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Research Article

Cross-species analysis of transcriptome emphasizes a critical role of TNF-α in mediating MAP2K7/AKT2 signaling in zearalenone-induced apoptosis

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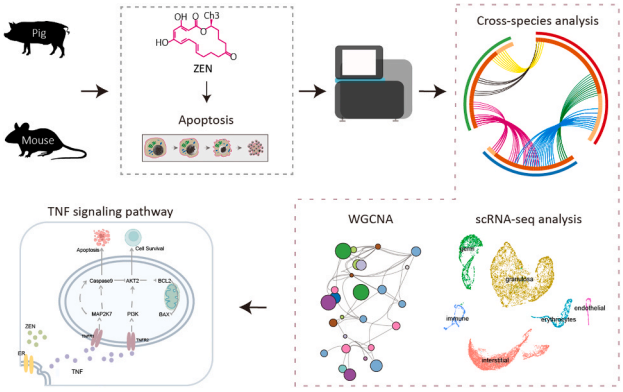
HIGHLIGHTS

- Cross-species analysis strengthen that zearalenone-induced apoptosis of granulosa cells was more detrimental to pigs.
- Zearalenone-induced apoptosis of granulosa cells *via* TNF-α-mediated MAP2K7/AKT2 signaling pathway was highlighted.
- Perinatal Zearalenone exposure impairs ovarian development in offspring mice.
- Crosstalk between TNF signaling pathway and PI3K-AKT signaling pathway during zearalenone-induced apoptosis was highlighted.

GRAPHICAL ABSTRACT



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ABSTRACT

Zearalenone (ZEN) is a widespread and transgenerational toxicant that can cause serious reproductive health risks, which poses a potential threat to global agricultural production and human health; its estrogenic activity can lead to reproductive toxicity through the induction of granulosa cell apoptosis. Herein, comparative transcriptome analysis, single-cell transcriptome analysis, and weighted gene co-expression network analysis (WGCNA) combined with gene knockout *in vivo* and RNA interference *in vitro* were used to comprehensively describe the damage caused by ZEN exposure on ovarian granulosa cells. Comparative transcriptome analysis

Abbreviations: TNF, Tumor necrosis factor; MAPK, Mitogen-5 activated protein kinase; MAP2K7, Mitogen-activated protein kinase 7; AKT, Protein kinase B; AKT2, AKT serine/threonine kinase 2; IFN, Interferon; IL, Interleukin; PI3K, Phosphoinositide 3-kinases; BCL2, B-cell lymphoma 2; BAX, BCL2 Associated X; CASP9, Caspase 9; ZEN, Zearalenone; mGCs, mouse granulosa cells; pGCs, pig granulosa cells; siRNA, exogenous double-stranded RNA; PBST, PBS containing 10% Triton X-100; DEGs, differentially expressed genes; GO, Gene ontology; KEGG, Kyoto Encyclopedia of Genes and Genomes; UMAP, uniform manifold approximation, and projection; FPKM, fragments per kilobase of exon model per million mapped fragments; WGCNA, weighted gene co-expression network analysis; MM, Module membership; GS, Gene significance; GSEA, Gene set enrichment analysis.

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