How does exposure to pesticide residues impact gut health?

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Exposure

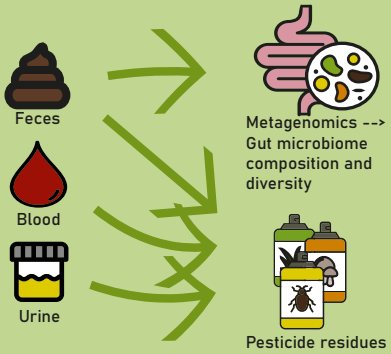
The gut microbiome and gut epithelium are exposed to pesticide residues via contaminated food, water, unintentional oral intake of dust, or via dust particles in swallowed mucus.

Gut microbiome

The gut microbiome plays an important role in resistance to pathogens, digestion of fibers and production of vitamins. A disrupted gut microbiome is linked to the pathophysiology of many diseases including cancer, neurodegenerative disease, metabolic disease and IBD.
Among others, glyphosate, chlorpyrifos, pyrethroids, carbendazim and imazalil are pesticides that have been shown to have a disruptive effect on the gut microbiome.

Findings in SPRINT

The gut microbiomes from all ~792 participants in SPRINT were analysed and pesticide residues were measured in their feces, blood and urine. **An association between gut microbiome composition and concentration of pyrethroids, glyphosate, DDE p,p' and spirotetramat-enol-glucoside in feces was found.**



Gut epithelium

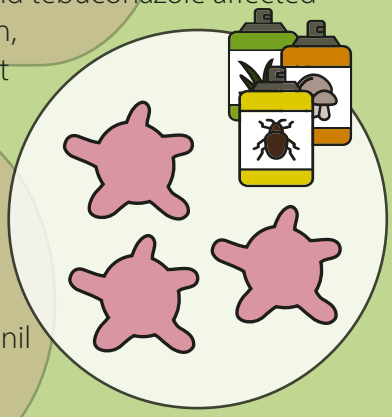
Organoid experiments

Gut epithelial organoids were exposed to glyphosate, tebuconazole, piperonyl butoxide (PBO), fludioxonil and cyprodinil. Effects at the molecular level were evaluated using gene expression analysis (RNA sequencing).

Treatment with fludioxonil and PBO resulted in the highest number of differentially expressed genes, while the effects of glyphosate and tebuconazole were comparibly minor. **All five treatments induce changes in gene expression consistent with increased oxidative stress and mitochondrial dysfunction. Fludioxonil and PBO upregulated genes involved in endoplasmic reticulum (ER) stress.**

Gut barrier function

The gut epithelium provides a physical and chemical barrier between the intestinal lumen and the bloodstream; it keeps microbes and potentially harmful molecules including pesticide residues out of the bloodstream, protecting the gut and the rest of the body from inflammation and disease.
Gene expression analysis revealed that all 5 treatments potentially impact gut barrier function. Gene ontology terms related to cell-cell adhesion and cell junctions were downregulated by glyphosate, PBO, fludioxonil and cyprodinil. Fludioxonil affected genes involved in glycosylation and tebuconazole affected genes involved in sialylation, both of which could impact gut barrier integrity.
OLFM4, a glycoprotein known to play a multifaceted role in the gut and in regulation of gut barrier function, was downregulated by fludioxonil and cyprodinil.



Increases in ER stress, mitochondrial dysfunction, oxidative stress and decreases in gut barrier integrity may contribute to chronic disease including IBD, cancer nd neurodegenerative disease.

1. Human gut microbiota in health and disease: Unveiling the relationship. Afzaal, 2022
2. Low-dose glyphosate exposure alters gut microbiota composition and modulates gut homeostasis. Lehman, 2023
3. Effects of environmental pollutants on gut microbiota. Jin, 2017
4. The gut microbiota: a major player in the toxicity of environmental pollutants? Claus, 2016
5. Human intestinal Barrier Function in Health and Disease. König, 2016
6. Olfactomedin-4 deletion exacerbates DSS-induced colitis through a matrix metalloproteinase-9-dependent mechanism. Wang, 20223
7. Mitochondrial Dysfunction in Cancer and Neurodegenerative Diseases. Barrera, 2016

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