in vivo*.

1. EcR expression fluctuates at a low level after recovery.
2. E75b expression dramatically decreases 30min after ecdysone clearance.
3. DHR3 expression spikes post-ecdysone clearance but quickly declines.
4. BFtz-f1 expression gradually increases during recovery.

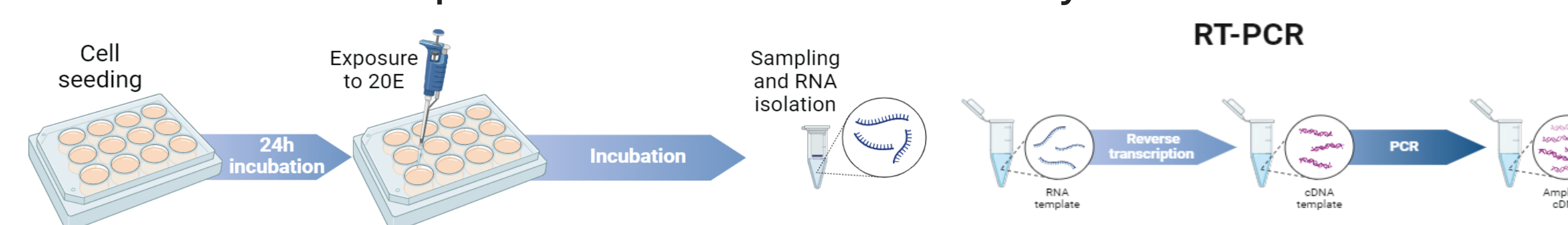
S2 cells show initial KEs potentially leading to adverse effect.
S2 cells seem to be a promising model for insect specific *in vitro* assay.

METHODS

Recovery response following exposure



Adverse continuous exposure scenario



REFERENCES:

1. Ankley G, et al. (2010) DOI: 10.1002/etc.34
2. Song Y, et al. (2017); DOI: 10.1021/acs.est.7b00480
3. Sullivan A and Thummel C, (2003); DOI: 10.1210/me.2002-0430

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