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Glycation: from inflammation to ageing



HOW DO EARLY AND LIFE-LONG EXPOSURE TO DIETARY AGE_s AFFECT TISSUE, GUT SENSITIVITY, AND MICROBIOTA IN MICE?

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Conflict of interest
Nothing to Disclose

Summary

1 | **Introduction**
Origin and implications of AGEs on health

2 | **Goals and experimental design**

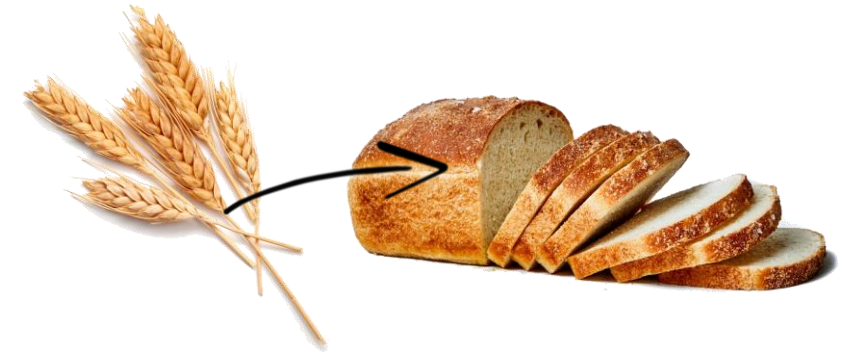
3 | **Findings**

4 | **Conclusions and perspectives**

The root of the problem



The good....
Palatability/Digestibility



and the bad....
Food exposome



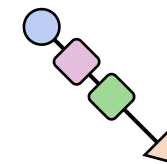
AGEs
Neoformed compounds



Dysbiosis
(Taguchi et al., 2021)



Tissular dysfunction
(Steenbeke et al., 2022)



RAGE vs. Inflammageing
(Frimat et al., 2019)


Goal



Understand the early (including perinatal period) and life-long physiological effects of dietary AGEs consumption and depict the real contributions to cellular stress trigger in a healthy animal model

Investigating the effects of dAGEs


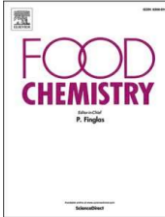
Dietary protocols



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Food Chemistry

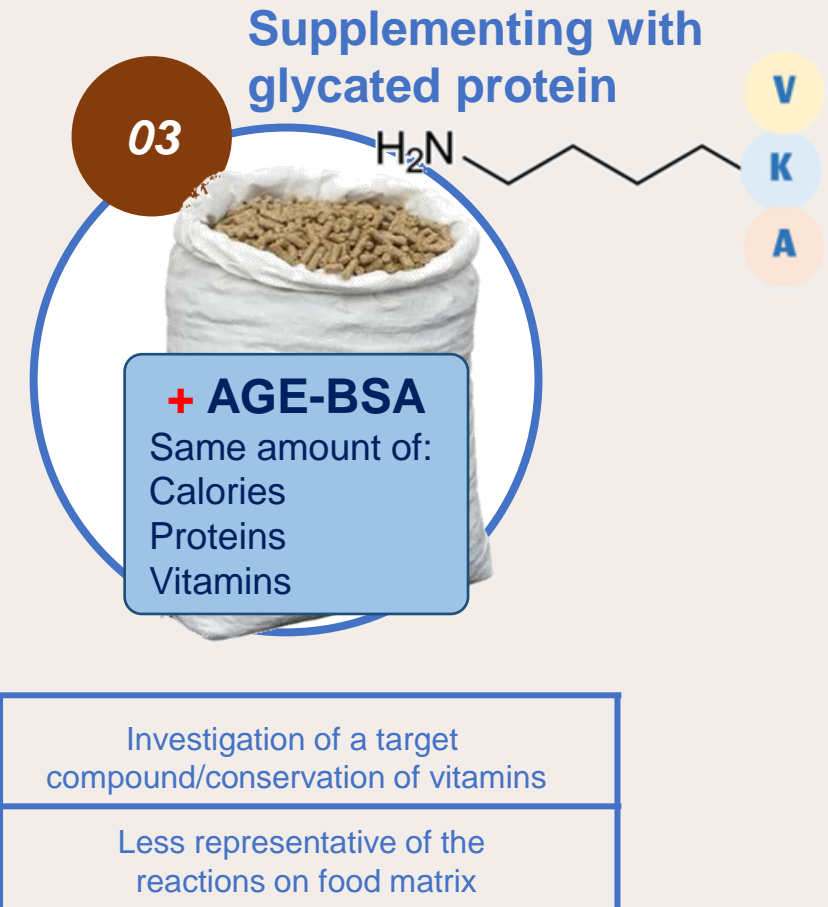
journal homepage: www.elsevier.com/locate/foodchem



Glycated bovine serum albumin for use in feeding trials with animal models – In vitro methodology and characterization of a glycated substrate for modifying feed pellets

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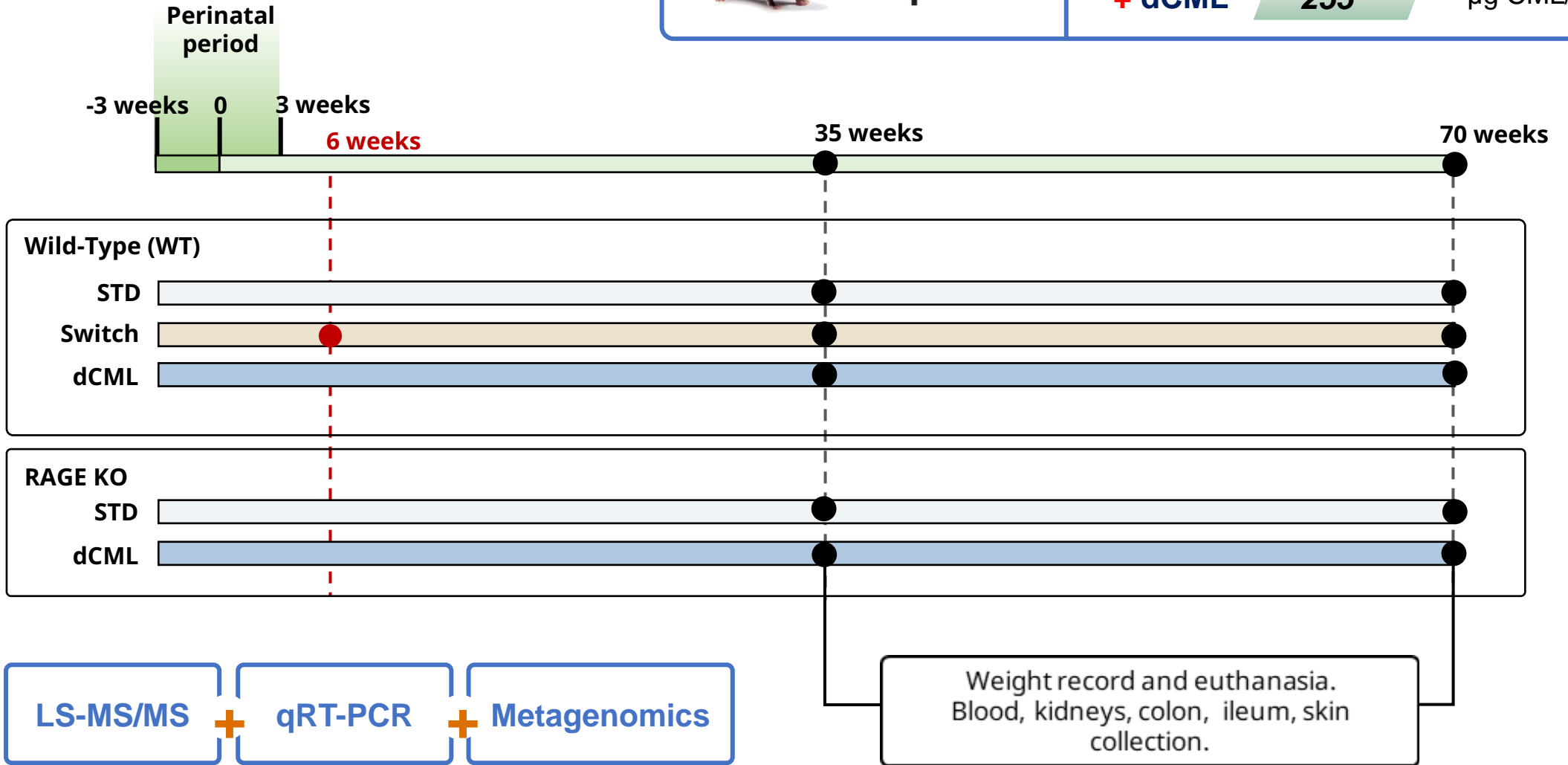
Experimental design

Model: Healthy C57BL/6

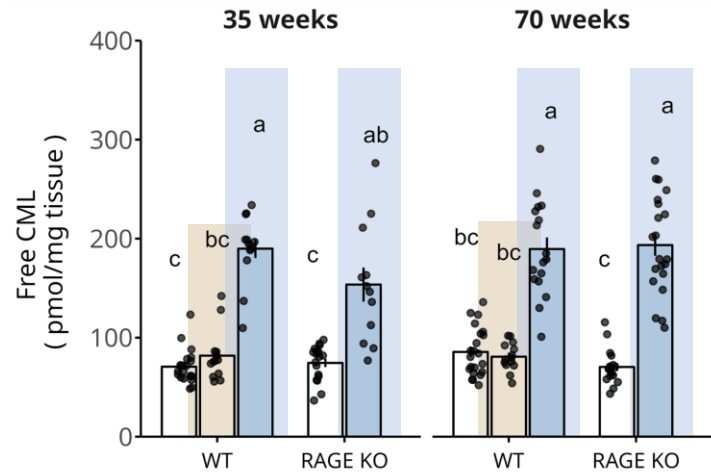


Diet:

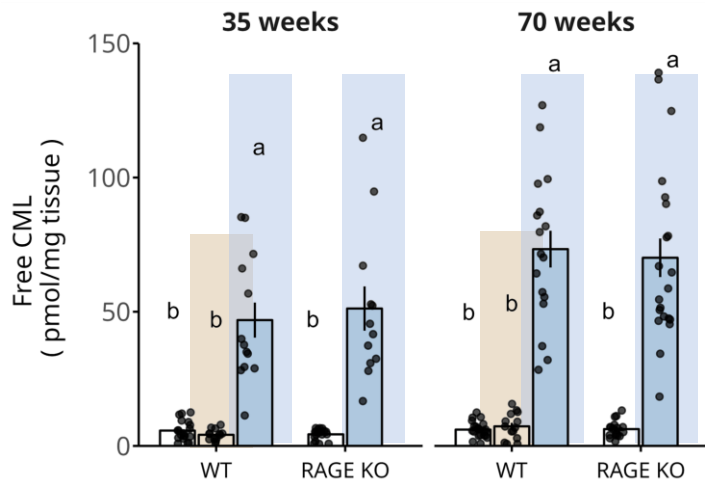
| | | |
|--------|-----|---------------|
| + STD | 20 | µg CML/g food |
| + dCML | 255 | µg CML/g food |



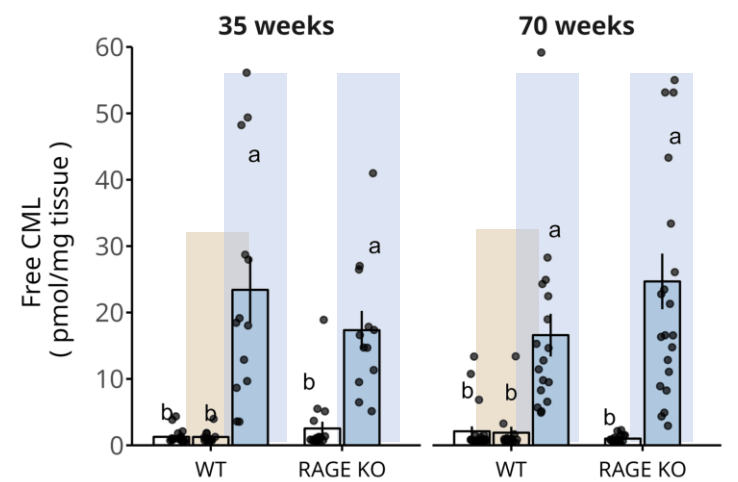
Kidneys – Free CML



Ileum – Free CML



Colon – Free CML



Free CML was significantly increased in the **kidneys, ileum, colon**

Such increase was RAGE independent

but...

the accumulation of free CML can be **reversed to levels compared to the controls**

...even if animals were exposed to dAGEs during perinatal period

van Dongen et al., 2021

Kidneys

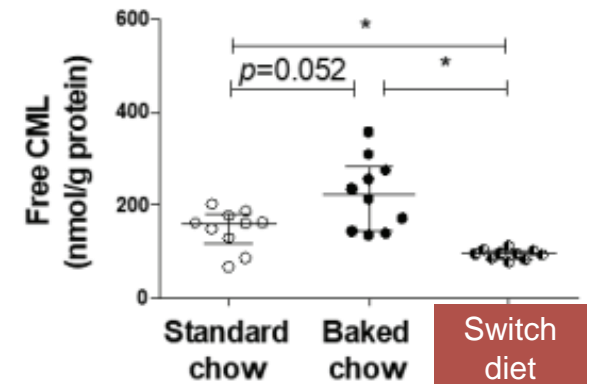
Age: 9 weeks

Sex: Males

Diet: Baked chow

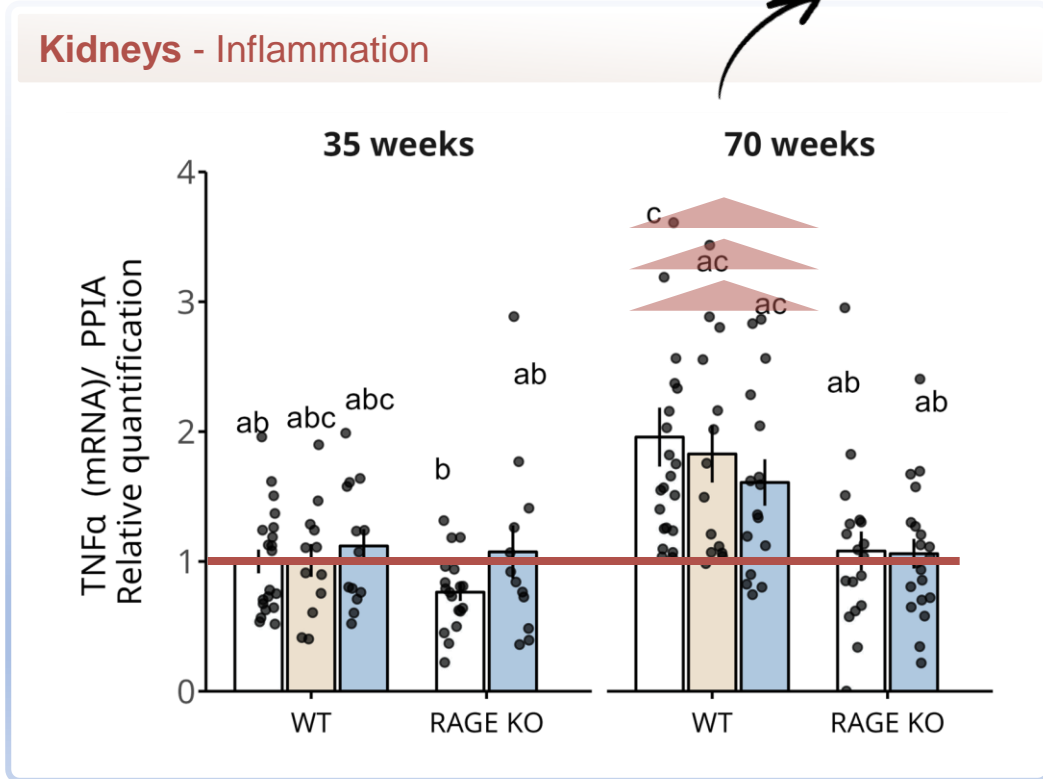
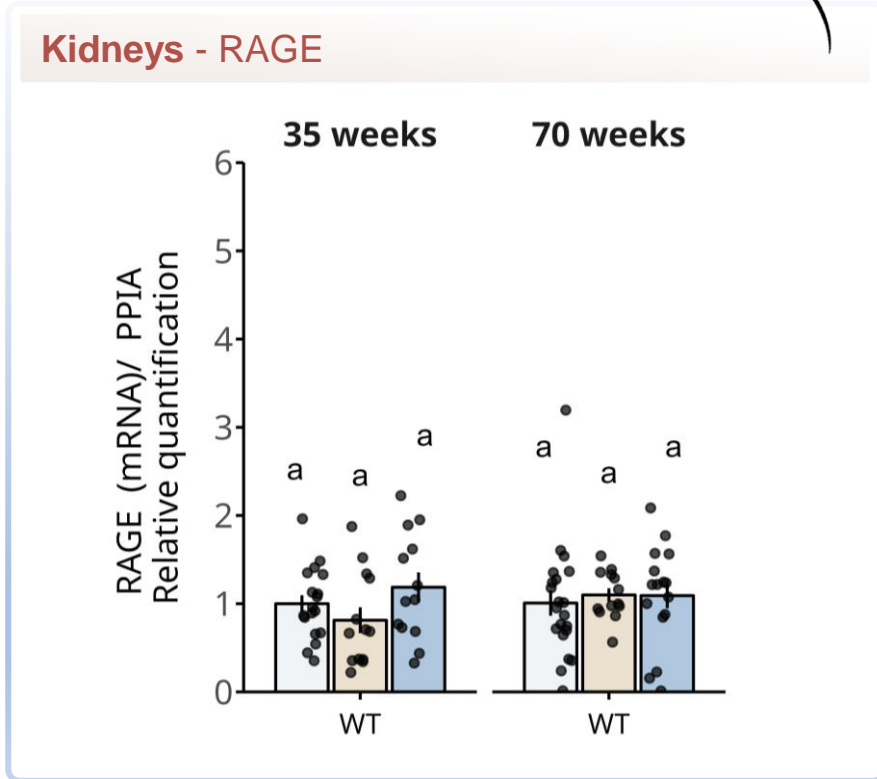
Exposure: 10 weeks

Switch after 5 weeks



RAGE gene expression does not seem to correspond to dAGE intake

RAGE depletion protects against **age** related low-grade inflammation

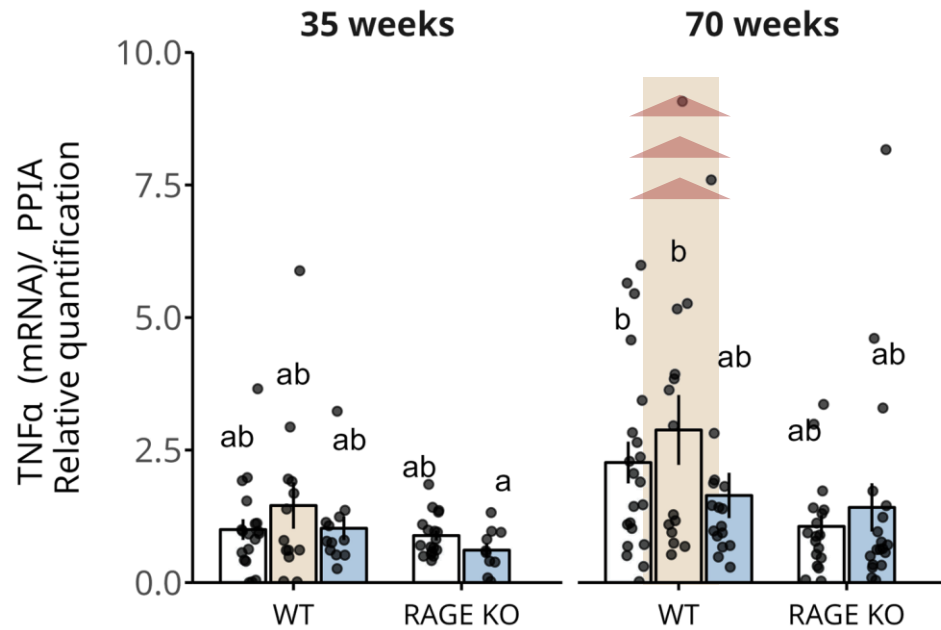


- Protein-bound CML
- Oxidative stress

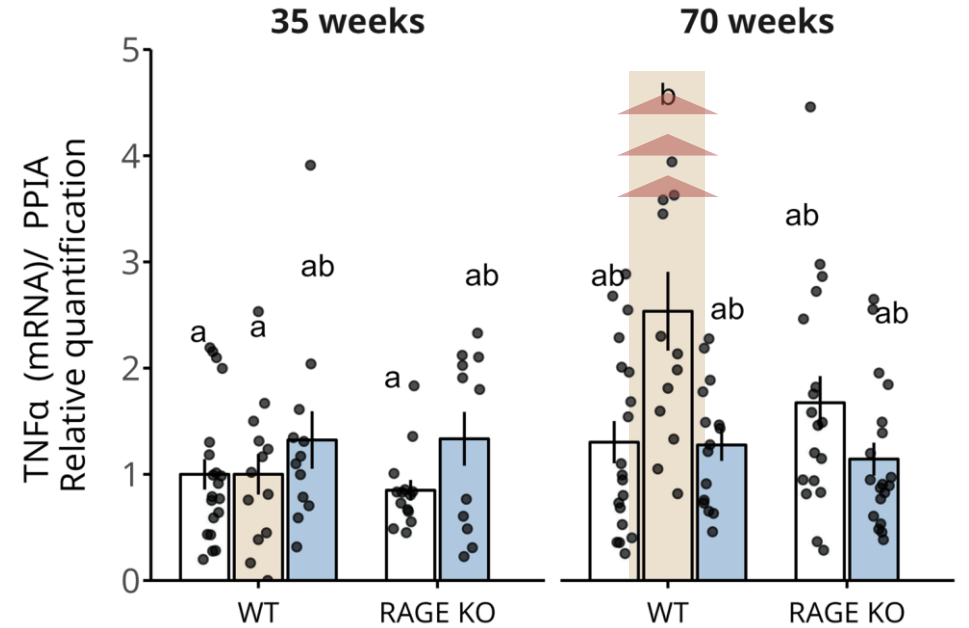
The increase in RAGE expression is not required for inflammation upregulation

dAGE concentrations did not trigger inflammation in the kidneys – age is most relevant

Ileum - Inflammation



Colon - Inflammation



The timing of diet diversification matters

Early-life diet switch results in long term intestinal sensibility to inflammation

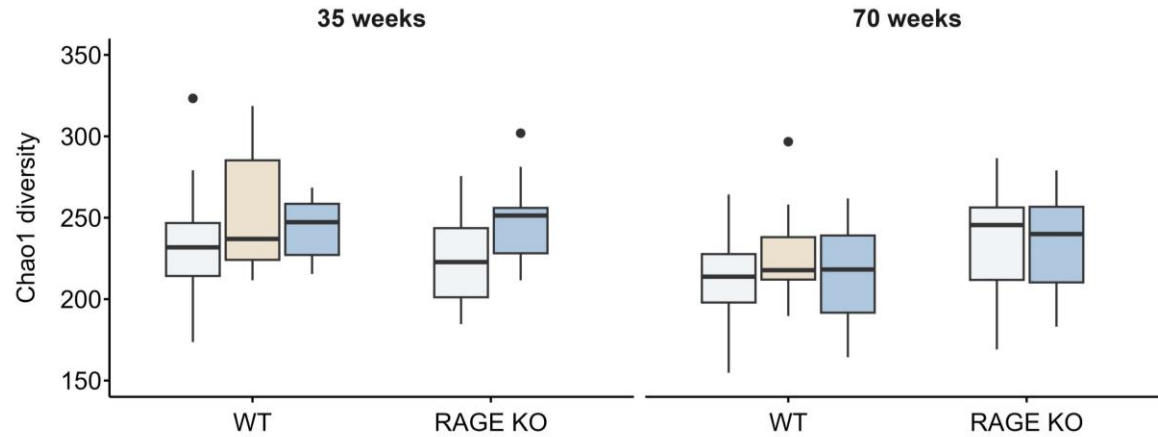
Early dietary changes have been suggested to reduce integrity of the intestinal epithelium vs. protein allergenicity (Differding et al., 2020)

Suggested mechanism

Microbiota ecology changes

How the gut microbiota ecology is affected by a diet enriched in dAGES?

Caecum – Alpha diversity



Microbial communities within the samples were resilient, with no dominant taxon significantly emerging from influences of diet, age, or genotype

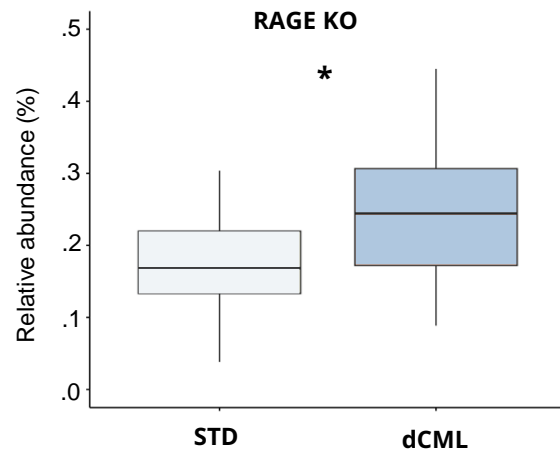
Equilibrium between the main phyla, Firmicutes and Bacteroidota

Anaerovoracaceae and Mirinifilaceae

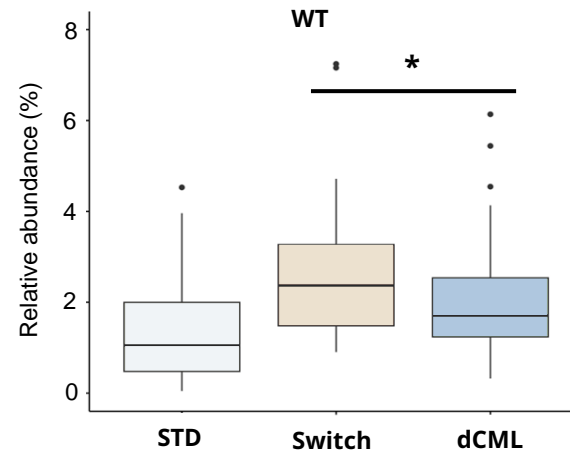
These taxa are known for their roles in glycan metabolism and mucin degradation, processes vital for maintaining intestinal homeostasis and overall gut health.

(Beaumont et al., 2020; Raimondi et al., 2021).

Anaerovoracaceae – Abundance



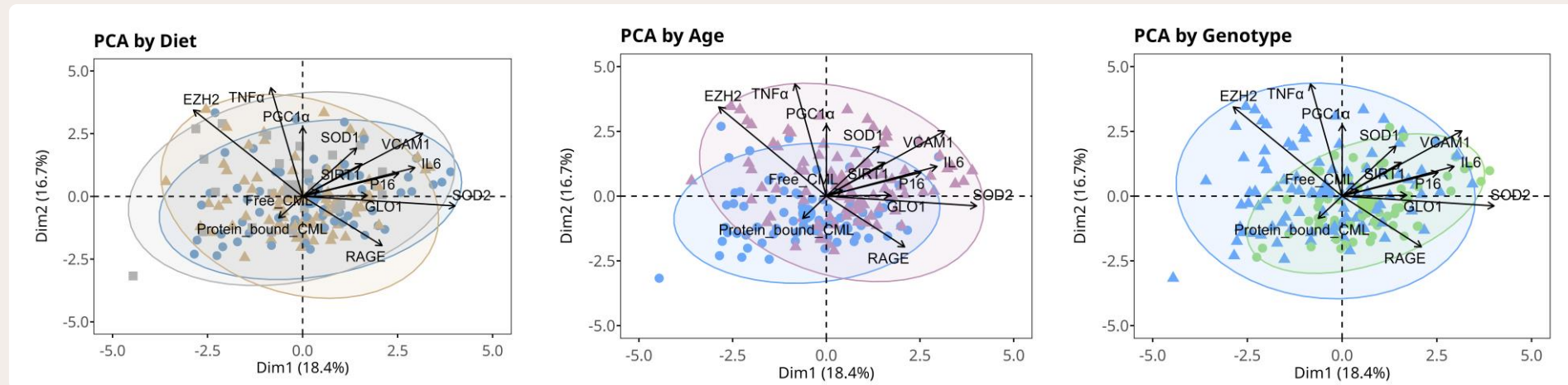
Mirinifilaceae – Abundance



A mechanism involved in changes in gut homeostasis

Main findings

- > **dCML accumulation** in different organs **is reversible** (even when animals were exposed to dAGEs during perinatal period)
- > **dCML accumulation** is RAGE independent and **RAGE knockout** contributed to **reduced inflammaging**
- > **Age and RAGE** deletion were **major factors** influencing the observed molecular changes



- > **Early-life diet switch** contributed to **intestinal sensitivity** to inflammation, including changes in gut microbiota abundance changes.
- > **dAGE** *per se* did not provoke unequivocally harmful effects in a **healthy** rodent model.

Major perspectives

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Early- and life-long intake of dietary advanced glycation end-products (dAGEs) leads to transient tissue accumulation, increased gut sensitivity to inflammation, and slight changes in gut microbial diversity, without causing overt disease

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For early career stage researchers of all ages researching AGEs
For PhDs by PhDs, and junior postdocs too

Location: Café Zuid (across the square from here) Maastricht

More info? Ask us or email:  young-agers@outlook.com

Nogueira Silva Lima, MT, M Howsam, C Delayre-Orthez, P Jacolot, S Jaisson, J Criquet, M Billamboz, et al. “Glycated bovine serum albumin for use in feeding trials with animal models – In vitro methodology and characterization of a glycated substrate for modifying feed pellets”. *Food Chemistry* 428 (1o de dezembro de 2023): 136815. <https://doi.org/10.1016/j.foodchem.2023.136815>.

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