

Mapping of the DNA adductome to study the genotoxic effects of red meat consumption

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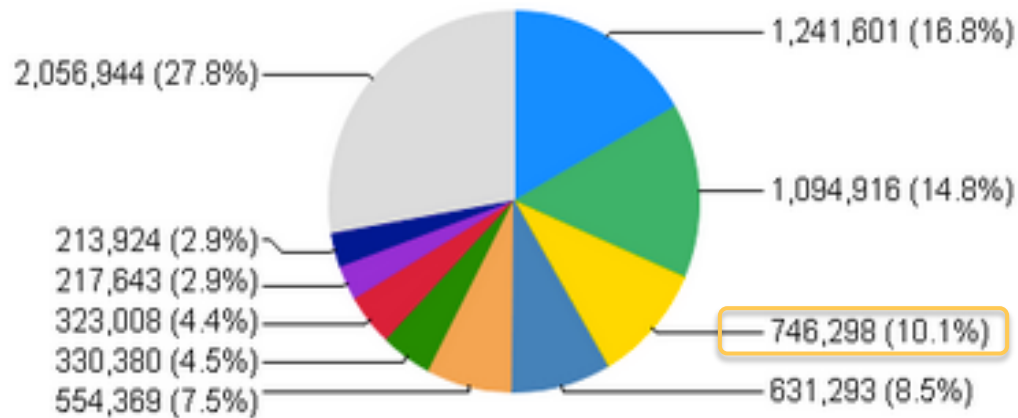


Worldwide cancer incidence

International Agency for Research on Cancer



Incidence



Globocan 2012 (IARC)

- Lung
- Prostate
- Colorectum
- Stomach
- Liver
- Bladder
- Oesophagus
- Non-Hodgkin lymphoma
- Kidney
- Other and unspecified

Colorectal cancer risk factors

≅ 10 % genetic

≅ 90 % non-genetic

– Tobacco

– Alcohol

– Unhealthy diet

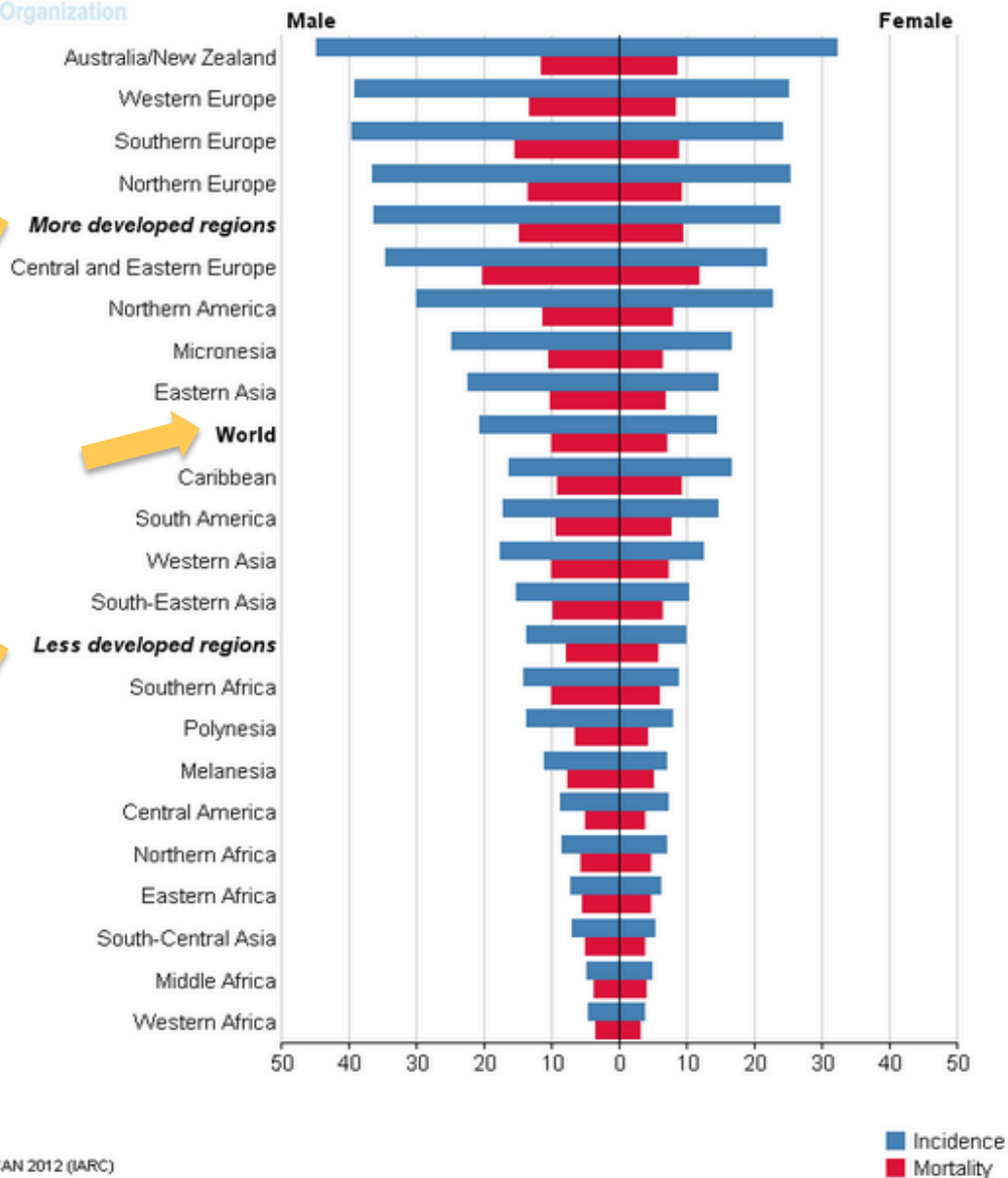
– Physical inactivity

– ...



Doll & Peto, J. Natl. Cancer Inst., 1981
Willett, Environ. Health Perspect., 1995

Colorectal cancer incidence rates per 100,000 men/women worldwide



Colorectal cancer risk factors

Western-type diet

80 %

Unhealthy diet

Doll & Peto, J. Natl. Cancer Inst., 1981
Willett, Environ. Health Perspect., 1995



Epidemiological data



100 g / day

→ Increased risk of 29 %

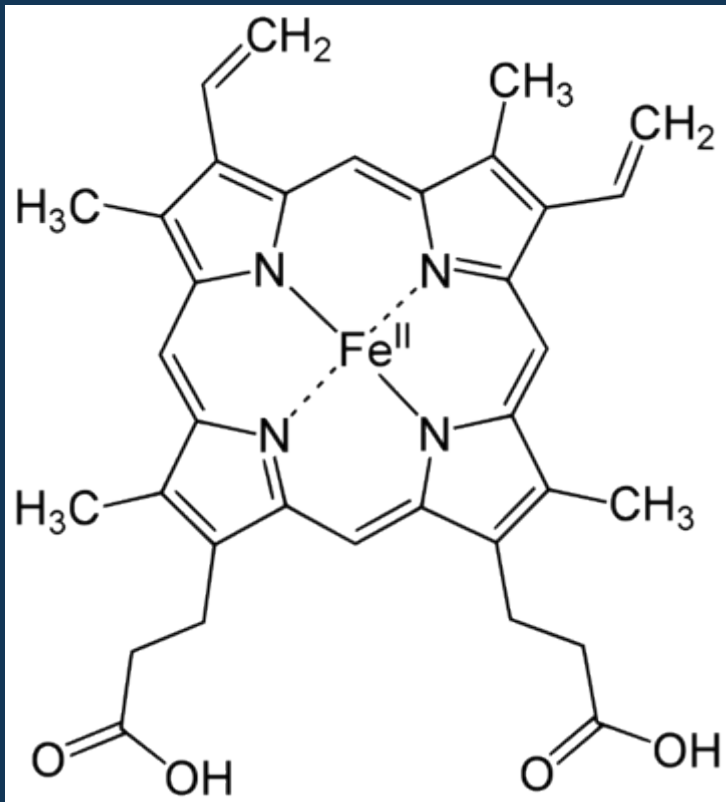


50 g / day

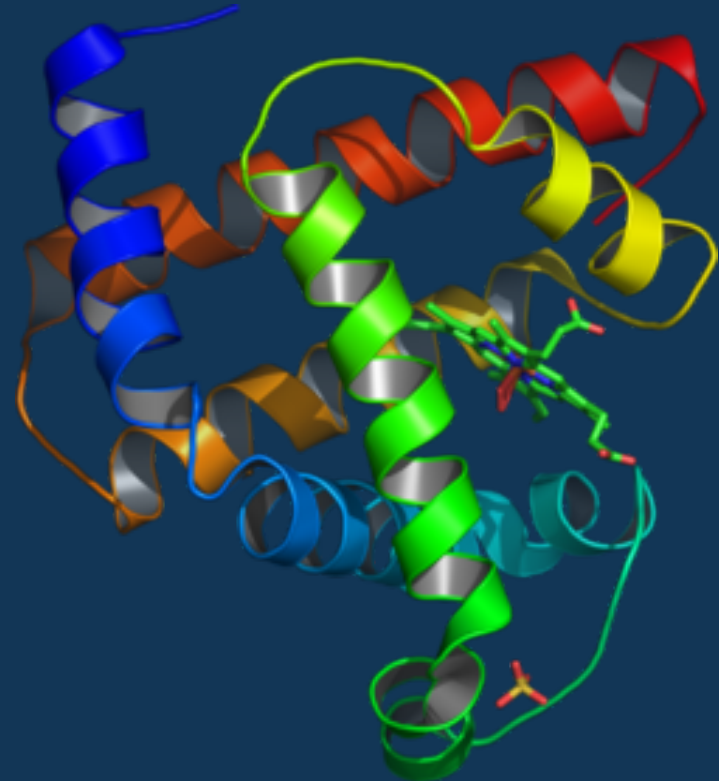
→ Increased risk of 21 %

Red meat and colorectal cancer hypothesis

Haem!



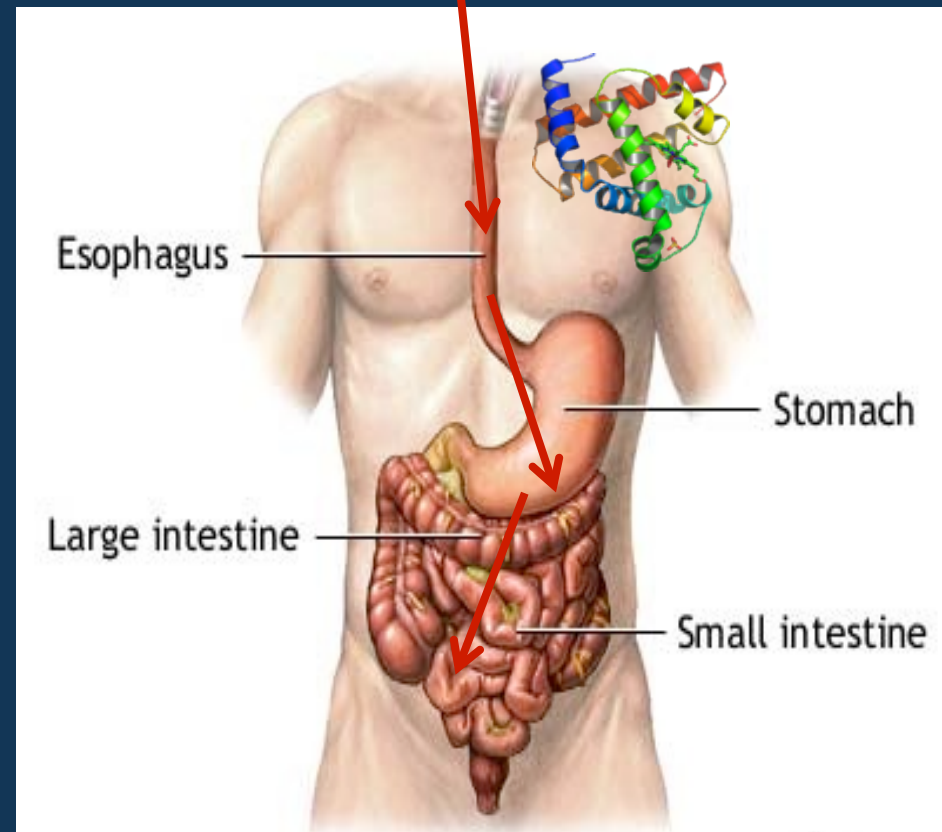
Myoglobin



Red meat vs. colon cancer: role of GI red meat digestion?

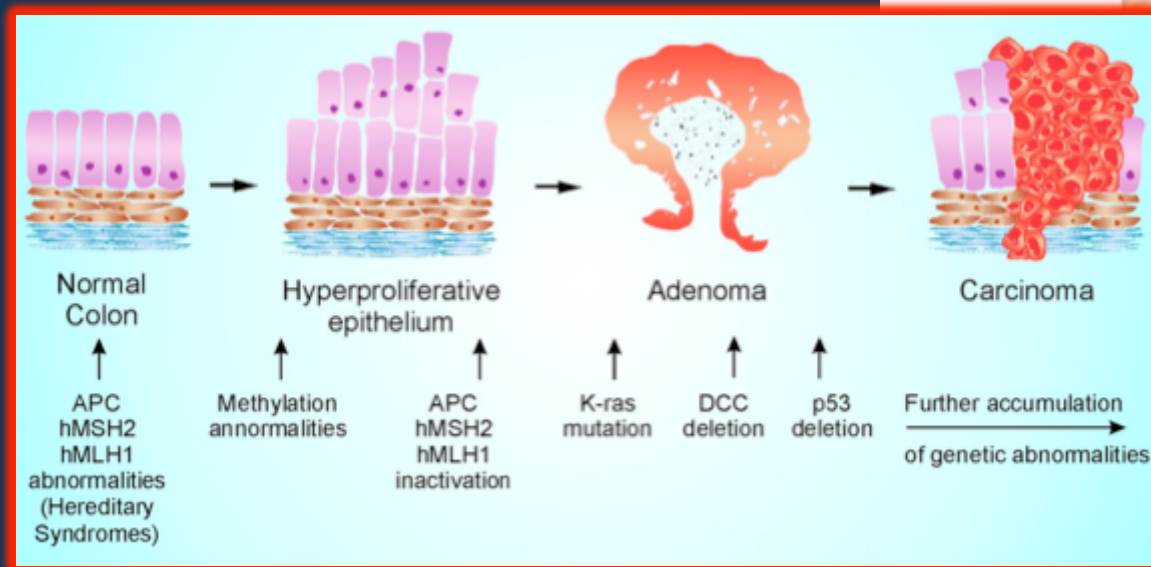
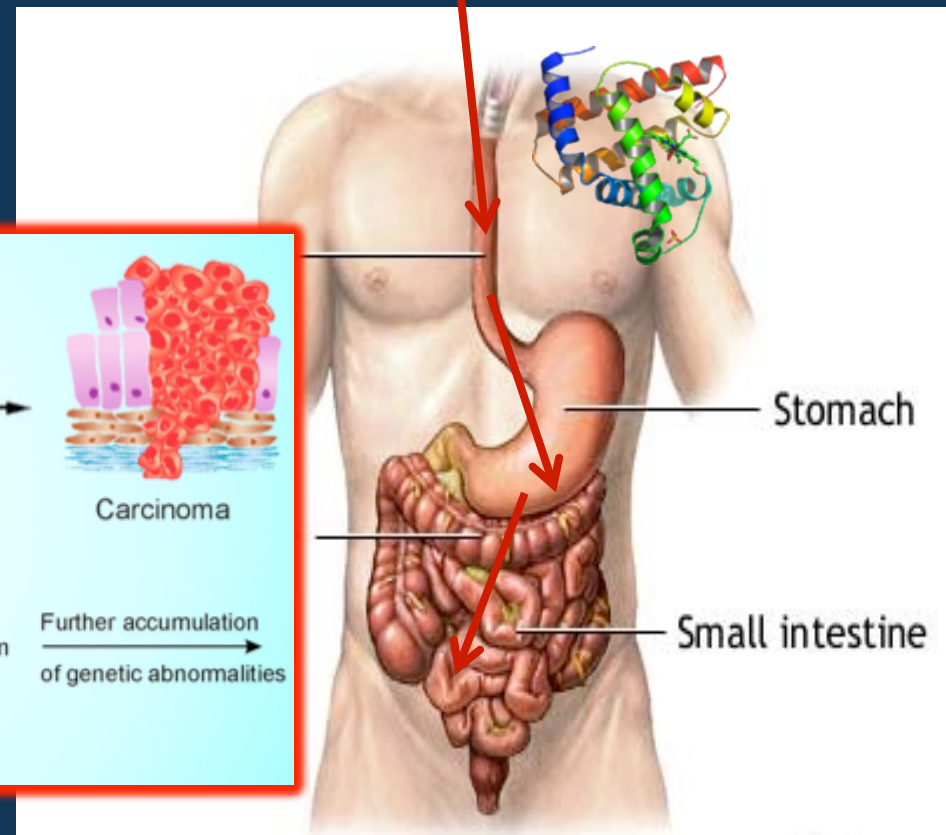
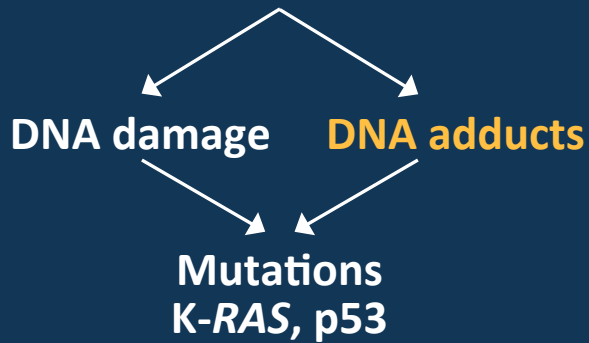
Meat with haem pass through GIT and stimulate formation of:

1. Lipid peroxidation products (LPOs)
2. N-Nitroso compounds (NOCs)



Red meat vs. colon cancer: role of GI red meat digestion?

NOCs and LPOs

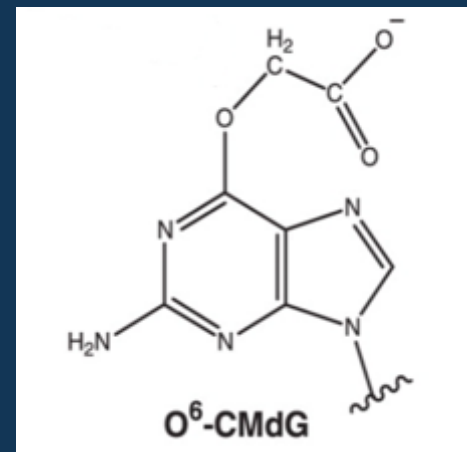


Experimental setup

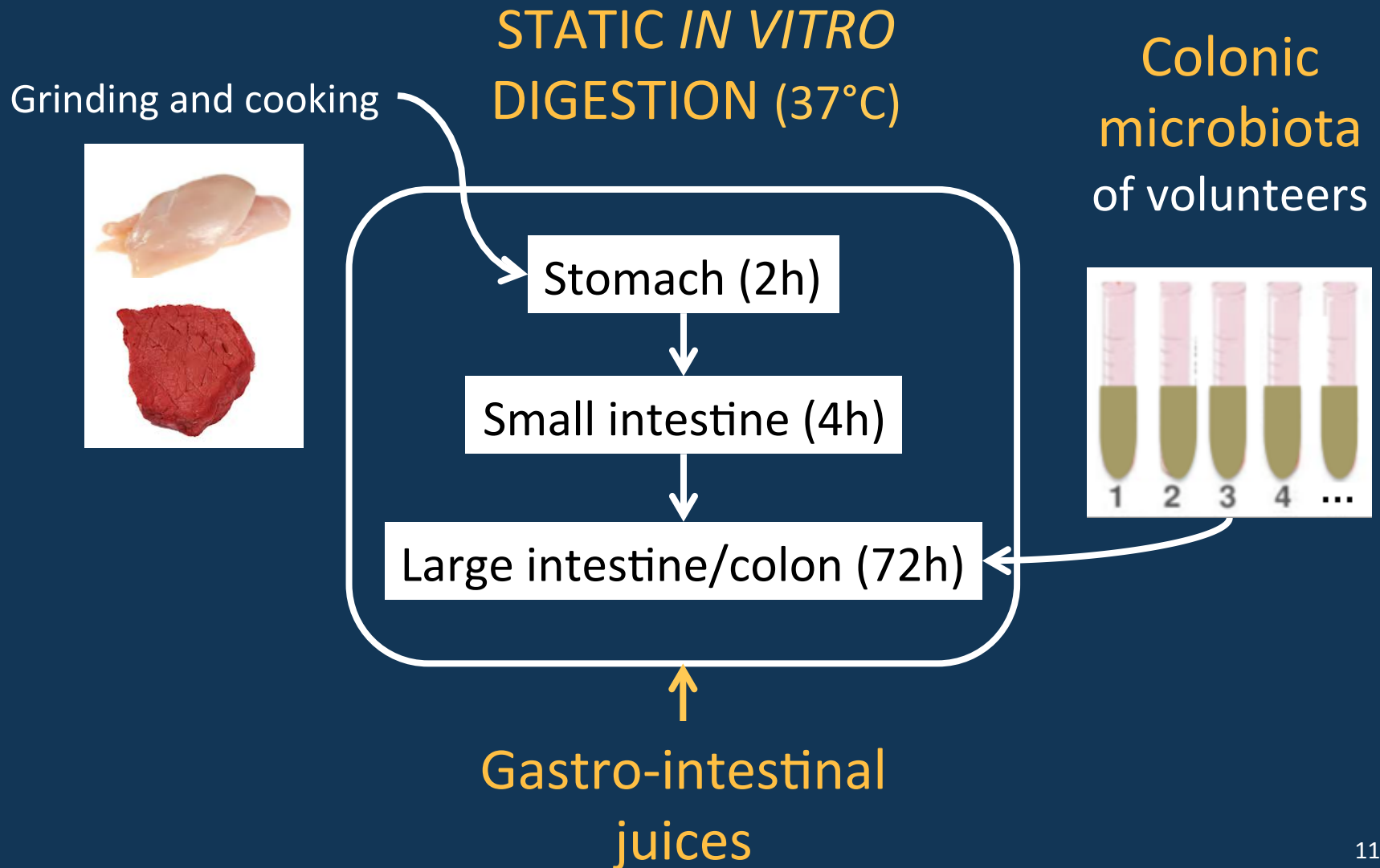
1. *In vitro* digestion of red (vs. white) meat
2. Mapping of DNA adducts by means of UHPLC-HRMS in meat digests

DNA adduct?

- When a chemical covalently binds to a DNA nucleobase
- First step in chemically induced carcinogenesis
- Different types:
 - By NOCs
 - By LPOs
 - And many others...



In vitro digestion of meat



DNA adduct analysis: DNA adductome mapping

1. **Sample preparation:**
 - a. Acid DNA hydrolysis (0.1 M HCl)
 - b. Solid Phase Extraction
2. **UHPLC-HRMS analysis**
 - a. Targeted (“profiling”)
 - b. Untargeted (“fingerprinting”)
3. **Data processing**
 - a. ToxID™
 - b. SPSS®
 - c. Sieve™
 - d. Simca™



Results (1):

- What?
 - Digestion of beef
 - Colonic digestion by means of the colonic microbiota obtained from 5 different volunteers
 - Increase, decrease or shift during colonic digestion?
 - How?
 - ToxID™ data processing based on m/z of known diet-related DNA-adducts
- N.D.
 - Rise in DNA adduct levels:
 - DNA adduct formation
 - Decrease in DNA adduct levels:
 - DNA adduct degradation or dilution
 - *(*)(*) isomers

Results (2):

- What?

- Digestion of beef vs. chicken
- + vs. with or without added calcium
- Microbiota of 2 volunteers:
 - P1 & P2
 - 3 biological replicates
- Increase, decrease or shift?

- How?

- ❖ ToxID™ data processing

- N.D.

- Beef (B) > Chicken (C) OR beef/chicken without added calcium > with added calcium (+Ca)

- Chicken (C) > Beef (B) OR beef/chicken with added calcium (+Ca) > without added calcium

- *(*)(*)(*) isomers

Results (3):

- What?

- Comparison of digestion of beef vs. chicken
- + vs. with or without added calcium
- 2 volunteers
 - P1 & P2
 - 3 biological replicates
- Discriminative DNA adducts?

- How?

- ❖ Sieve™:

- spectral data processing*

- ❖ Simca™:

- OPLS discriminant analysis*

Most prominent findings

- **Colonic microbiota**
 - Active production/formation of (genotoxic) molecules
- **DNA adduct profiling**
 - Several DNA adduct types significantly higher or lower in different meat preparations...
 - ...
- **Discriminant analysis**
 - ...



3RD INTERNATIONAL SYMPOSIUM OF

PP
robotics
rebotics
In Pediatrics
2016

APRIL 28 - 30, 2016
AT "THE PAND", GHENT
www.PreProPed2016.be



The international congress of Prebiotics & Probiotics in Pediatrics 2016, organized by Prof. Y. Vanderplas, will take place at "The Pand" in Ghent from April 28 until April 30 2016. The program will cover all major topics related to prebiotics, probiotics, microbiota and gut health. Many key opinion leaders are invited and confirmed their participation.

The scientific program highlights the current advances in the research, production and use of probiotics and prebiotics in children, with particular focus on their role in maintaining health and preventing diseases. The major goal is to provide a scientific forum for stakeholders and to enable the interactive exchange of state-of-the-art knowledge. Ghent is a beautiful city, just 50 km away from Brussels, easy to reach from the national airport (direct train connection every half hour), and offers a unique mixture of medieval and modern architecture. The symposium will be held in the heart of the city, at a distance of only 30 km from Bruges.

You will hear about the novel clinically-relevant studies emphasizing the importance of pro/prebiotics for new indications. Subscribe before January 31, 2016 (and early bird registration) and join us in Ghent, Belgium.

*Check out the Scientific
program and other important
information on the website!*

Date: April
28-30, 2016



MORE INFORMATION:

Find out more about this event by visiting our website: www.PreProPed2016.be

Subscribe to this symposium
before January 31, 2016 and
join us in Belgium!



Thank you!

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