Mycotoxin risk and the role of intestinal immunity in animal performance

Maria Angeles Rodriguez, OLMIX Technical Manager - Spain

Health & Nutrition Poultry Seminar - *Dubai* **-** 19th January 2018

THE MYCOTOXIN CHALLENGE

- Mycotoxins are 'fungal metabolites which when ingested, inhaled, or absorbed through the skin cause **decreased performance, sickness or death in man or animals, including birds'** (Pitt, 1996)

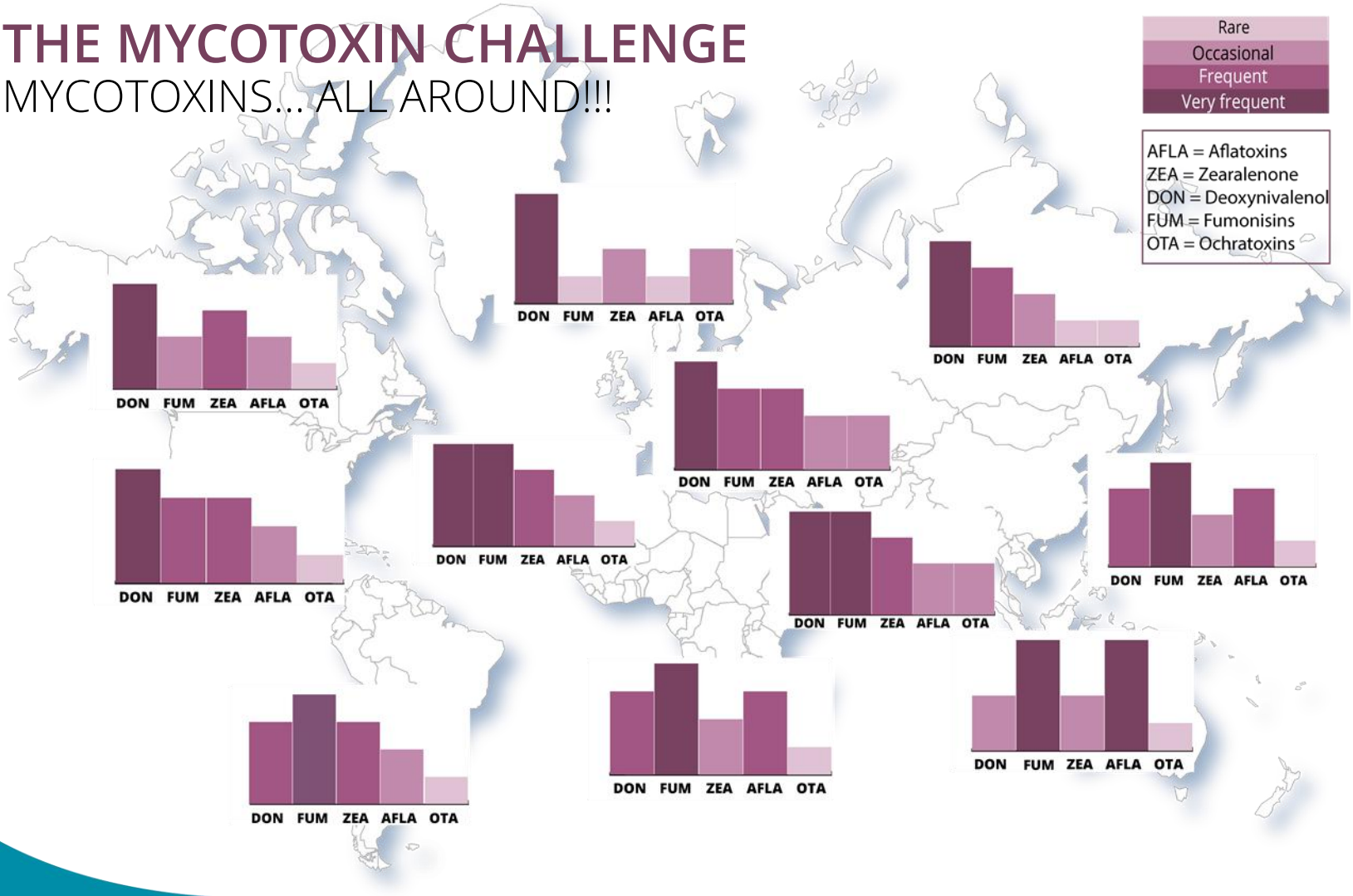
- Mycotoxin:
  - Greek word for fungus: « **Mykes** »
  - Latin word for poison: « **Toxicum** »

- Any potential toxic substance produced by **molds secondary metabolism**

Mycotoxins are a high potential threat to human and animal health through the ingestion of food or feed prepared from infected commodities.

THE MYCOTOXIN CHALLENGE

MYCOTOXINS… ALL AROUND!!!



THE MYCOTOXIN CHALLENGE

EFFECT OF MYCOTOXINS ON RUMINANTS

FIELD MYCOTOXINS

Fumonisins
Immune depression, gastrointestinal disturbances, lower productivity, pulmonary edema, liver toxicity

Trichothecenes (DON, T2-HT2)
Immune depression (SCC, mastitis), gastrointestinal disturbances, liquid or non digested feces, lower productivity

Zearalenone
Hyperestrogenism, poor fertility, abortions/ returns, cysts development

STORAGE MYCOTOXINS

Aflatoxins
Immune depression, lower productivity, transfer of Aflatoxin M1 to milk (carcinogenic for humans)

Ochratoxins
Immune depression, weakened kidneys and liver, dehydration/high water consumption, lower productivity

THE MYCOTOXIN CHALLENGE
EFFECT OF MYCOTOXINS IN POULTRY

FIELD MYCOTOXINS

Fumonisins
Immune depression, gastrointestinal disturbances, high feed conversion ratio, pulmonary edema, liver toxicity

Trichothecenes (DON, T2-HT2)
Immune depression, gastrointestinal disturbances, high feed conversion ratio, decreased feed consumption, dermal lesions, alteration of egg production and quality

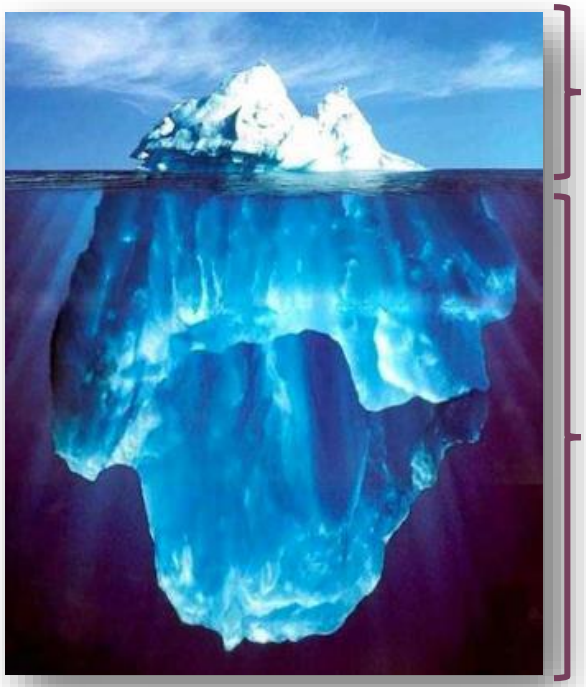
Zearalenones
Hyperestrogenism, poor fertility / lower hatchability

STORAGE MYCOTOXINS

Aflatoxins
Immune depression, limited productivity, leg problems, poor fertility / lower hatchability

Ochratoxins
Immune depression, renal lesions, liver troubles, higher feed conversion ratio, low productivity

THE MYCOTOXIN CHALLENGE
ACUTE AND SUBACUTE MYCOTOXICOSIS



Visible part: acute mycotoxicosis

- high contamination
- clinical symptoms

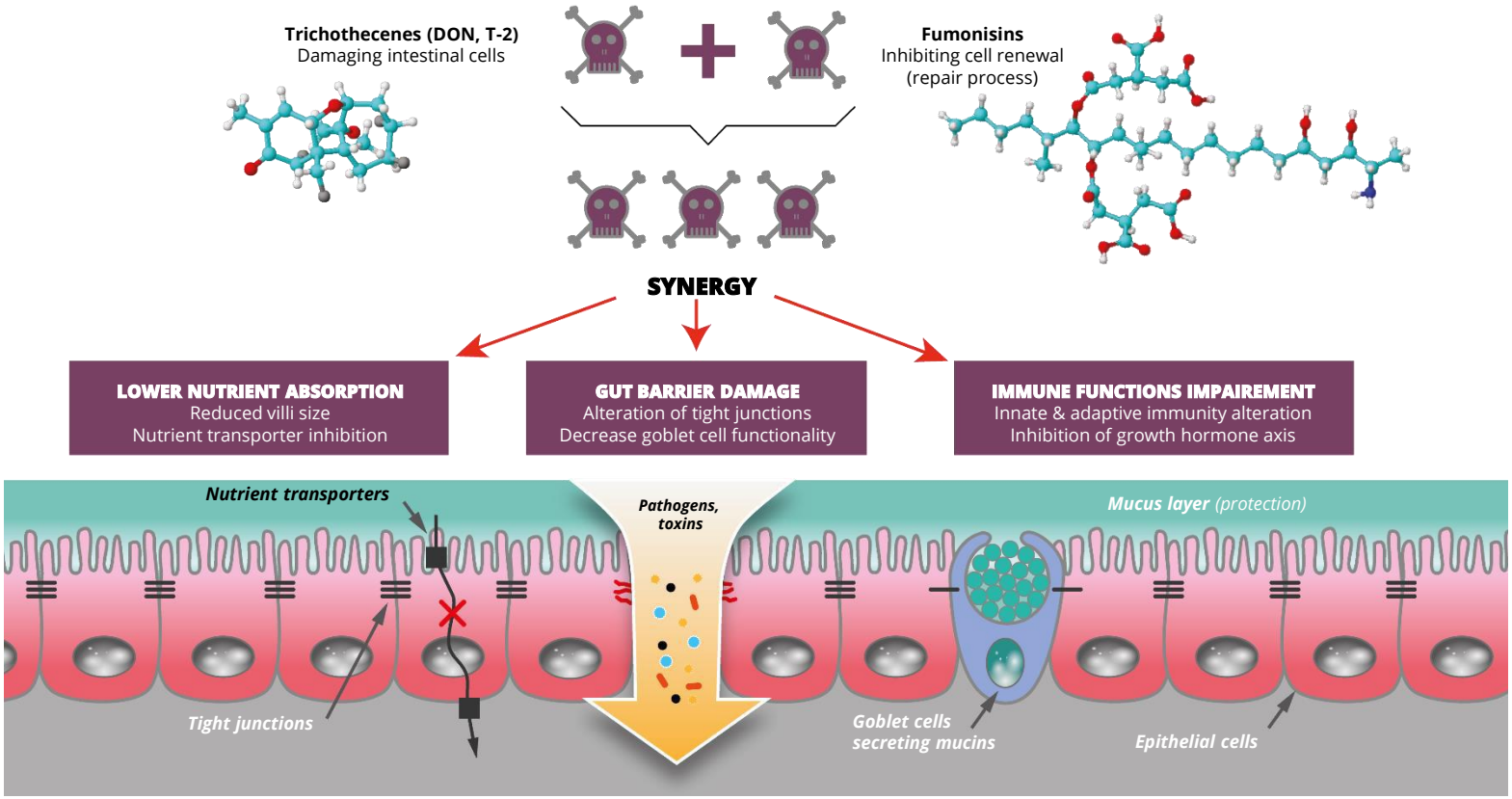
Hidden part: subacute mycotoxicosis

- chronic exposure
- polycontamination
- poor performance

Subacute mycotoxicosis is now widely considered to be the most important impact of mycotoxins, particularly in developing countries. (FAO, 2001)

THE MYCOTOXIN CHALLENGE

EFFECT OF MYCOTOXINS ON THE GUT



THE MYCOTOXIN CHALLENGE
EFFECT OF MYCOTOXINS ON NUTRIENT ABSORPTION

Reduced villi size

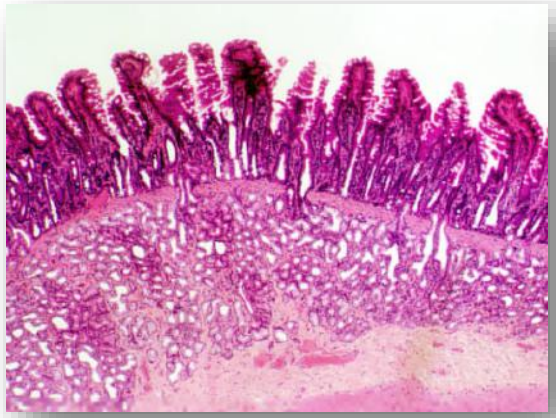
Deoxynivalenol (DON)

Inhibitor of protein synthesis

Decreases villus height

Lower absorptive surface area

Reduces nutrient absorption thus alters FCR



Adapted from Grenier and Applegate, 2013

THE MYCOTOXIN CHALLENGE
EFFECT OF MYCOTOXINS ON NUTRIENT ABSORPTION

Reduced villi size

Fumonisins (FUM)

Inhibitor of lipid synthesis

Decreases epithelial cells proliferation

Impair villus renewal

Reduces nutrient absorption thus alters FCR

Villus height *(µm)*	**CONTROL**	**FB1**
Proximal jejunum	300 ±16[a]	259 ±17[b]
Median jejunum	321 ±13[a]	259 ±21[b]
Distal jejunum	265 ±13[a]	182 ±13[b]

Adapted from Pinton *et al*, 2012

THE MYCOTOXIN CHALLENGE
EFFECT OF MYCOTOXINS ON NUTRIENT ABSORPTION

Reduced villi size

DON

Decreases villus height

FUM

Impair villus renewal

SYNERGISTIC EFFECT ON VILLI:
Less nutrient absorption surface

From Pinton *et al*, 2012 ; Grenier and Applegate, 2013

THE MYCOTOXIN CHALLENGE
EFFECT OF MYCOTOXINS ON NUTRIENT ABSORPTION

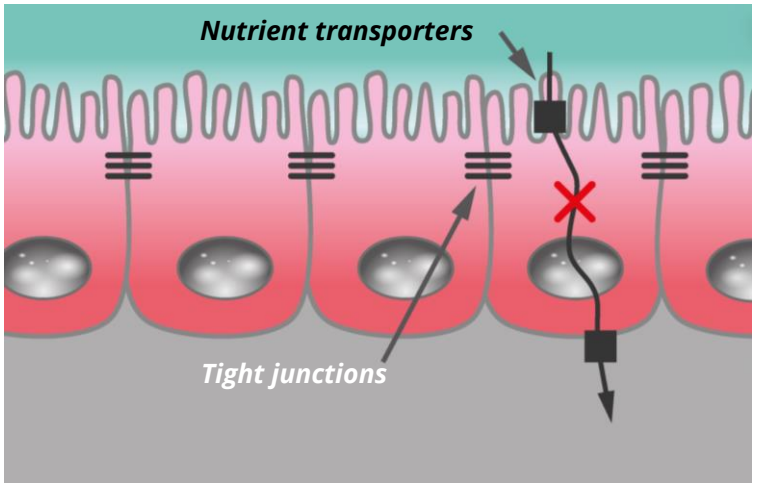
Nutrient transporter inhibition

Deoxynivalenol (DON)

inhibits SGLT1*
(glucose co-transporter)

Decreases glucose absorption and water reabsorption

↗ FCR



** Sodium-Glucose Linked Transporter 1*

Grenier and Applegate, 2013; and Awad *et al.*, 2011

THE MYCOTOXIN CHALLENGE
EFFECT OF MYCOTOXINS ON NUTRIENT ABSORPTION

Impact on digestive health

Deoxynivalenol (DON)
inhibits SGLT1*
(glucose co-transporter)

Decrease of
water reabsorption

Mycotoxins (DON, T-2, FUM)
Reduce nutrient
absorption

Change in microbial
community

↗ risk of diarrhea

* *Sodium-Glucose Linked Transporter 1*

Tenk *et al*, 1982 ; Wache *et al*;, 2009

THE MYCOTOXIN CHALLENGE

EFFECT OF MYCOTOXINS ON GUT BARRIER

Alteration of tight junctions

Mycotoxins, especially DON have the ability to increase intestinal permeability.

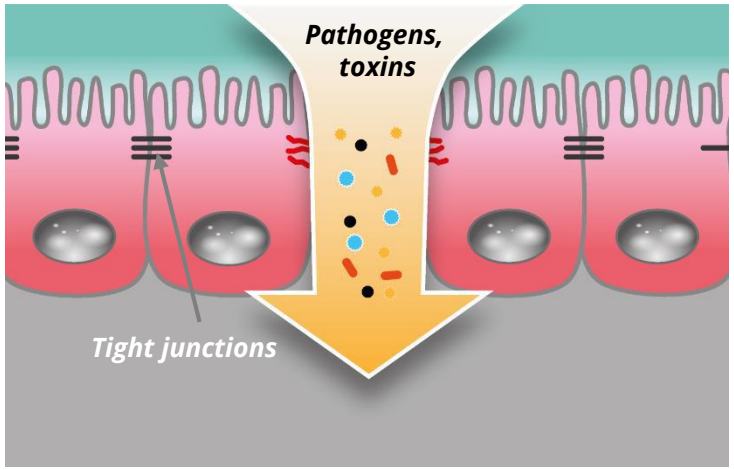
DON and FUM

Activation of MAPK*

↘ claudin expression

Open tight junction proteins

↘ Intestinal barrier function



** Mitogen activated protein kinases*

Extracted from Grenier and Applegate, 2013

THE MYCOTOXIN CHALLENGE
EFFECT OF MYCOTOXINS ON GUT BARRIER

Decrease of goblet cell functionality

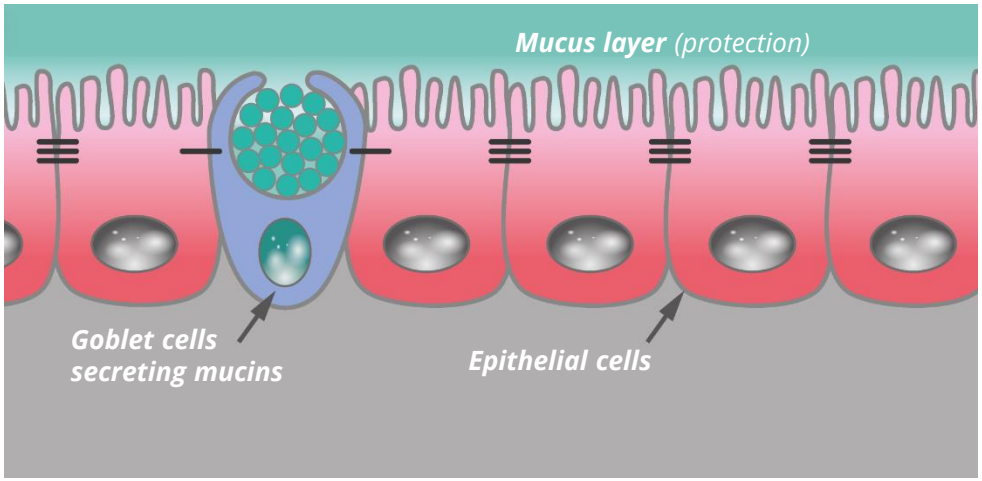
DON + T-2

Reduction in the number of goblet cells

↘ Mucus production

↘ TEER*

↗ risk of diarrhea



* *Transepithelial electric resistance*

Maresca *et al.*, 2013

THE MYCOTOXIN CHALLENGE
EFFECT OF MYCOTOXINS ON IMMUNE FUNCTIONS

Innate & adaptive immunity alteration

- Mycotoxins are one of the most immunosuppressive factors coming from feed (Surai and Dvorska, 2005)
- **Mycotoxins leading to immune depression** (in descending order): (Devegowda and Murphy, 2005)

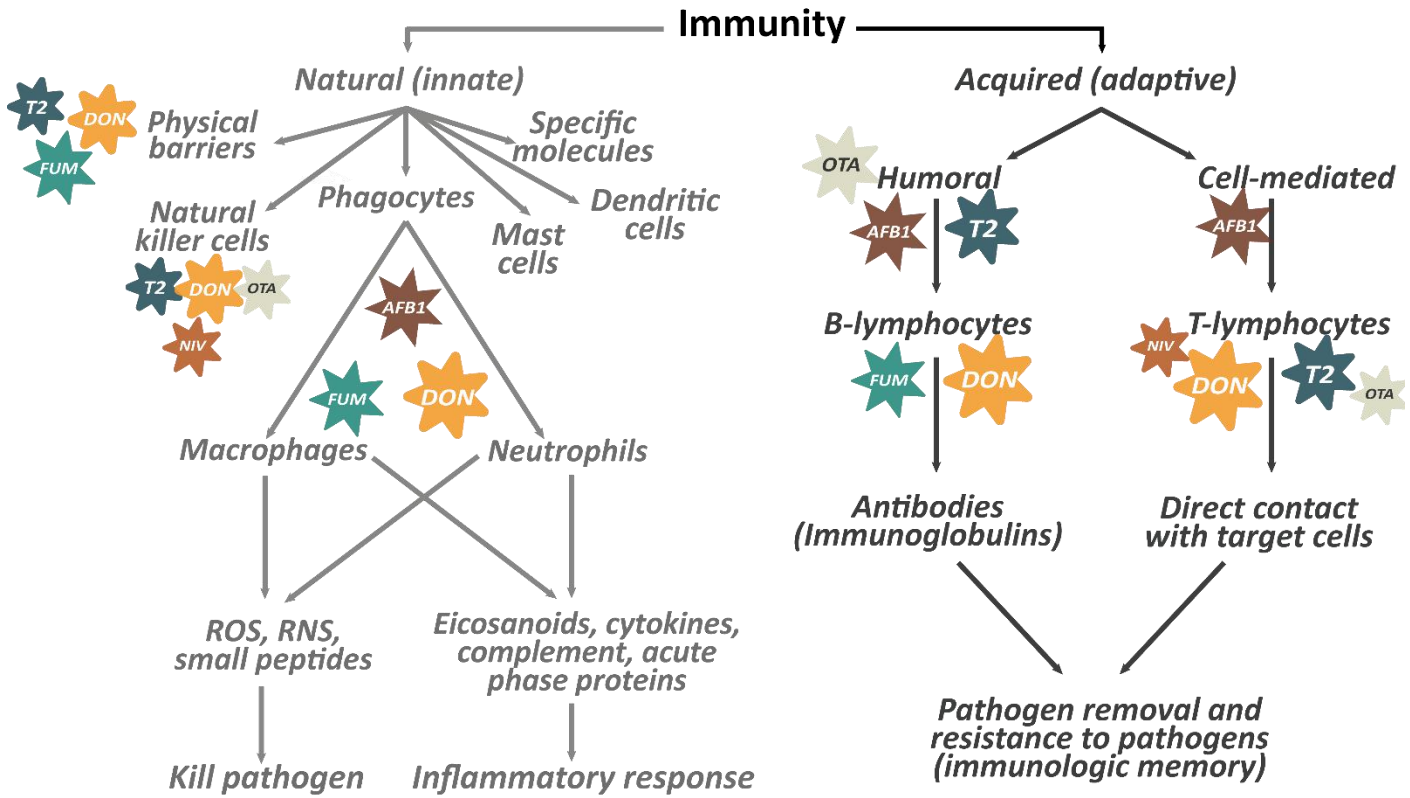
Aflatoxins
Trichothecenes (T-2/HT-2, DON)
Ochratoxins
Fumonisins

- It is estimated that **up to 70% of the immune defenses of the organism are located in the intestine**.

THE MYCOTOXIN CHALLENGE

EFFECT OF MYCOTOXINS ON IMMUNE FUNCTIONS

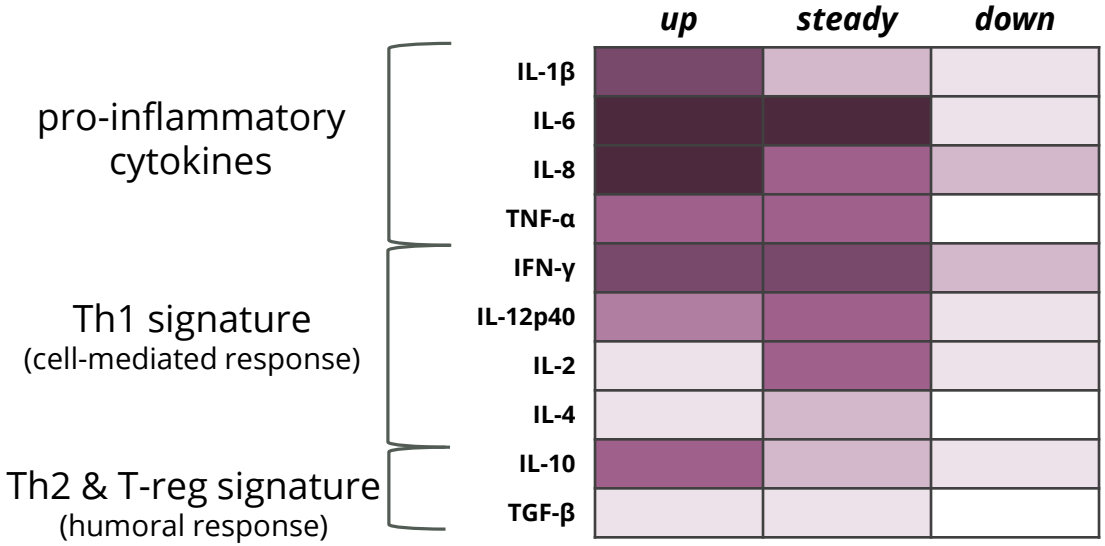
Innate & adaptive immunity alteration



Adapted from Surai et Dvorska, 2005

THE MYCOTOXIN CHALLENGE
EFFECT OF MYCOTOXINS ON IMMUNE FUNCTIONS

Innate & adaptive immunity alteration



Heat map of mycotoxins interaction with gut epithelium (Grenier and Applegate, 2013)

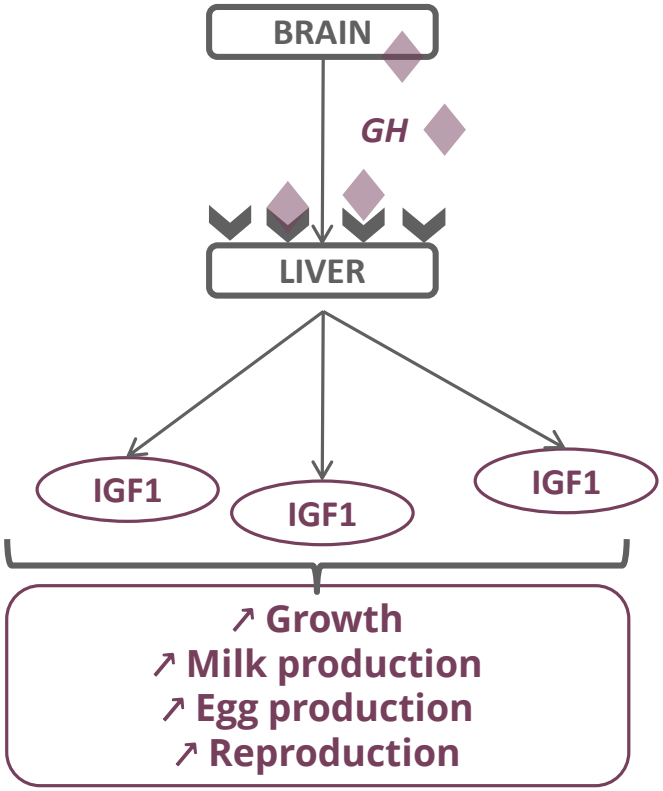
Effect of mycotoxins on pro-inflammatory cytokines is the most important one

THE MYCOTOXIN CHALLENGE

EFFECT OF MYCOTOXINS ON GROWTH HORMONE AXIS

What is IGF1?

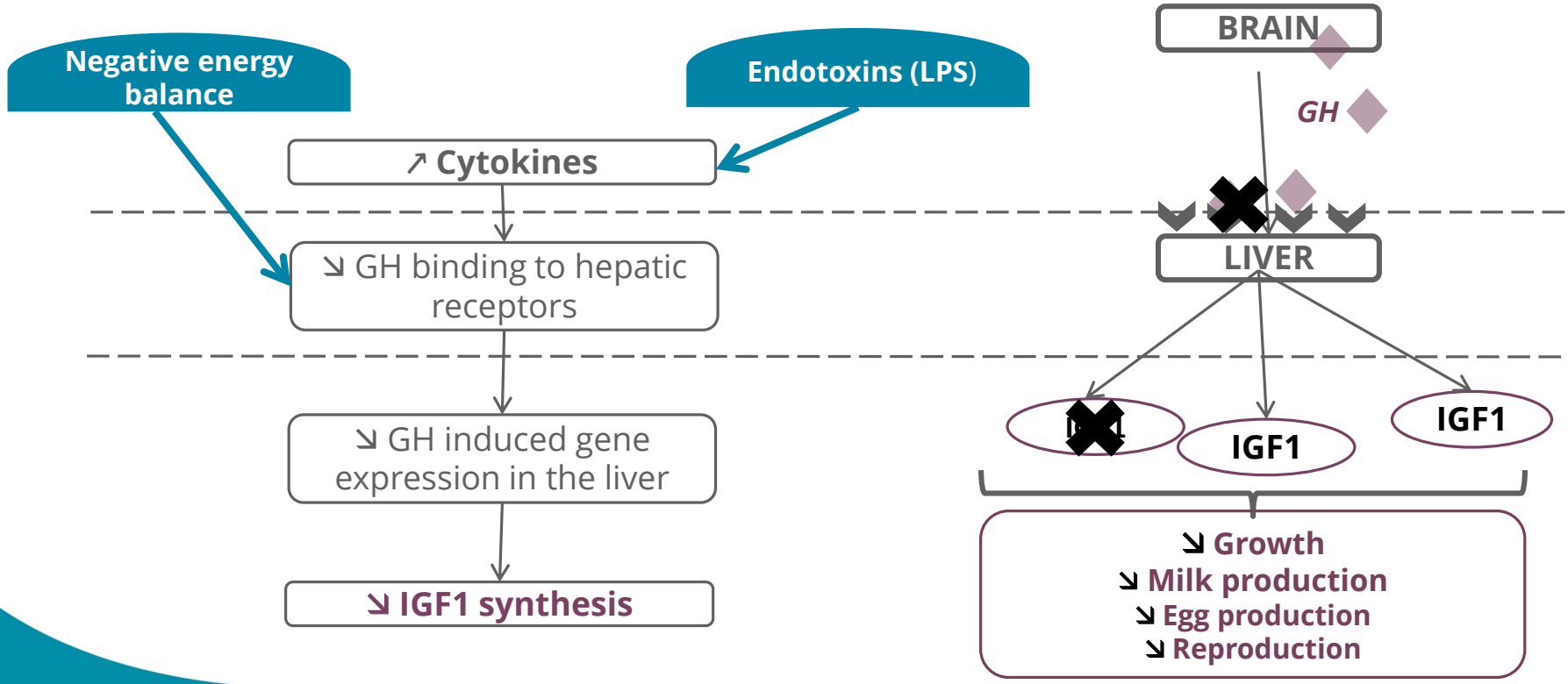
- Insulin-like Growth Factor 1
- IGF1 mediates many actions of growth hormone (GH) and stimulates cell replication, cell differentiation and the synthesis of cellular products.
- IGF1 modulates FSH and LH sensitivity, influencing follicle development and ovulation cycles.
- As for their biological effects, in general, IGF1 is mainly responsible for cell multiplication.



THE MYCOTOXIN CHALLENGE

EFFECT OF MYCOTOXINS ON GROWTH HORMONE AXIS

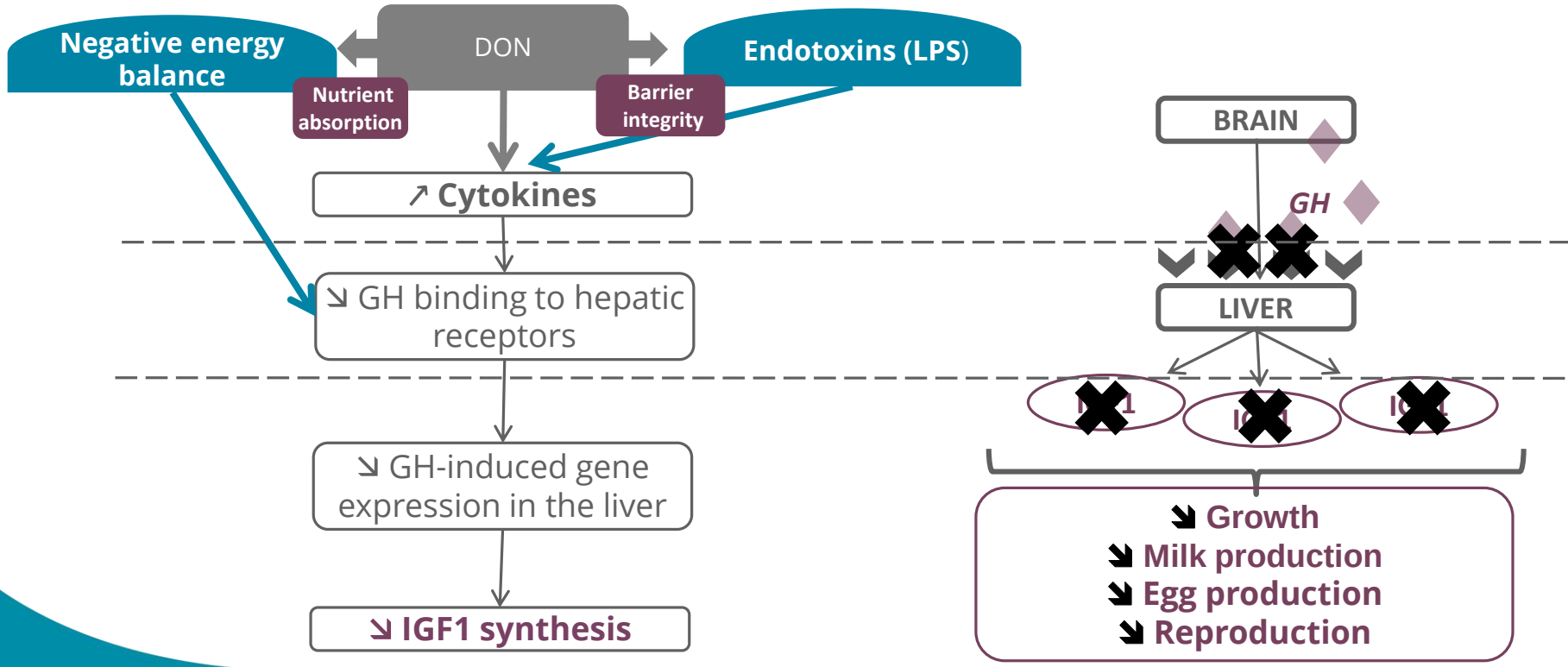
Synergistic effects



THE MYCOTOXIN CHALLENGE

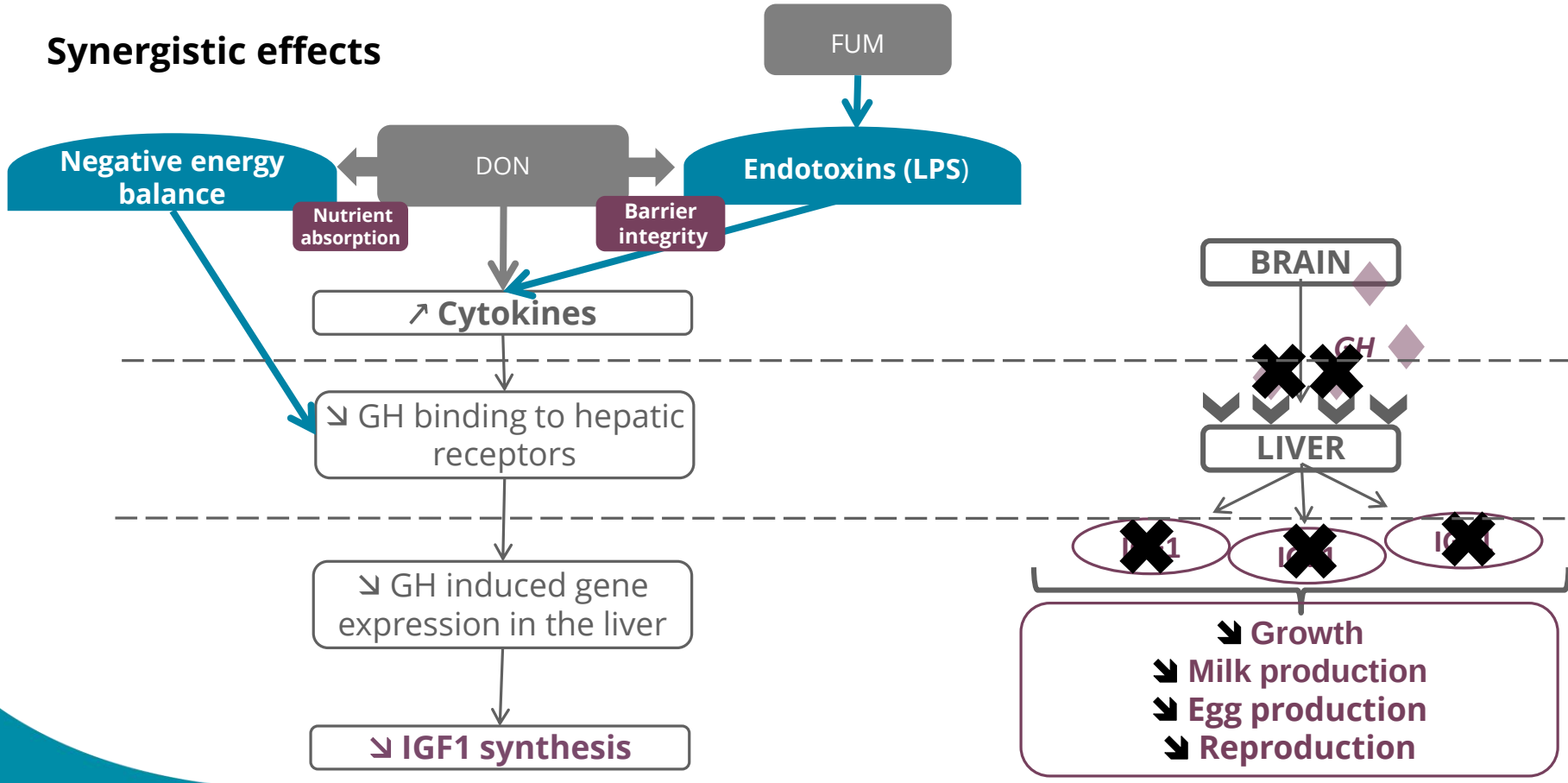
EFFECT OF MYCOTOXINS ON GROWTH HORMONE AXIS

Synergistic effects



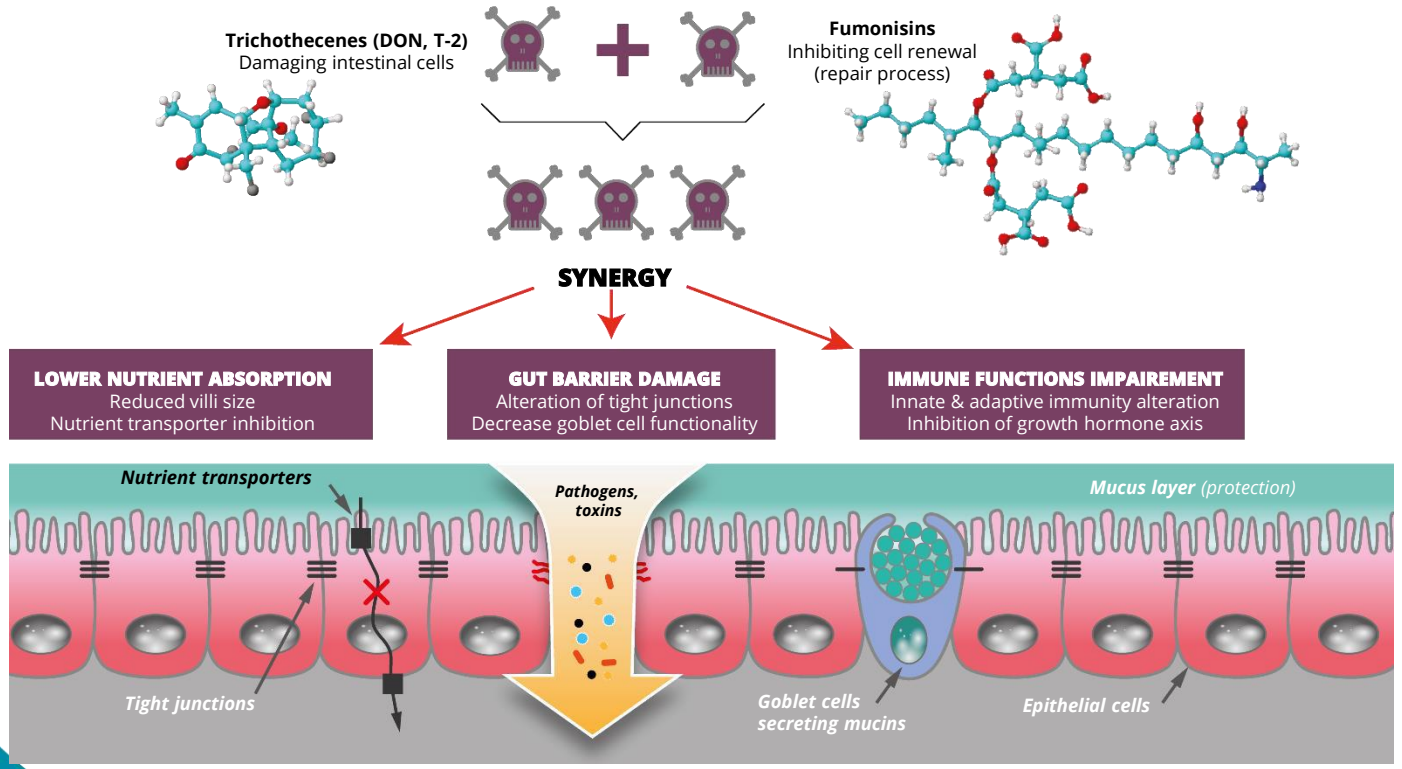
THE MYCOTOXIN CHALLENGE

EFFECT OF MYCOTOXINS ON GROWTH HORMONE AXIS



THE MYCOTOXIN CHALLENGE

EFFECT OF SUBACUTE MYCOTOXICOSIS ON PERFORMANCE

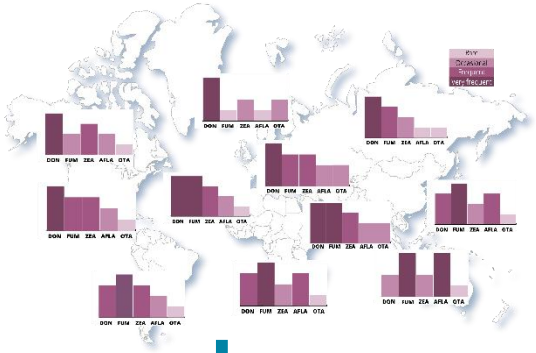


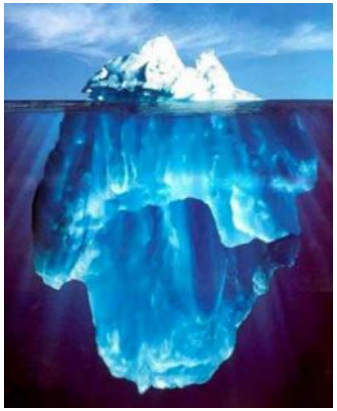
POOR PERFORMANCE

- ↘ Meat
- ↘ Milk
- ↘ Reproduction

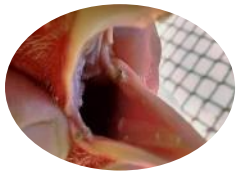
THE MYCOTOXIN CHALLENGE
SUMMARY

Mycotoxins are everywhere

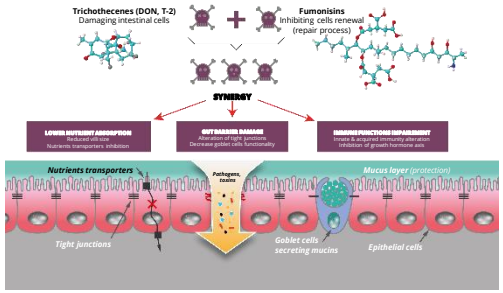




Acute mycotoxicosis



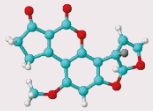
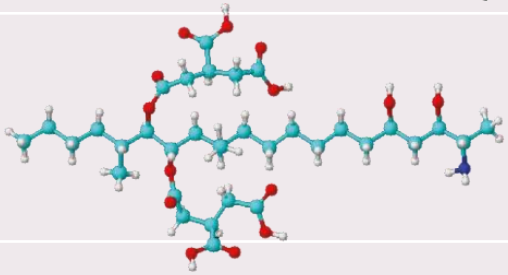
Subacute mycotoxicosis



How to protect the animals?

TOXIN BINDERS EFFICACY

MYCOTOXIN VARIABILITY

	**Aflatoxins** - Planar molecules, rigid - Medium polarity	Easily adsorbed by aluminosilicates (clays), especially the Montmorillonite type.
	**Zearalenone and ochratoxins** - Larger molecules and very flexible - Medium polarity	Not adsorbed by unmodified clays. Adsorbed by specific polysaccharides.
	**Fumonisins** - Much larger molecules, very flexible - More polar	Due to their size and structural configuration, they are the most difficult mycotoxins to adsorb.
	**Trichothecenes** - Larger volume, globular shape, epoxy ring = **VERY rigid** - Medium polarity	

Toxin binders must have the capacity to bind mycotoxins with different properties

MT.X+: THE OLMIX SOLUTION

A SINGULAR COMBINATION OF NATURAL ADSORBENTS

- Interspaced Montmorillonite

- Micronized Montmorillonite

- Diatomaceous earth

- Yeast cell walls

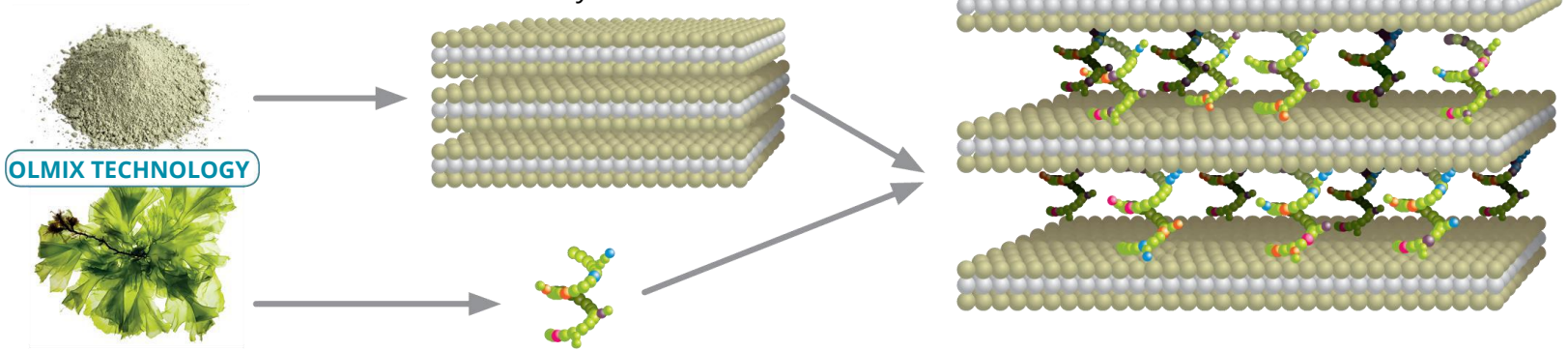
- Seaweed extracts (Marine Polysaccharides)

MT.X+: THE OLMIX SOLUTION

INTERSPACED MONTMORILLONITE TECHNOLOGY

Selected Montmorillonite

Micronized Montmorillonite with layered structure



Selected algae
Ulva sp

Algae extracts (Structuring polysaccharides)

Interspaced Montmorillonite

Interspacing Montmorillonite with algae extracts allows:

- Accessible adsorptive surface
- Available adsorption sites
- Types of adsorption sites
- Complexity of structure decreasing desorption

→ **Wide adsorption spectrum**

MT.X+: THE OLMIX SOLUTION

INTERSPACED MONTMORILLONITE TECHNOLOGY

Standard Montmorillonite

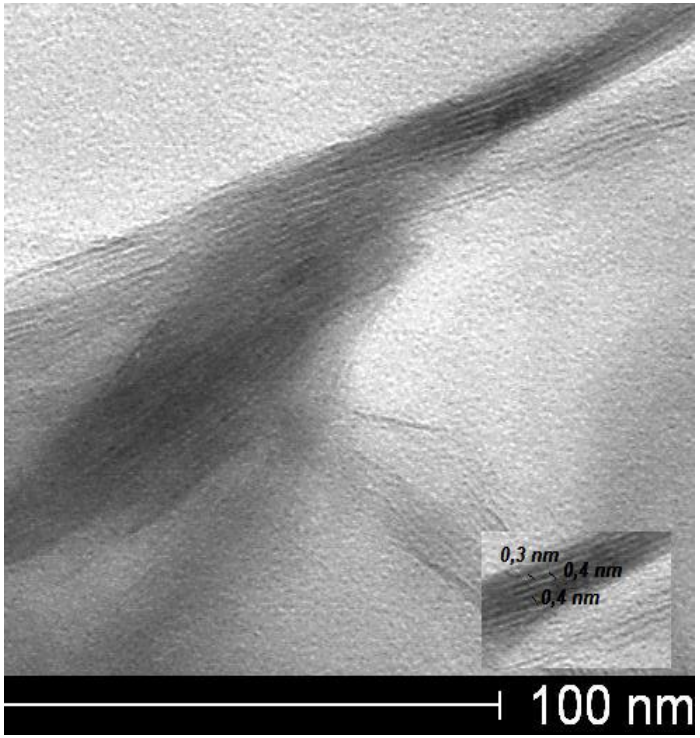


Figure 1: Standard MMT in TEM image

Interspaced Montmorillonite

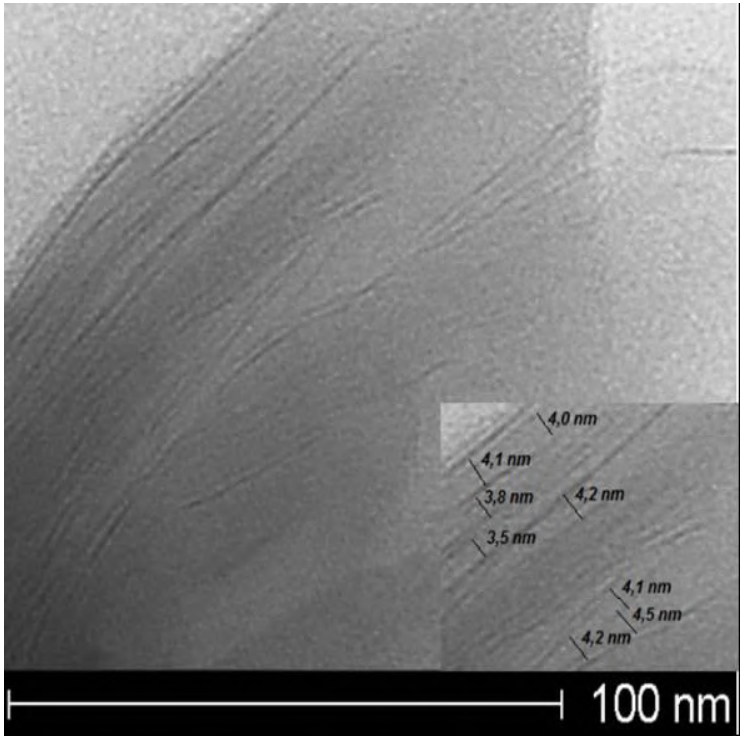


Figure 2: Interspaced MMT in TEM image

MT.X+: THE OLMIX SOLUTION

INTERSPACED MONTMORILLONITE IN DYNAMIC *IN VITRO* TEST

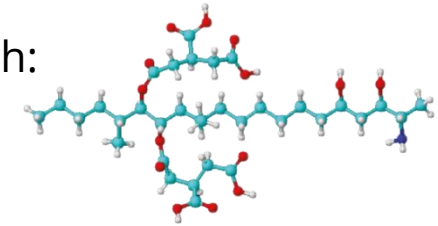
(*Demais and Havenaar, 2006)*

- Measurement of the availability for absorption (bioaccessibility) of mycotoxins in the jejunum by simulating gastrointestinal conditions of monogastrics in the TIM-1 system.

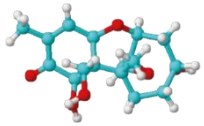
- Use of **complete feed** contaminated with both:
  - DON (1 ppm) and,
  - Fumonisin B1 (2 ppm).

- Level of interspaced MMT in feed: 0%; 0.01% and 0.1%.

FUM



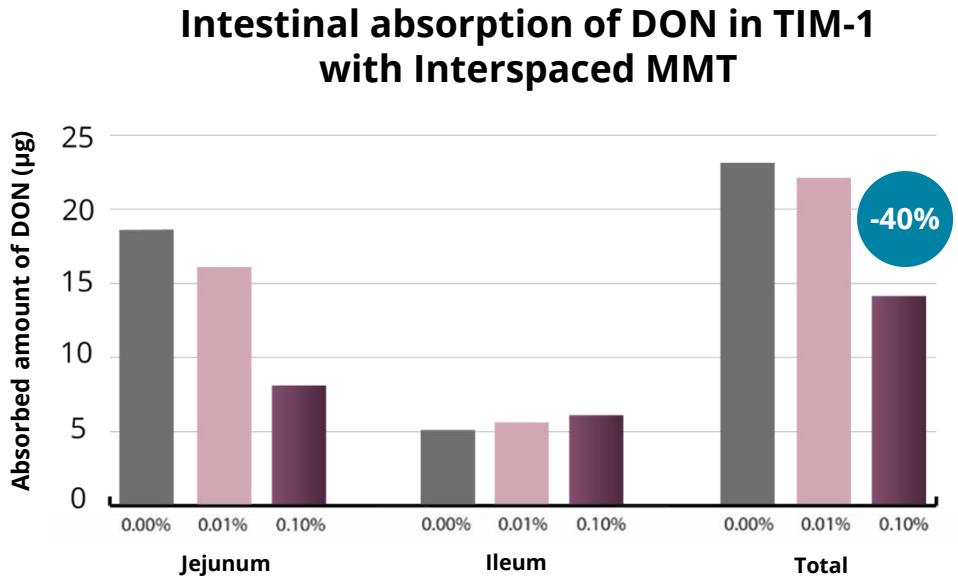
DON



MT.X+: THE OLMIX SOLUTION

INTERSPACED MONTMORILLONITE IN DYNAMIC *IN VITRO* TEST

(*Demais and Havenaar, 2006)*



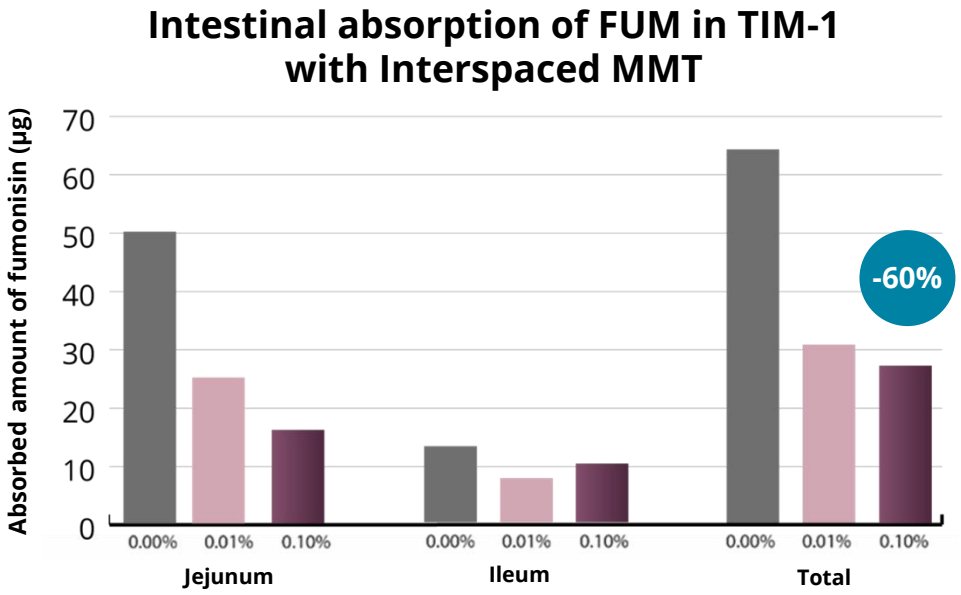
Remember! 2% of active carbon reduces the bioaccessibility of DON by 45% in TIM-1.
(Avantaggiato *et al*, 2004)

DON intestinal absorption was reduced by 40% with 0.1% interspaced montmorillonite.

MT.X+: THE OLMIX SOLUTION

INTERSPACED MONTMORILLONITE IN DYNAMIC *IN VITRO* TEST

(*Demais and Havenaar, 2006)*



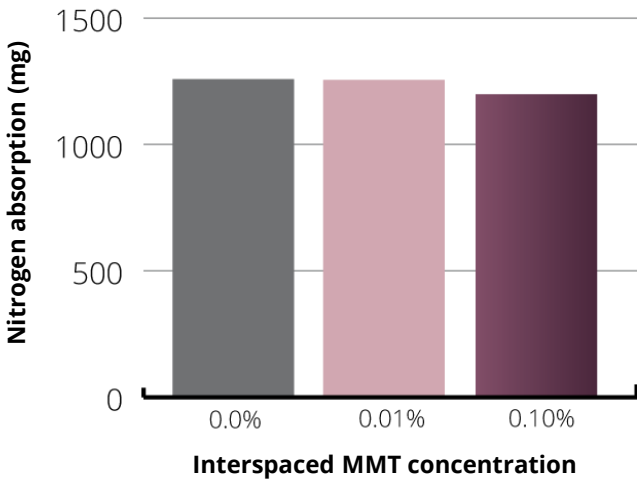
Fumonisin intestinal absorption was reduced by 50 to 60% with 0.01% and 0.1% interspaced montmorillonite.

MT.X+: THE OLMIX SOLUTION

INTERSPACED MONTMORILLONITE IN DYNAMIC *IN VITRO* TEST

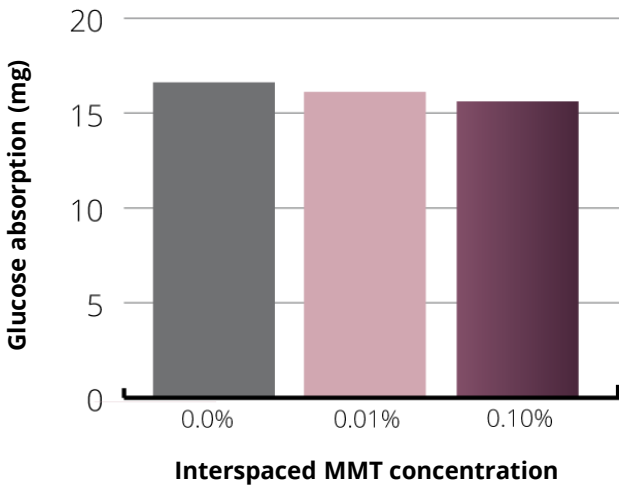
(*Demais and Havenaar, 2006)*

Effect of Interspaced MMT on PROTEIN intestinal absorption in TIM-1



Interspaced MMT did not change the intestinal absorption of nitrogen.

Effect of Interspaced MMT on CARBOHYDRATE intestinal absorption in TIM-1



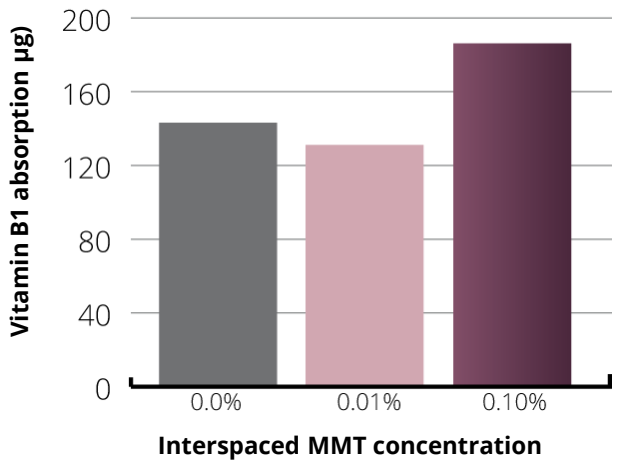
Interspaced MMT did not change the intestinal absorption of glucose.

MT.X+: THE OLMIX SOLUTION

INTERSPACED MONTMORILLONITE IN DYNAMIC *IN VITRO* TEST

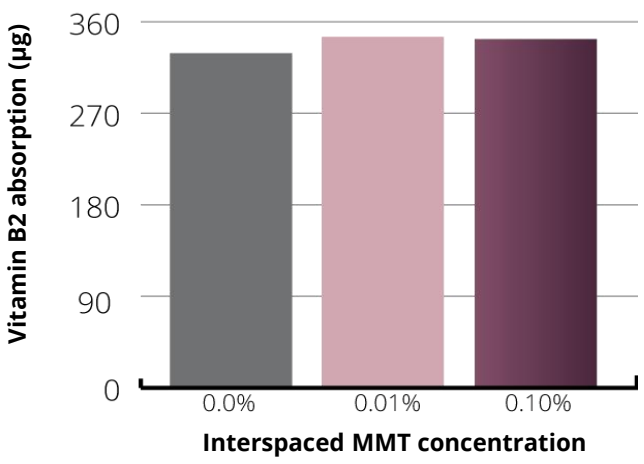
(*Demais and Havenaar, 2006)*

Effect of Interspaced MMT on VITAMIN B1 intestinal absorption in TIM-1



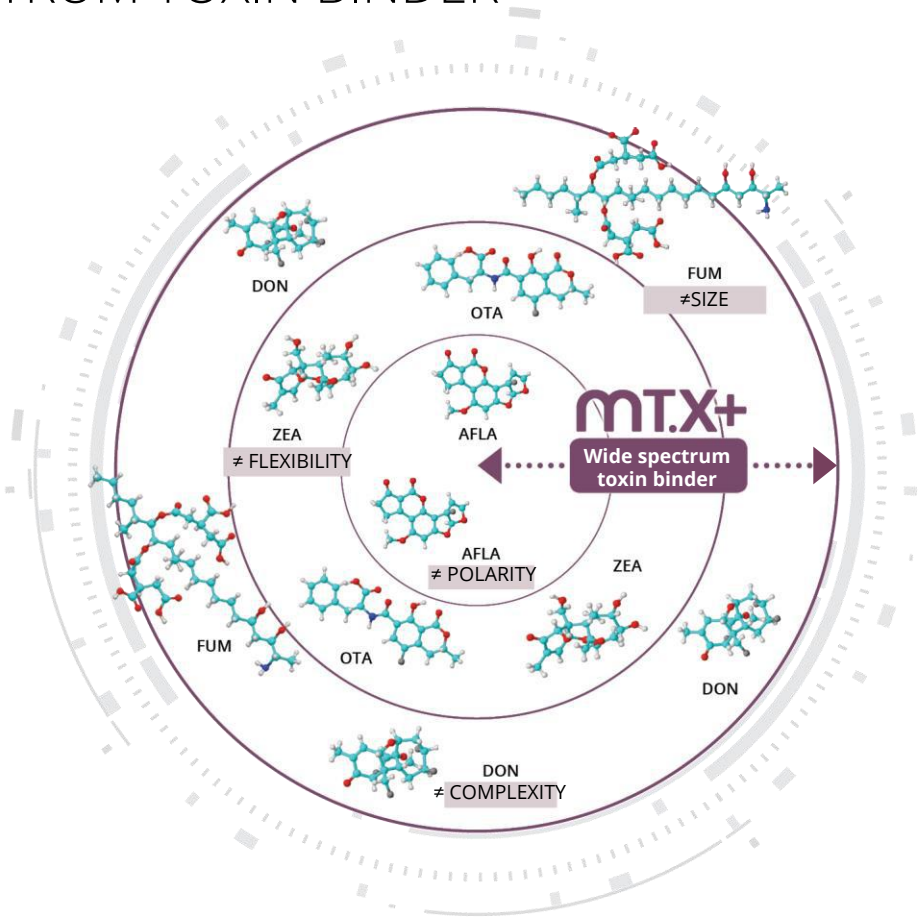
Interspaced MMT did not change the intestinal absorption of vitamin B1 at 0.01%.

Effect of Interspaced MMT on VITAMIN B2 intestinal absorption in TIM-1



Interspaced MMT did not change the intestinal absorption of vitamin B2.

MT.X+: THE OLMIX SOLUTION
WIDE SPECTRUM TOXIN BINDER



MT.X+: THE OLMIX SOLUTION
PRODUCT PRESENTATION

Fine powder MT.X+

Microgranular MMi.S

- No dust
- Easy to use

MMi.S is dedicated for a direct use on farm, for use in mash feeds in order to improve its homogenization in feed.

Same formula, same efficacy!

TOOLS - SERVICES

EXPERTISE TOOLS

Olmix
Myco'Evaluator

Interactive tool to evaluate the mycotoxin risk on the farm.
Calculate a percentage of risk to have a significant level of mycotoxins in the feed.

Olmix
Myco'Screen
expertise on Mycotoxin Analysis

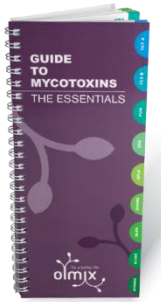
Olmix provides customized advices on mycotoxin analysis in order to better handle the risk in feed mills and farms.
An overview of over 40 mycotoxins and metabolites.
Olmix experts give you the keys to interpret the analysis and turn it into practical actions.

Olmix
Myco'Calculator
Optimizes toxin binder dosage

Depending on each situation, Olmix helps you to determine the most suitable dosage of MT.X+/MMi.S.

Olmix
Myco'Essentials
Olmix kwowledge

The Guide to Mycotoxins, The Essentials, helps you to better understand each mycotoxin specificity.



Olmix
Myco'News

(newsletter) provides you the latest scientific findings about mycotoxins.

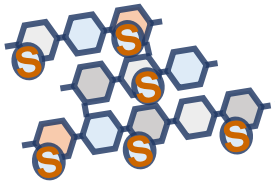
IF ANIMALS ARE ALREADY CONTAMINATED……

- COUNTERACTING MEASURES

MSP®MUCIN

MSP®MUCIN
MODE OF ACTION

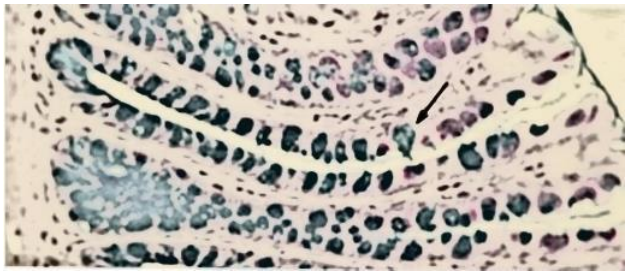
MSP®



Increased excretion of mucin

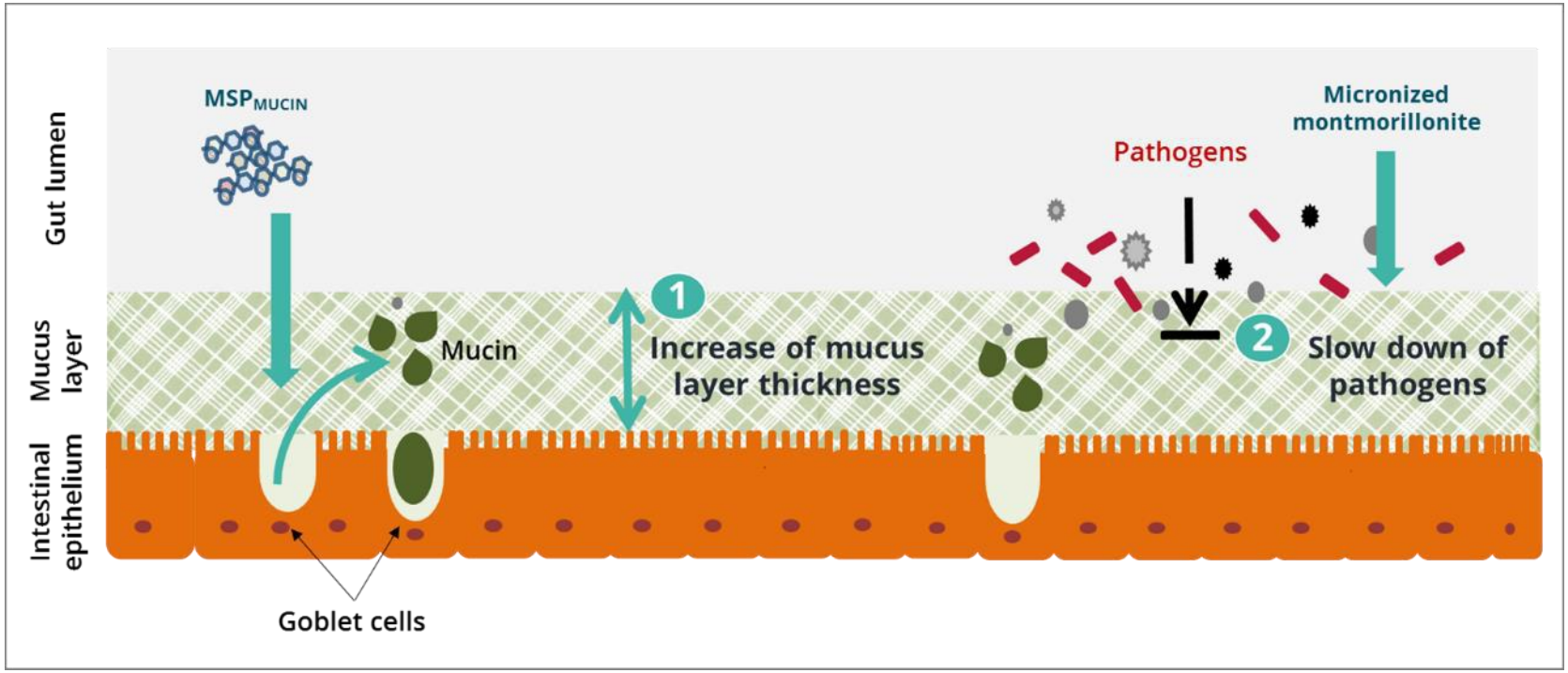
Increasing the thickness of the mucin macromolecular system covering the epithelial cells

Preservation of the intestinal wall integrity



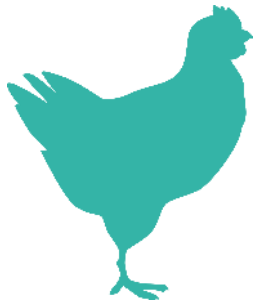
Intestinal mucosa
Barcelo et al., 2000

MSP®MUCIN
MODE OF ACTION

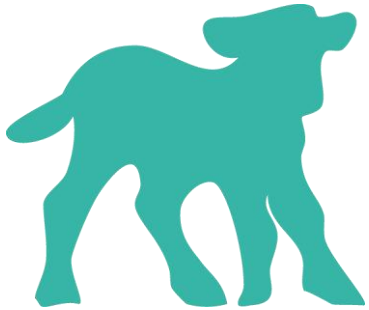


MSP®MUCIN
USE IN ANIMAL CARE RANGE

SeaLyt



Diet



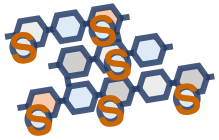
Preventing and managing digestive troubles

MSP®IMMUNITY

MSP®
IMMUNITY

MSP®IMMUNITY MODE OF ACTION

MSP®IMMUNITY



Innate Immunity

Increase of cytokines production

Production or recruitment vector of immune cells

(i.e. chemokines, interferons, ...)

Stimulation of immune cells

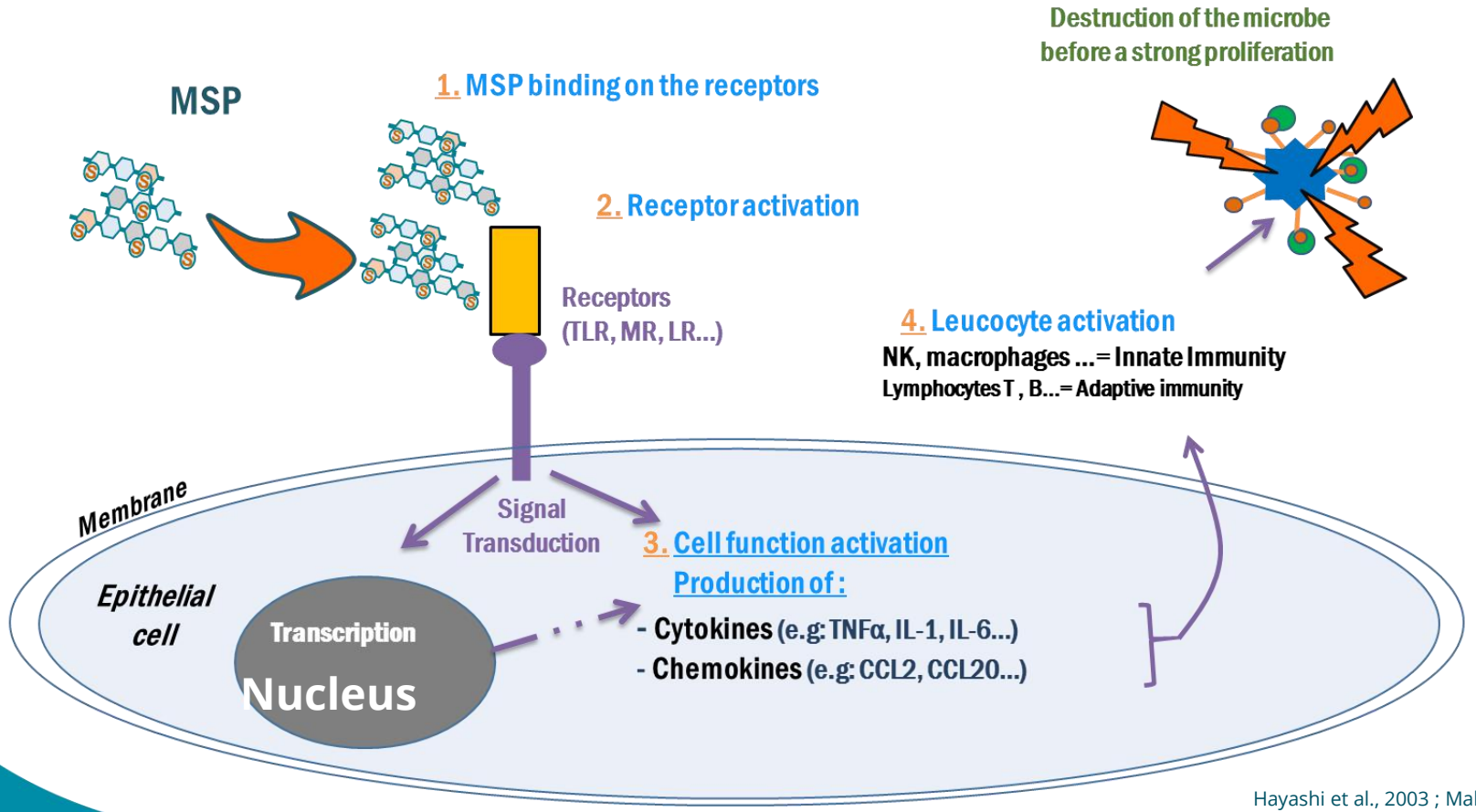
(i.e. macrophages,...)

Adaptive Immunity

Migration and stimulation of immune cells

(i.e. Lymphocytes,...)

MSP® IMMUNITY
MODE OF ACTION

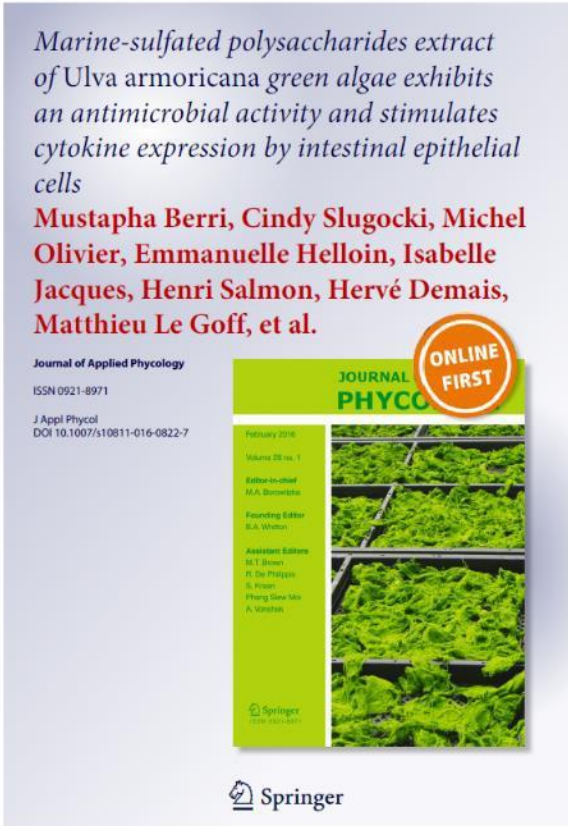


Hayashi et al., 2003 ; Makarenkova, I.,2012

MSP®IMMUNITY
SCIENTIFIC RESULTS (*in vitro*) – Berri *et al.*, 2016

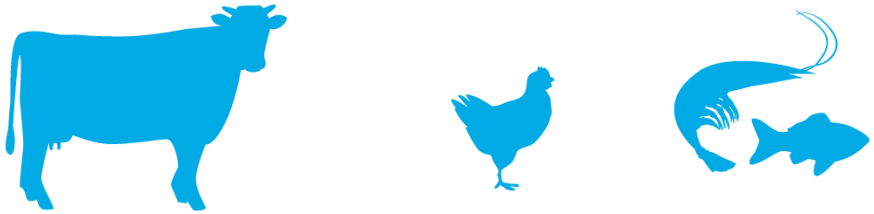
Mediator			Degree of stimulation of expression compared to control
TNFα	Pha		**82.63** ± 15.79**
IL-1α	Proliferation of CD4-	n of B-cells.	**22.96** ± 3.16**
IL-8			**313.53** ± 47.54**
CCL20	Recruitment	vity.	**159.44** ± 42.52 **
IL-6	Differentiation of	ells and	**30.58** ± 7.03 **
IL-1β	Proliferation, differer	olecules and	**4.92** ± 1.63**
IL-12p40	Production of IF	lls and	**3.88** ± 0.66**
TGFβ	Differentiation	T-cells.	**4.83** ± 0.66**
PPARγ	Transcription factor	α and IL1β	**3.71** ± 0.78**

** *P<0.01*



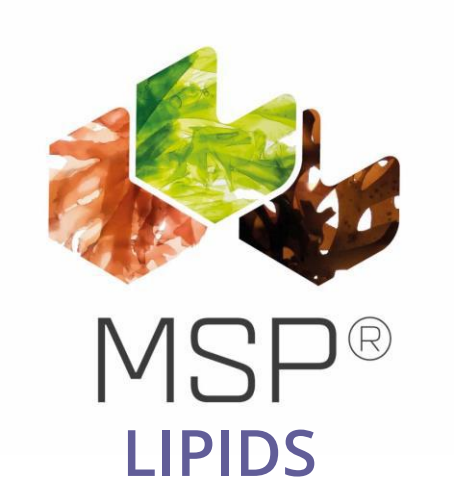
MSP®IMMUNITY
USE IN ANIMAL CARE RANGE

Searup



In support of vaccination
For increased immune transfer via the colostrum
For faster recovery in case of illness

MSP®LIPIDS

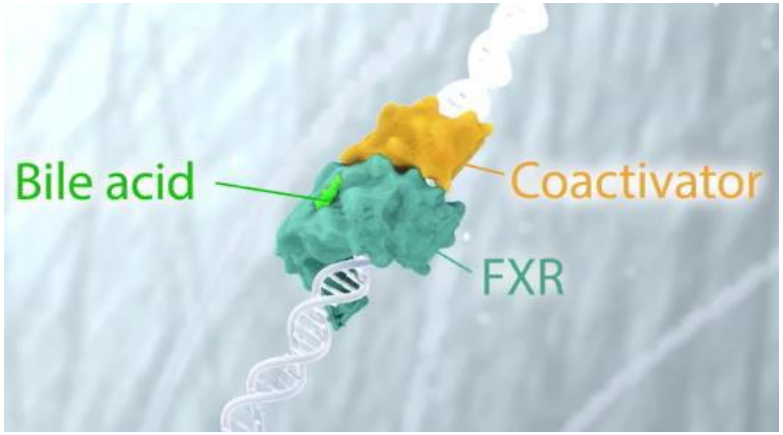


MSP®$_{LIPIDS}$
MODE OF ACTION

- Ulvans present in MSP®$_{LIPIDS}$ has the capacity to increase FXR expression by 3 when added to animal's diet (Qi *et al*., 2015).

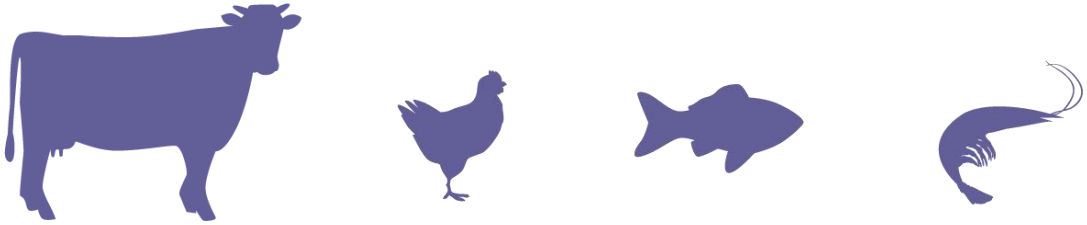
- FXR = Farnesoid X Receptor

- FXR in the hepatocytes and enterocytes is a key receptor for the cholesterol, bile acids and lipid metabolism.



MSP®LIPIDS
USE IN ANIMAL CARE RANGE

DigestSea



COMPOSITION

- Algae *(water-soluble extracts)*:
- Sorbitol
- Choline
- Amino acids *(Methionine…)*
- Vitamins *(B group)*
- Plant extracts *(artichoke, boldo)*
- Vitamins and minerals naturally present in the algae

MSP®

CONCLUSION

TAKE HOME MESSAGES

- Mycotoxins are a real threat in nowadays husbandry
- Main target is intestinal integrity and immunity
- Silent thief impairing performance and reducing profitability
- There are effective ways to counteract their deleterious effects with innovative technologies

AMADÉITE®

MT.X+ FOR FEED

MMi.S FOR FARM

- Other measure can be taken to reduce symptomatology when animals are already contaminated.

MSP® MUCIN

MSP® IMMUNITY

MSP® LIPIDS

SeaLyt Diet

Searup

DigestSea

Thank you for your attention!