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## **Mycotoxins, a part of the dietary exposome: a challenge for toxicologists**

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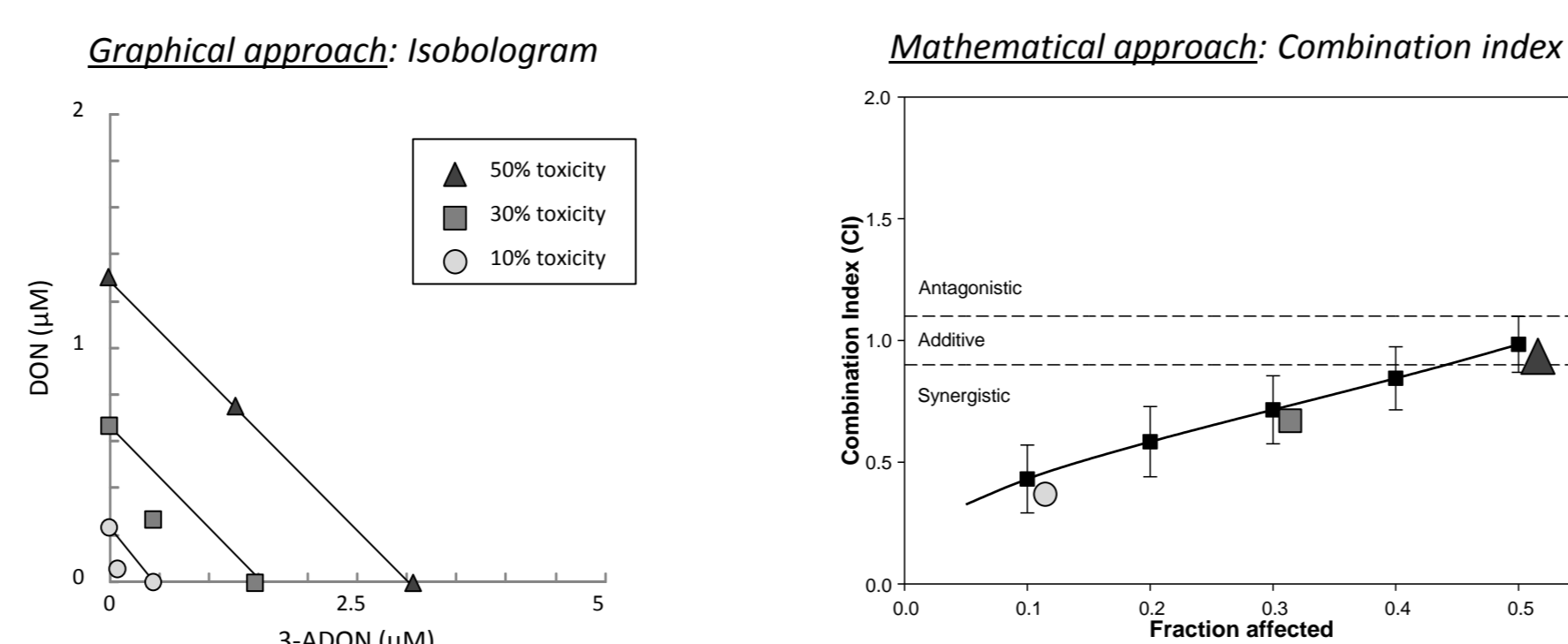
## STATE OF THE ART

- Humans are exposed throughout their lives to a wide range of food contaminants, bacterial toxins or neoformed products.
- Mycotoxins are the most frequently natural food contaminants.
- Co-contamination of mycotoxins in food is confirmed by their co-occurrence in food and co-exposure monitoring surveys.
- Few data exist on the combined toxic effects of mycotoxins or with other food compounds, and so the risk assessment of the exposure to a combination of food contaminants is incomplete.

## INTERACTIONS BETWEEN MYCOTOXINS

### Combined effects on cytotoxicity by Trichothecenes mycotoxins

The type of interaction depends on the dose.



The type of interaction is similar in different cell lines,

Mycotoxin association	Type of interaction at low doses	
	Human Caco-2 cells Alassane-Kpembé et al., Toxicol. Appl. Pharmacol. 2013	Porcine IPEC-1 cells Alassane-Kpembé et al., Arch. Toxicol. 2015
DON & 3-ADON	Synergy	Antagonism
DON & 15-ADON	Synergy	Synergy
15-ADON & 3-ADON	Synergy	Synergy
DON & NIV	Synergy	Synergy
DON & FX	Synergy	Antagonism
NIV & FX	Additivity	Additivity

→ At low concentrations, synergy is the main type of interaction.

Alassane-Kpembé et al., Toxicol. Appl. Pharmacol. 2013 ; Alassane-Kpembé et al., Arch. Toxicol. 2015

## INTERACTIONS BETWEEN MYCOTOXINS & HEAVY METALS

### Interaction between deoxynivalenol and cadmium

- Deoxynivalenol (DON) is a frequent food contaminant of cereals
- Cadmium (Cd) is a common and widespread toxic heavy metal, contaminating food, water and air.

**Objective: Evaluate the interactions DON/Cd in different organs, using cell lines *in vitro*.**

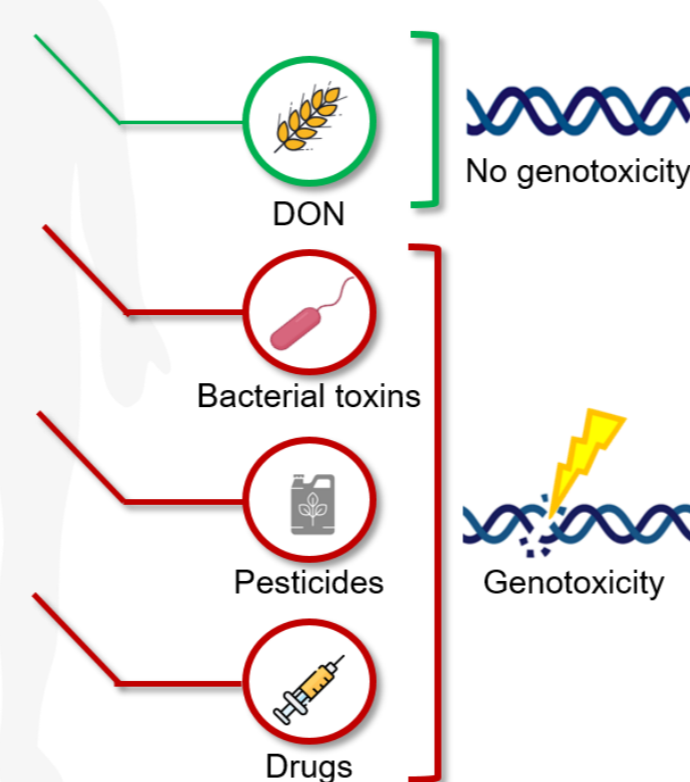
Fa	Cell type				Interaction
	Kidney HEK-293T	Intestine Caco-2	Blood HL-60	Liver HepG2	
0.2	1.51 ± 0.04	0.98 ± 0.28	0.43 ± 0.04	3.80 ± 1.07	Strong antagonism
0.3	1.27 ± 0.11	1.13 ± 0.22	0.65 ± 0.04	1.73 ± 0.02	Antagonism
0.4	1.18 ± 0.08	1.28 ± 0.18	0.94 ± 0.03	1.17 ± 0.06	Moderate antagonism
0.5	1.12 ± 0.07	1.45 ± 0.15	1.33 ± 0.04	0.95 ± 0.04	Slight antagonism
0.6	1.07 ± 0.06	1.64 ± 0.19	1.87 ± 0.08	0.82 ± 0.05	Nearly additive
0.7	1.02 ± 0.06	1.90 ± 0.33	2.73 ± 0.17	0.72 ± 0.05	Moderate synergism
0.8	0.98 ± 0.04	2.30 ± 0.61	4.32 ± 0.39	0.64 ± 0.05	Synergism

→ The interaction between DON and Cd is organ specific.

Le et al., Sci. Total. Env. 2018

## INTERACTIONS BETWEEN MYCOTOXINS & GENOTOXINS

### Exacerbation of genotoxicity by deoxynivalenol

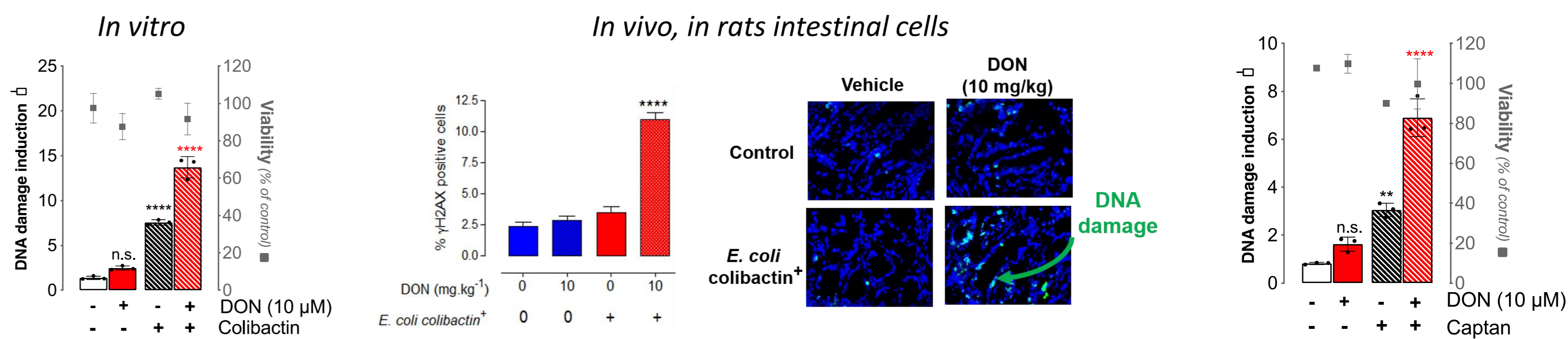


- Humans are exposed to a wide range of toxins and compounds from our microbiota, diet, ...
- Among them, numerous genotoxic compounds from bacteria, pesticides or drugs induce DNA damages in eucaryotic cells.
- However, DON is a non carcinogenic and genotoxic compound.

**Objective: Evaluate if the mycotoxin deoxynivalenol can influence the effects of diverse genotoxic compounds *in vitro* and *in vivo*.**

DON and genotoxic bacterial toxins

DON and genotoxic pesticide



→ DON and other trichothecens exacerbate DNA damages induced by multiple genotoxins such as drugs, pesticides or bacterial toxins.

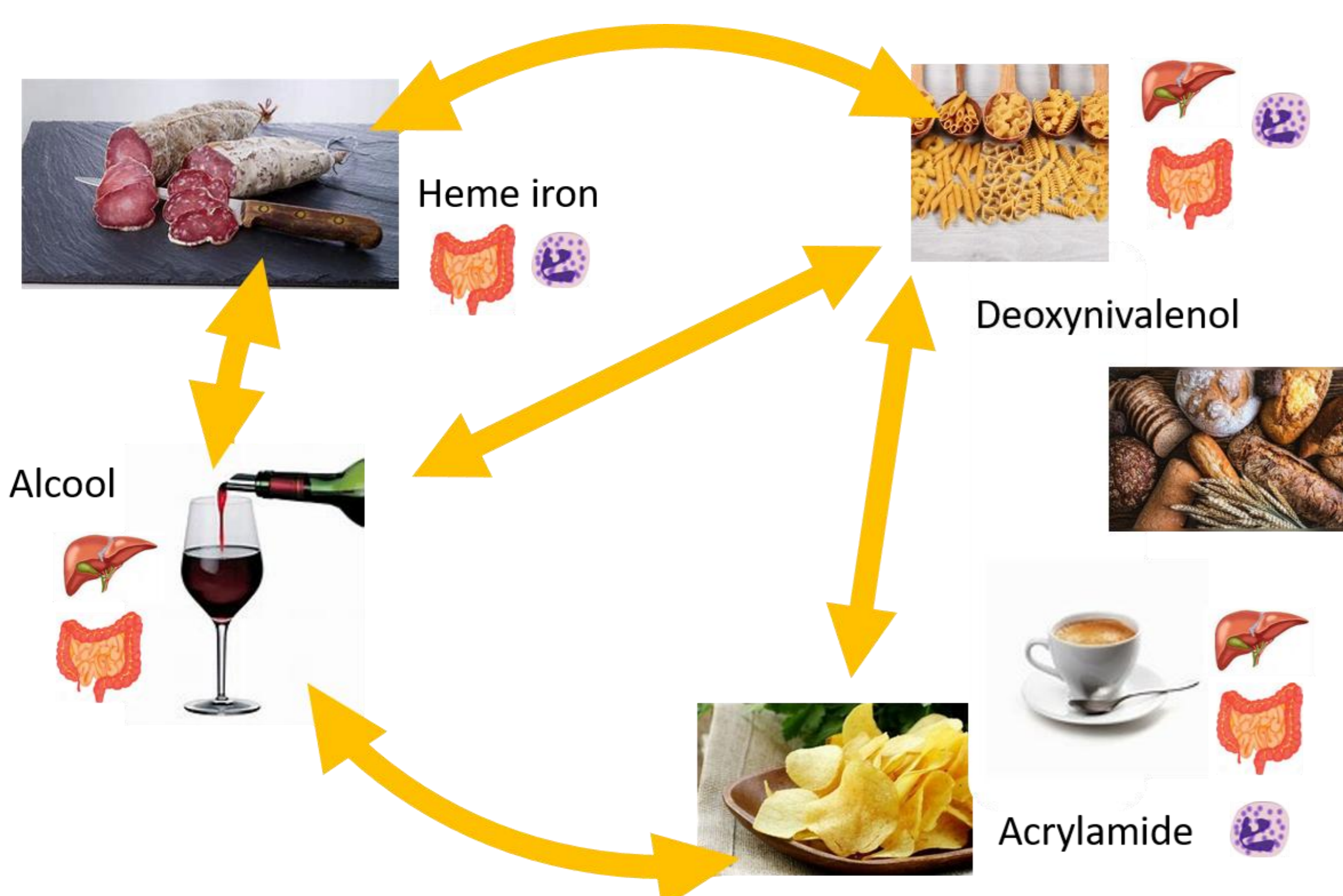
Payros et al., mBIO, 2017 ; Garofalo et al., Environ. Pollution., 2023 ; Garofalo et al., Sci. Total. Env. 2022

## ACTUAL PROJECT : DOES DON EXACERBATE THE GENOTOXICITY OF GENOTOXIC PRODUCTS PRESENT IN OUR FOOD ?

## CONCLUSIONS

### The Aperomix project

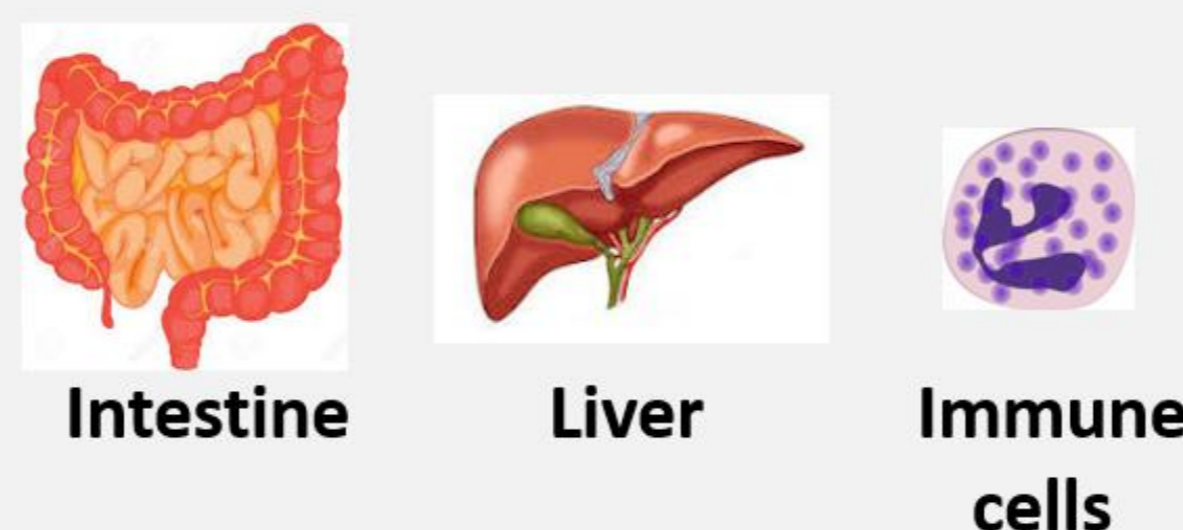
**Objective: Identify contaminants or neoformed products from food for which the health risk would be aggravated by DON**



**In vitro models**  
« Cocktails effect » « Doses effect »  
**Ex vivo models**  
**INCREASED COMPLEXITY OF MIXTURES**

**In vivo models**  
« chronic exposure » → role on cancer

**VARIOUS TARGET ORGANS**



- Mycotoxins cocktails can lead to synergistic interactions.
- Mycotoxins interact with other food contaminants such as heavy metal, pesticides, genotoxins, ...
- Co-contamination by several mycotoxins and food compounds is the RULE, not the exception and NEEDS more investigation.
- Regulation should evolve and take into account the co-contamination.