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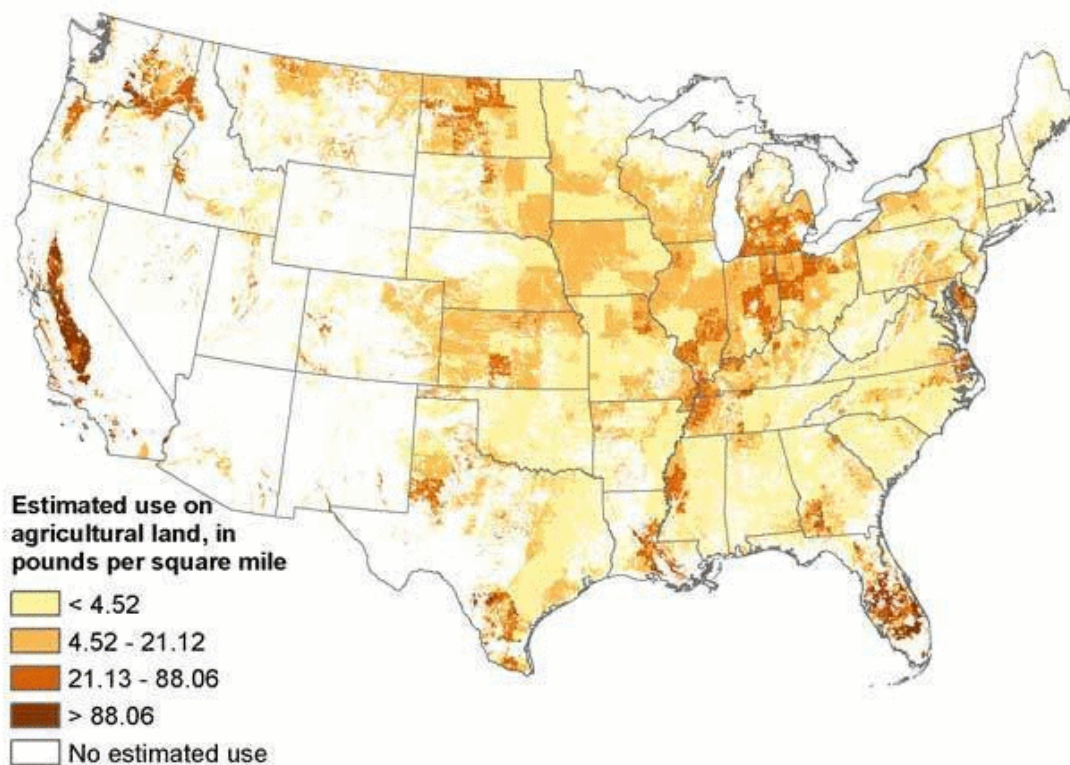
**New scientific concepts to improve the
regulatory assessment of pesticide toxicity**
The case of glyphosate

Robin Mesnage, PhD, King's College London, UK

Science, Precaution, Innovation:
towards the integrated governance of new technologies
14/15 October 2019

Glyphosate-based herbicides are the most heavily applied herbicide in the world and usage continues to rise

Estimated Agricultural Use for Glyphosate, 1992



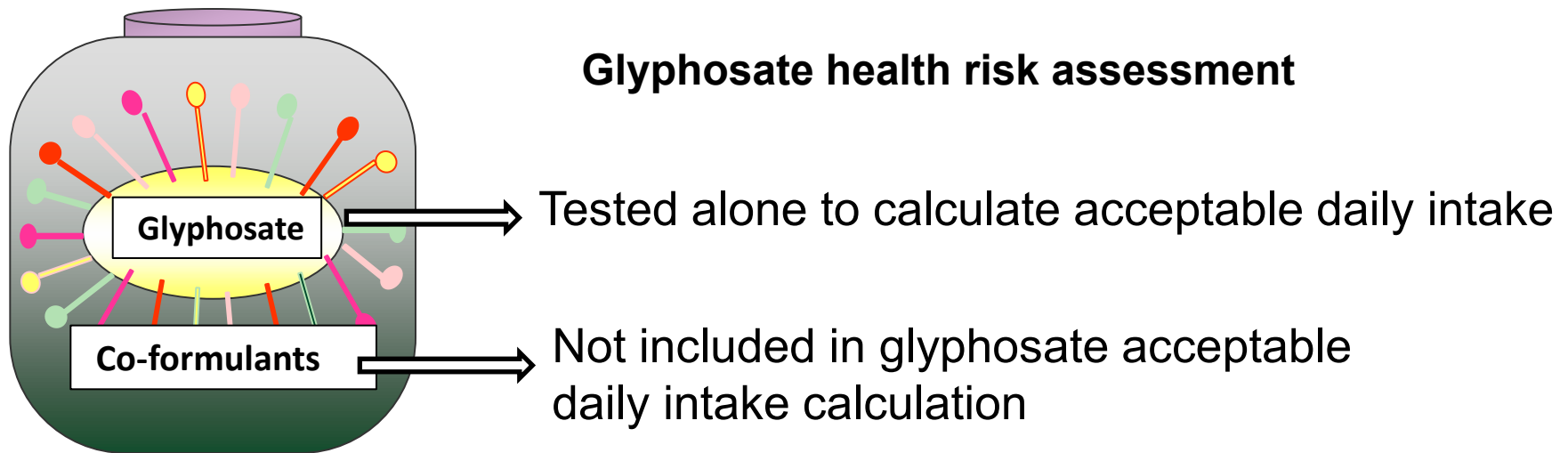
Human exposures to glyphosate are rising

New scientific concepts to improve the regulatory assessment of pesticide toxicity

- 1/ Testing chronic effects of commercial formulations**
- 2/ incorporate testing principles from endocrinology (hormone dosages)**
- 3/ Examination of the full lifespan, including a prenatal period**
- 4/ Test the effects of pesticides on the gut microbiome**
- 5/ Real-life exposures to chemical mixtures**
- 6/ Human biomonitoring of pesticide exposures**

1/ Chronic effects of commercial formulations have to be tested

COMMERCIAL FORMULATION



The company asking for the pesticide commercialization is free to choose the molecule that they want to declare as an active principle.

Are you sure co-formulants of pesticides are safe and do not need to be tested?



Glyphosate formulations are up to 1000 times more toxic than glyphosate alone

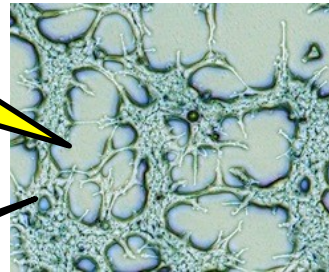
Formulations

X 1000



Glyphosate

X 1



If the toxic agent is not glyphosate, then what is it?

EU agrees ban on glyphosate co-formulant

By [Sarantis Michalopoulos](#) | [EURACTIV.com](#)

📅 12 Jul 2016



The licence for glyphosate was extended for another 18 months. [[Global Justice Now](#) / [Flickr](#)]

Languages: [Français](#) | [Deutsch](#)

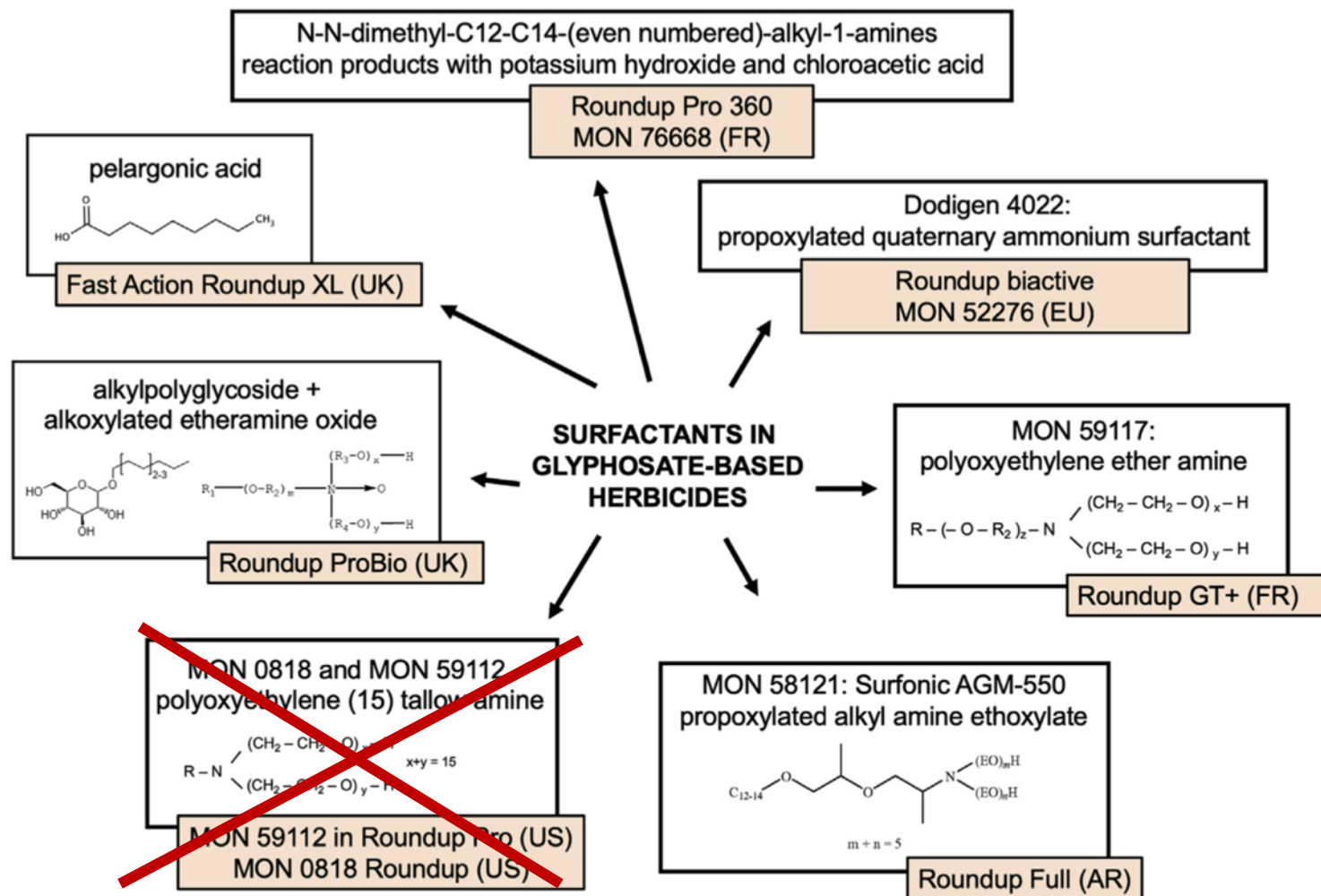


Comments



Print





Improving current animal testing strategies

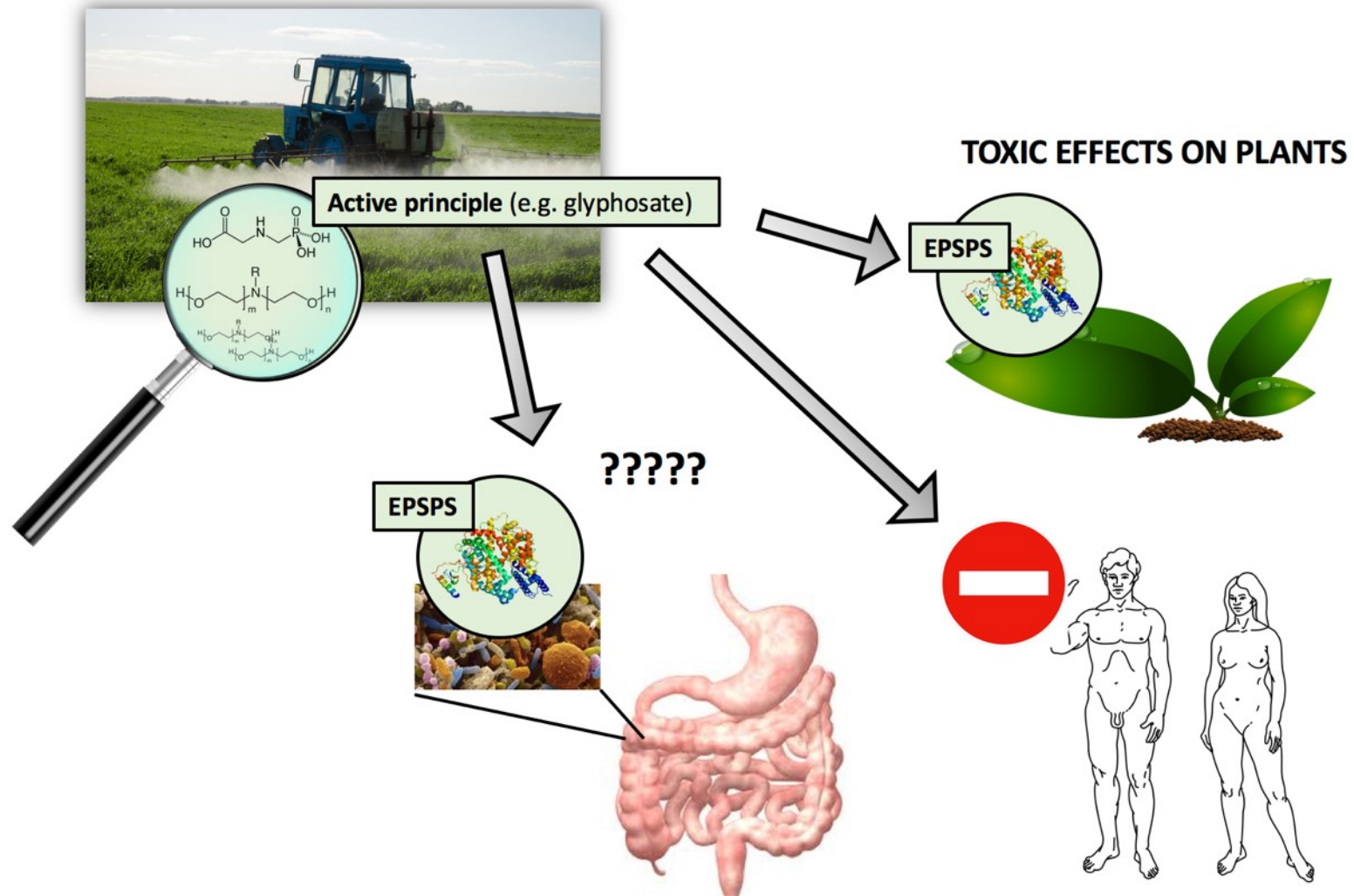
2/ Some pesticides are suspected endocrine disruptors.

Studies should incorporate testing principles from endocrinology (hormone dosages)

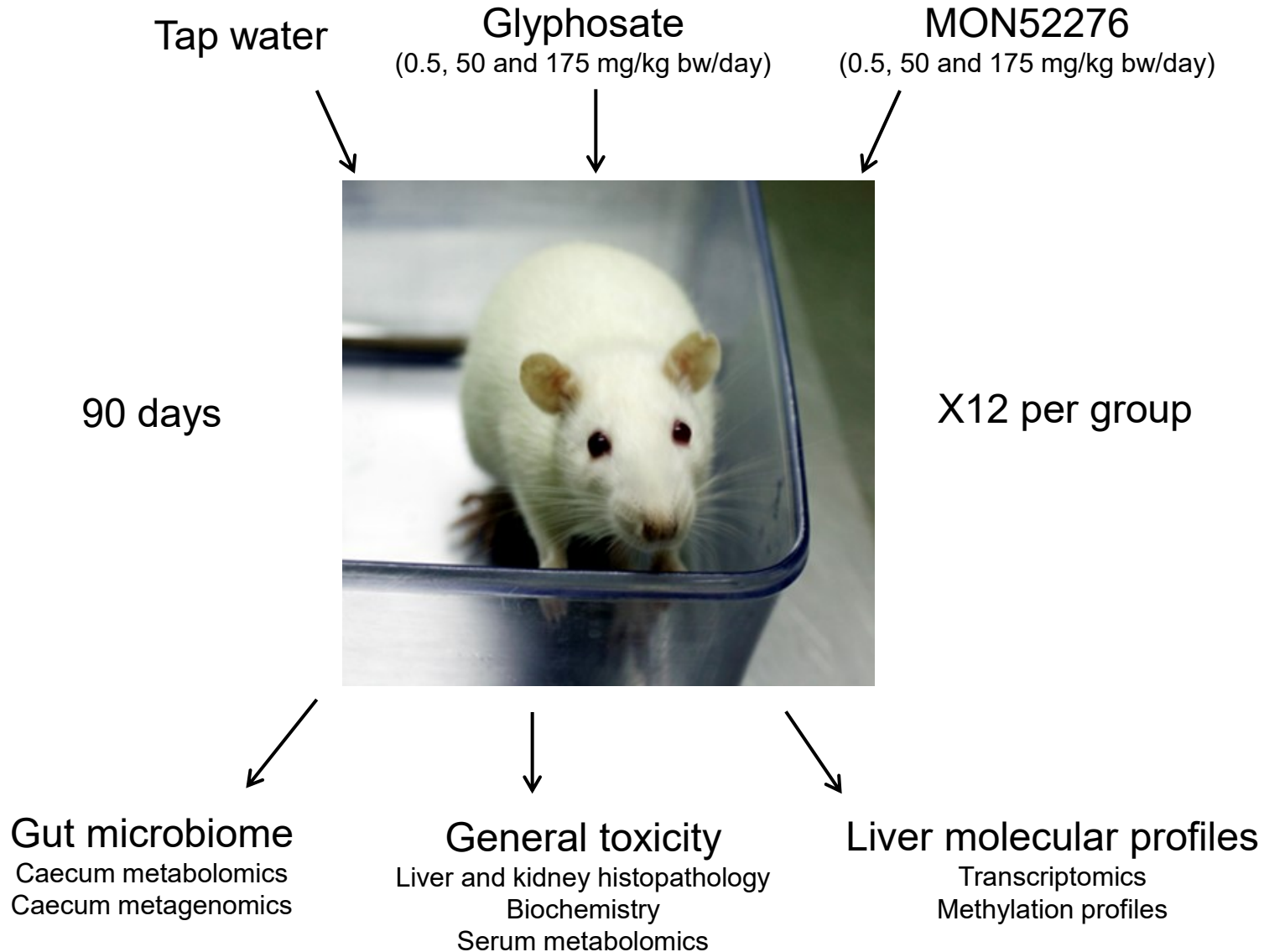
3/ Future studies should use designs that examine the full lifespan of the animal, including a prenatal period

3/ New studies should be performed to test the effects of pesticides on the gut microbiome

Glyphosate effects on the gut microbiome?



Glyphosate effects on the gut microbiome?



The most comprehensive study ever on Glyphosate & Glyphosate-based herbicides

- ➔ TOXICITY
- ➔ CARCINOGENICITY
- ➔ PRENATAL DEVELOPMENTAL TOXICITY
- ➔ NEUROTOXICITY
- ➔ MULTI-GENERATIONAL
- ➔ ENDOCRINE DISRUPTION
- ➔ MICROBIOME



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5/ Real-life exposures to chemical mixtures

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Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox



Short communication

New challenges in risk assessment of chemicals when simulating real exposure scenarios; simultaneous multi-chemicals' low dose exposure



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Six months exposure to a real life mixture of 13 chemicals' below individual NOAELs induced non monotonic sex-dependent biochemical and redox status changes in rats

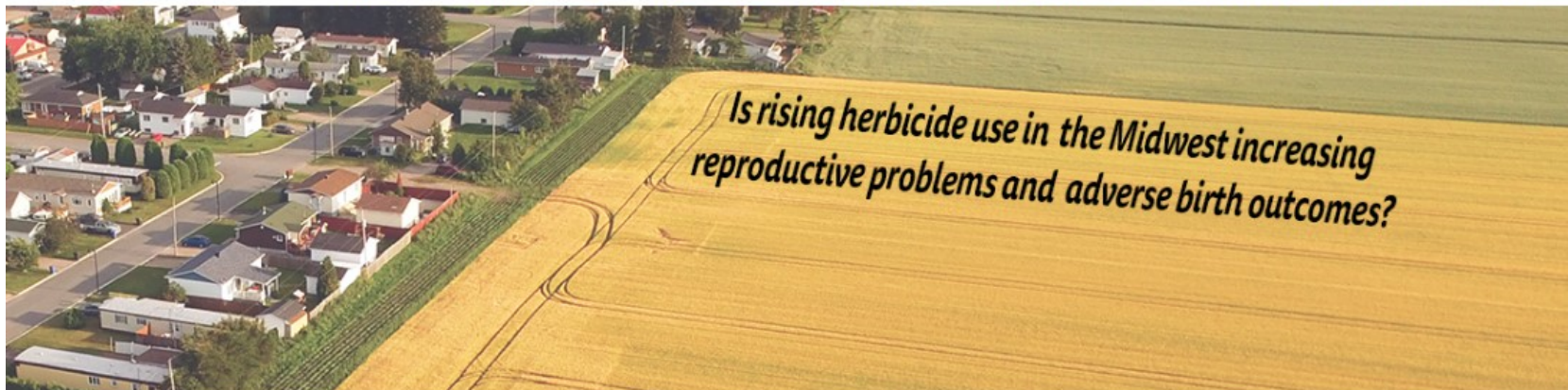


Anca Oana Docea^{a,1}, Eliza Gofita^{a,1}, Marina Goumenou^{b,1,1}, Daniela Calina^{c,1}, Otilia Rogoveanu^d, Marius Varut^e, Cristian Olaru^f, Efthalia Kerasioti^g, Polyxeni Fountoucidou^g, Ioannis Taitzoglou^h, Ovidiu Zlatianⁱ, Valerii N. Rakitskii^j, Antonio F. Hernandez^k, Dimitrios Kouretas^g, Aristidis Tsatsakis^{b,*}

Example: Caecal and blood multiomics reveals metabolic biomarkers in rats following subchronic exposure to a pesticide mixture typically found in EU foodstuff at their permitted acceptable daily intake

6/ Human biomonitoring of exposures to pesticides

- Since the ability of chemicals to cause complex diseases in human populations is not fully predictable with the current battery of regulatory toxicity tests, health effects are often detected in epidemiological studies several decades after the products are released on the market.
- The impregnation by most pollutants, and their effects at environmental levels, remains uncharacterised
- In the US (<https://www.cdc.gov/exposurereport/>): 17 sulfonylureas, atrazine, 2,4-dichlorophenoxyacetic acid, as well as pyrethroid, organophosphorus insecticide, and carbamate metabolites.
- In Europe (project HBM4EU): pyrethroids, chlorpyrifos, dimethoate, glyphosate and fipronil considered as priorities for future biomonitoring



KEY RESEARCH QUESTIONS

- How have prenatal herbicide exposure levels changed over time?
- Are herbicides contributing to heritable, epigenetic changes in newborns across the Midwest?
- How can we determine which herbicides pose the greatest risks, and which are low-risk?



<https://twinsuk.ac.uk>



Evaluating the effects of pesticide exposure through analysis of the gut microbiome in twins discordant for organic food consumption.

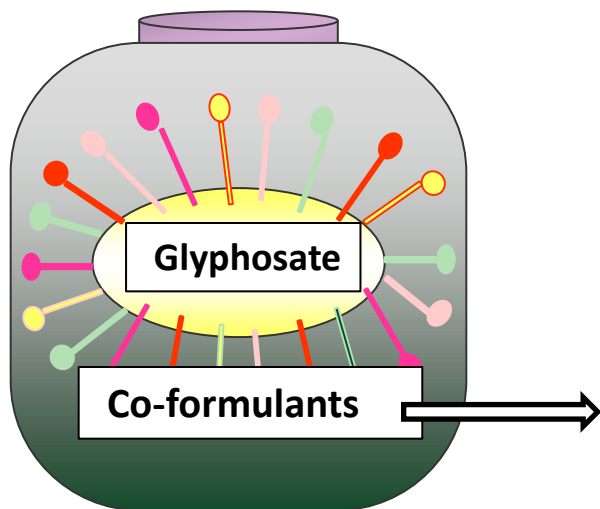
Exposure to 571 pesticides in 65 twin pairs that are discordant for an organic diet.

Gut microbiome of these twin pairs will be studied by shotgun metagenomics to allow correlations to be made between an organic diet, pesticide body burden, gut microbiome status, and health/disease indicators.

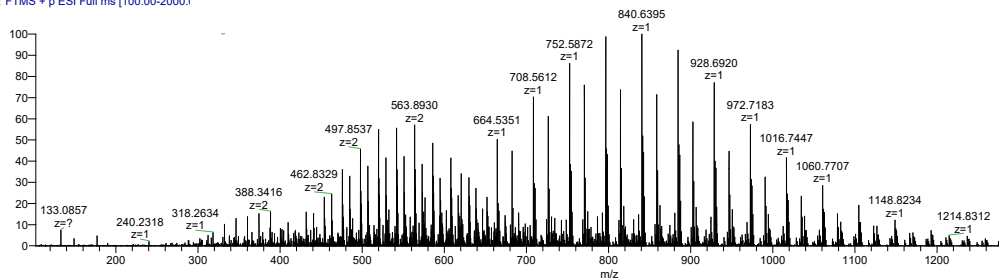
Chemicals used as co-formulants can be among the most toxic pollutants in the environment

Can surfactants be found in human foodstuffs? In human urine?

COMMERCIAL FORMULATION



129350 #20-35 RT: 0.23-0.34 AV: 16 NL: 3.24E6
T: FTMS + p ESI Full ms [100.00-2000.]



Taking into account toxic effects of glyphosate

Is there data showing health risks for human populations at environmental levels? In agricultural workers?

What are uncertainties?

Risk management: Should we ban glyphosate? what about substitutions?



Thank you for your attention!

Questions?

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