Raw milk and Raw milk Kefir for the dietary management of allergic diseases

FACE conference 2023

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Allergic diseases – a global health problem

4 BILLION PEOPLE WORLDWIDE

50% OF EU POPULATION

55-151 BILLION EURO

- Increased prevalence in Western countries
  - Loss of rural living conditions
    - Hygiene hypothesis: *'a little dirt does not hurt'*

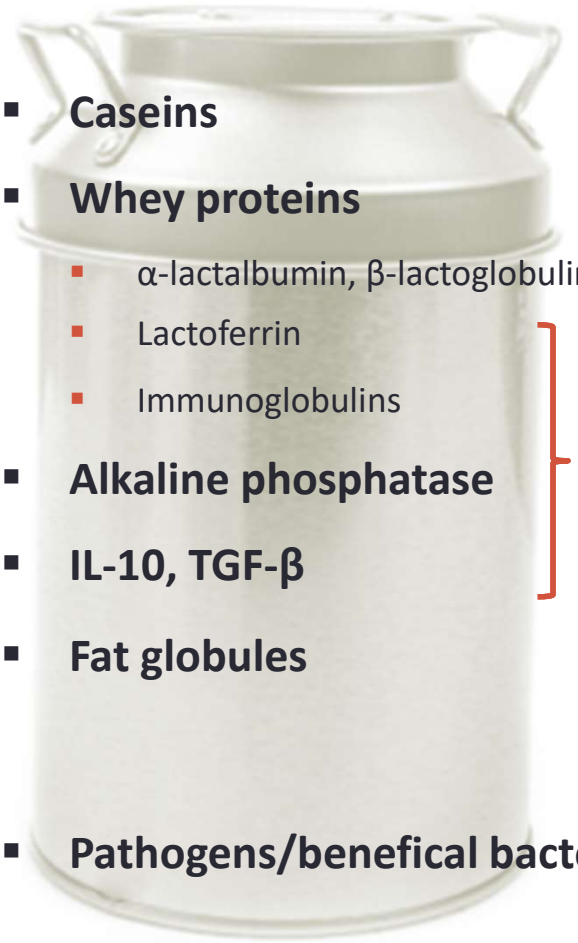
Raw milk – a natural solution?

- Growing up on a farm lowers the risk of developing asthma and allergies
  - Raw, unprocessed, farm milk consumption
- Consumption of raw cow's milk early in life protective against the development of allergies later in life
- Independent of:
  - Concomitant farm exposures
  - Farm status
- Only epidemiological evidence

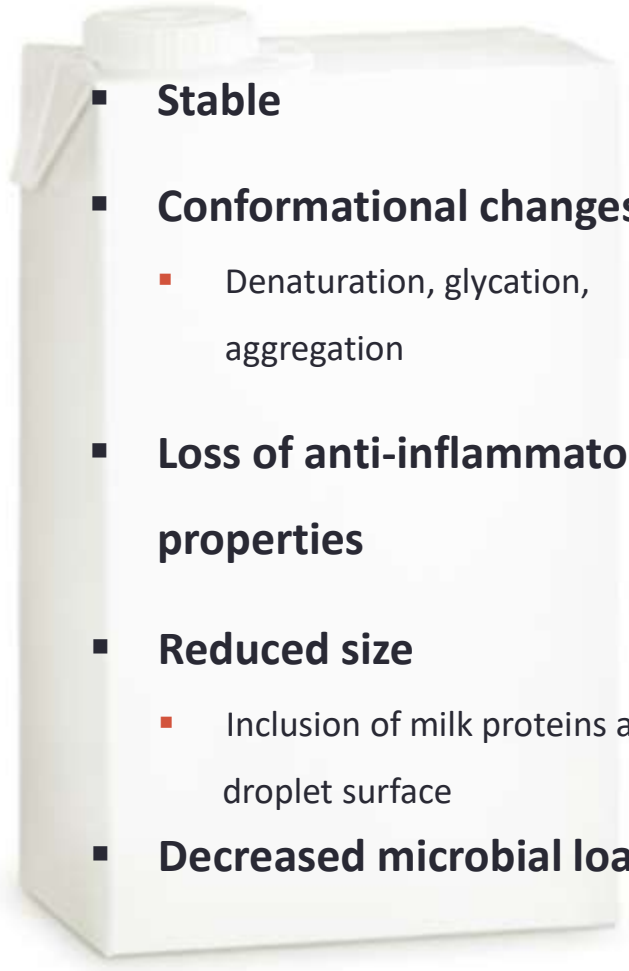
Kilpeläinen M *et al., Clin Exp Allergy* (2000)
Riedler J *et al., Clin Exp Allergy* (2000)
Waser M *et al., Clin Exp Allergy* (2007)
Perkin MR, Strachan DP, *J Allergy Clin Immunol.* (2006)

Milk processing (1)

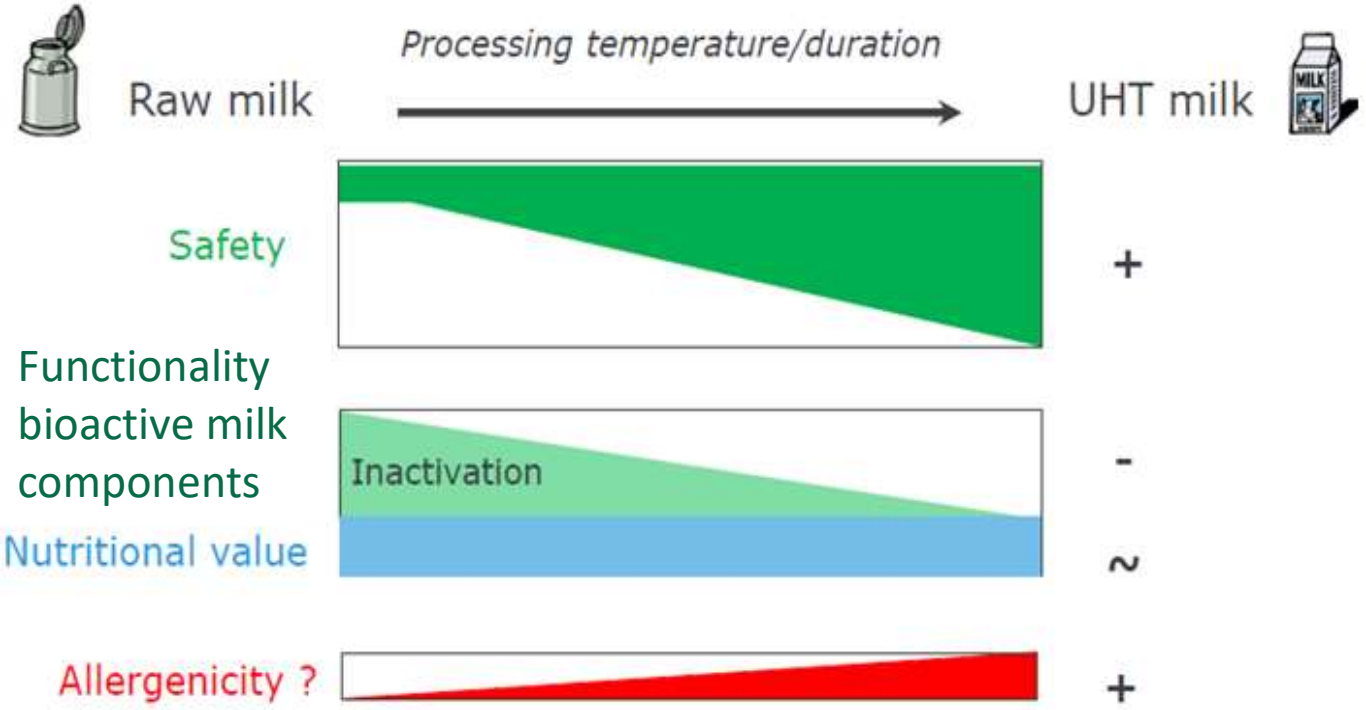
Heating and homogenization



- **Caseins** → **Stable**
- **Whey proteins** → **Conformational changes**
  - α-lactalbumin, β-lactoglobulin → Denaturation, glycation, aggregation
  - Lactoferrin
  - Immunoglobulins
- **Alkaline phosphatase**
- **IL-10, TGF-β** → **Loss of anti-inflammatory properties**
- **Fat globules** → **Reduced size**
  - Inclusion of milk proteins at droplet surface
- **Pathogens/benefical bacteria** → **Decreased microbial load**



Milk processing (2)



(Adapted from van Neerven, 2015)

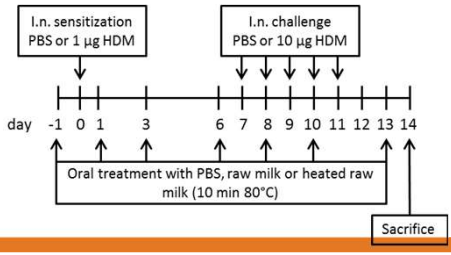
- WHO does not recommend raw milk consumption
- Sale of raw milk in the Netherlands only permitted with clear 'heat before consumption' label

Aim of our studies

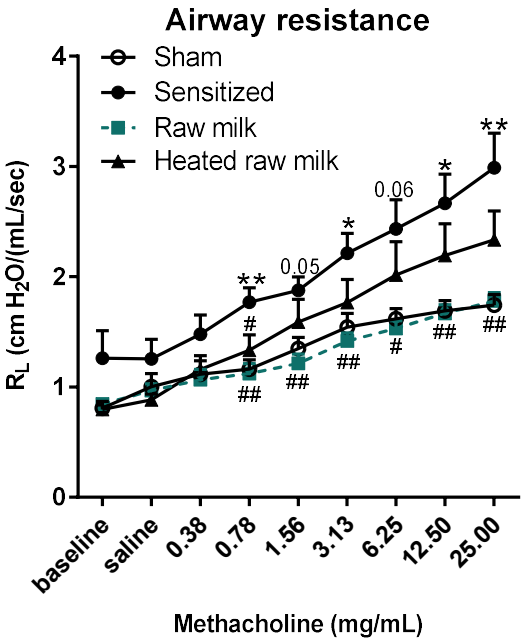
- Prove the allergy-protective effects of raw cow's milk by causality
- To achieve a better understanding of the raw milk components involved in the allergy-protective effects

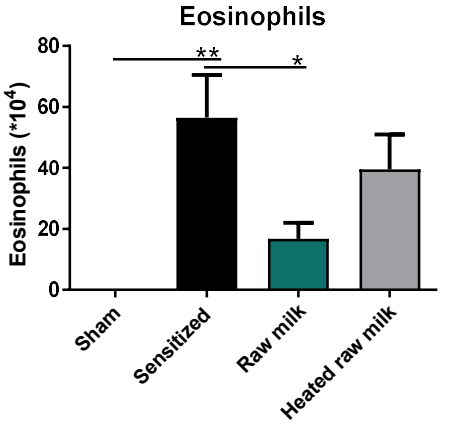
Vorzugsmilch since 1905

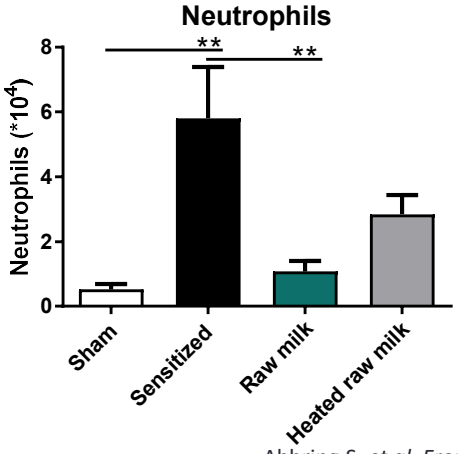
Allergic asthma



- *To investigate whether raw cow's milk can prevent the development of asthma in a murine HDM-induced allergic asthma model*

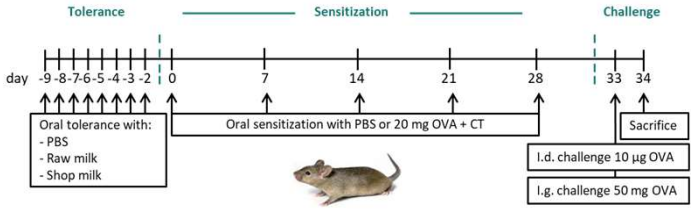




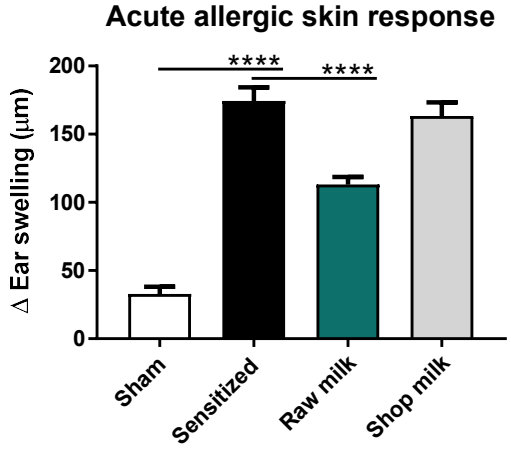


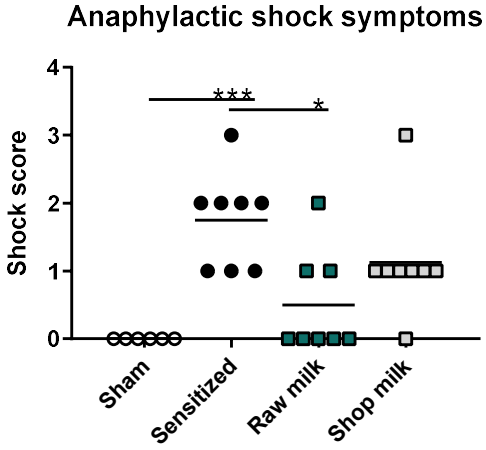
Abbring S, *et al, Frontiers (2017)*

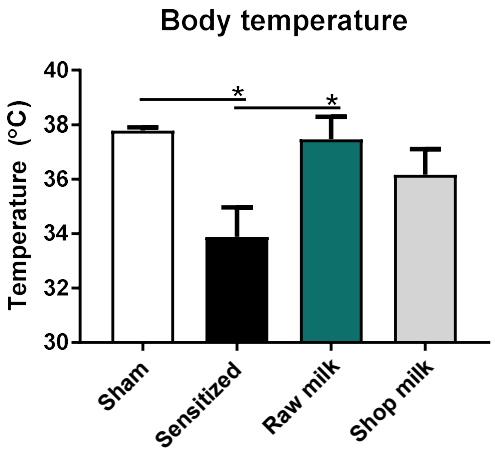
Food allergy

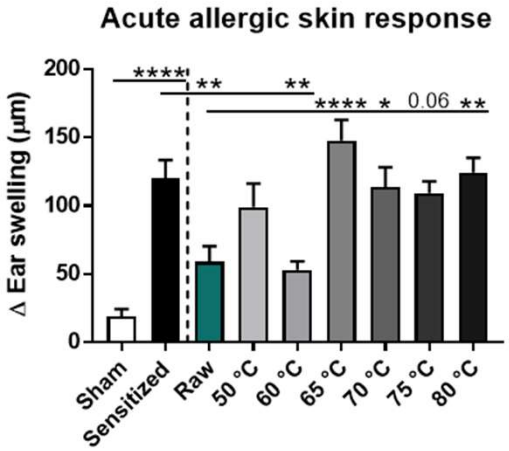


- *To investigate whether raw cow's milk also protective in a murine ovalbumin (OVA)-induced food allergy model*





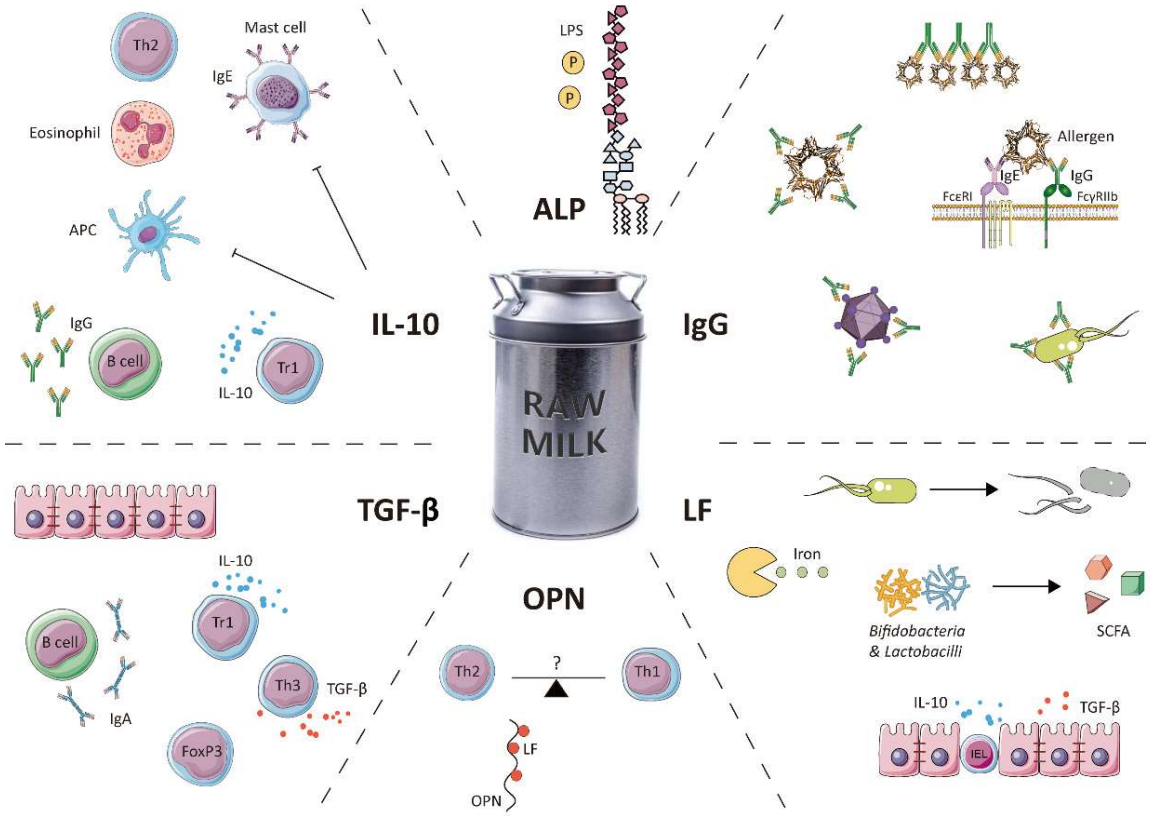




Abbring S, Ryan JT, *et al., Nutrients* (2019)
Abbring S, *et al, Food&Function (2020)*

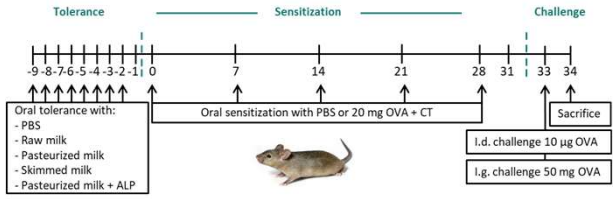
Heat-sensitive milk components

- Heat-sensitive raw milk components involved

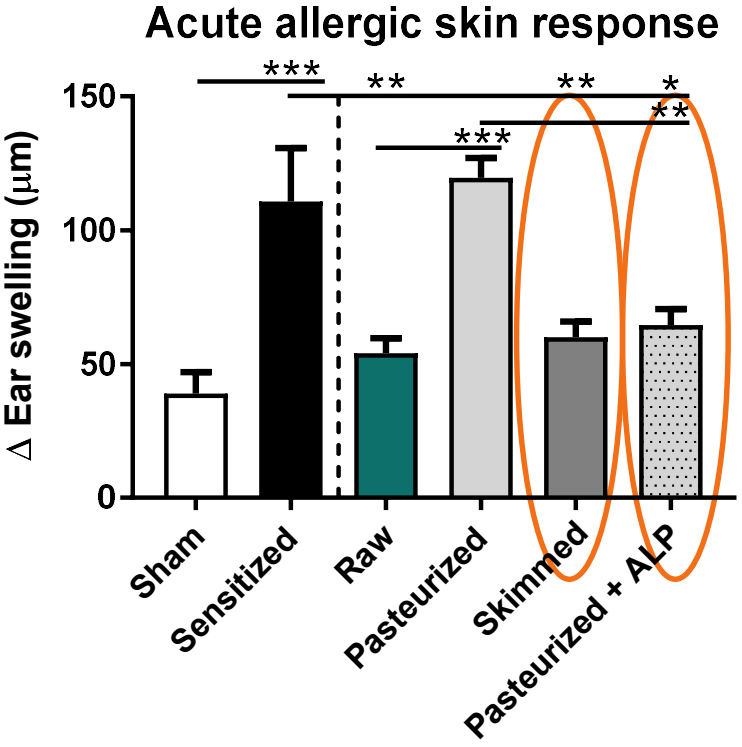


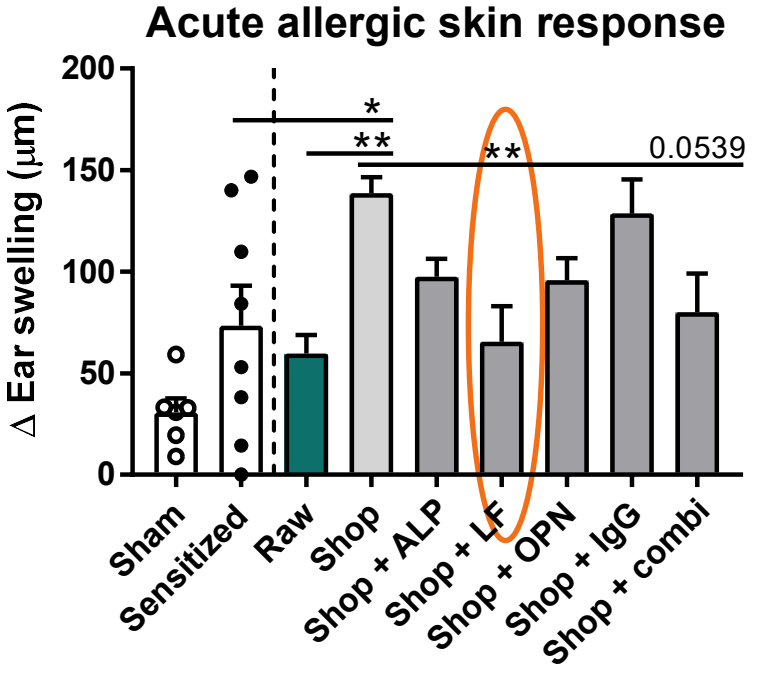
Abbring S *et al., Eur J Pharmacol.* (2019)

Milk components



- *To investigate the contribution of fat content and heat-sensitive milk components to the allergy-protective raw milk effect*





Abbring S, Ryan JT, *et al., Nutrients* (2019)
Van Esch, Abbring S *et al., unpublished result*

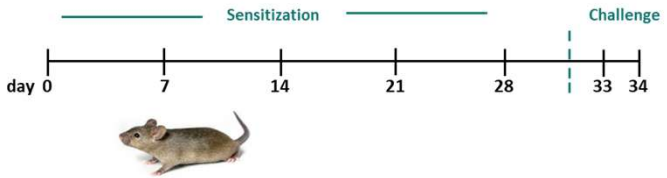
Conclusion

- Suppression of food allergic symptoms by raw cow's milk retained after skimming but abolished after pasteurization
  - No effect of fat content
  - Heat-sensitive milk components involved

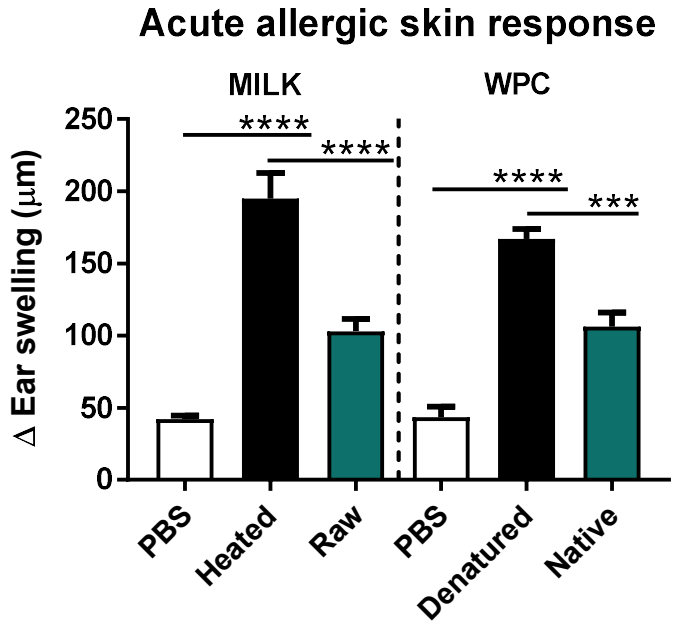
- Heating temperatures as low as those used during pasteurization are already detrimental to the allergy-protective effects

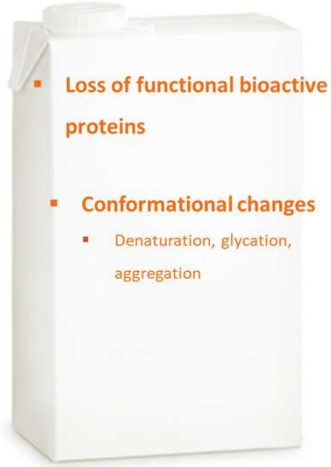
- Supplementing heat-treated milk with ALP and LF restored the protective effects

What about allergenicity?



- We mainly focused on tolerogenic feature of raw cow's milk
- *To investigate whether milk processing also affects the allergenicity of the milk*





➡ Milk processing negatively influences the allergenic potential of the milk

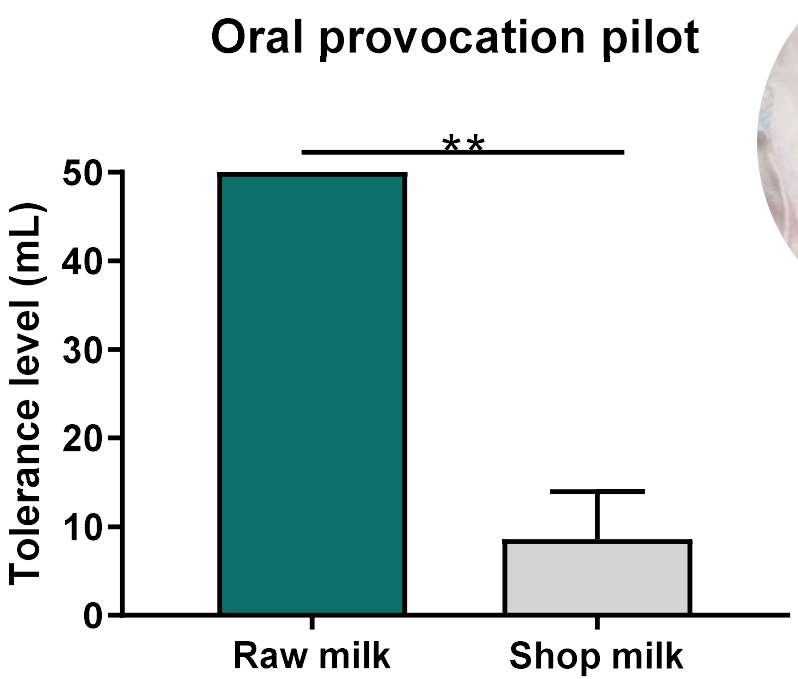
Abbring S *et al., Clinical experimental Allergy (2019)*

Human study (11 children): DBPCT

- Multiple allergic children were tested one by one (June 2009 – Nov 2010)
- 11 children were tested:
  - 2 children shows a negative SPT and could take up both shop and raw milk till 50 ml >> no milk allergy
- 9 children were left:
  - 6 males, 3 females
  - Age: 1.5 years
  - Tot IgE: 155 ku/l; Spec IgE: 10 ku/l
  - Raw vs shop milk: 50 ml vs 8.6 (range 0.5-50; SE = 16.0). P=0.002
  - No pathological reactions on raw milk
  - 1 child: no pathological reactions on shop milk, 8 children: increased rush, eczema, etc immediate or delayed

Abbring S *et al., Clinical experimental Allergy (2019)*

Allergic children showed no allergic symptoms after drinking raw milk



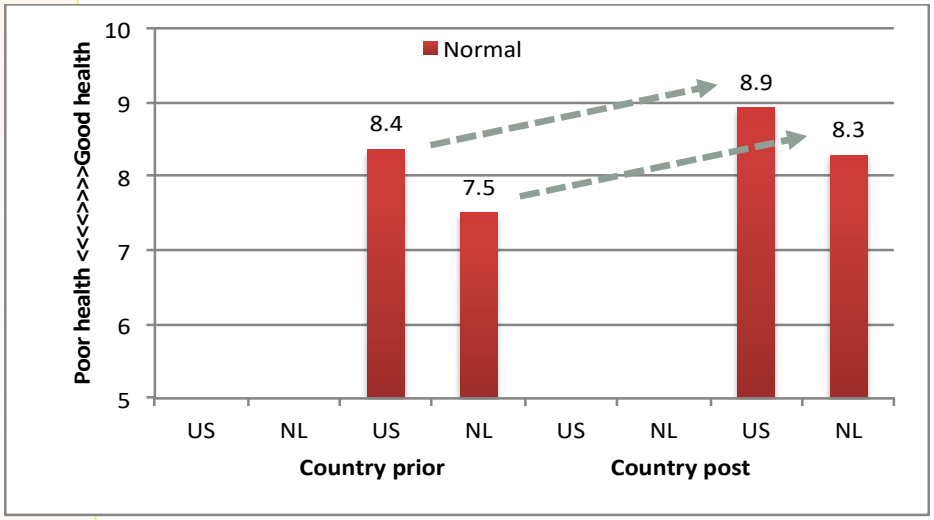
Abbring S *et al., Clinical experimental Allergy (2019)*

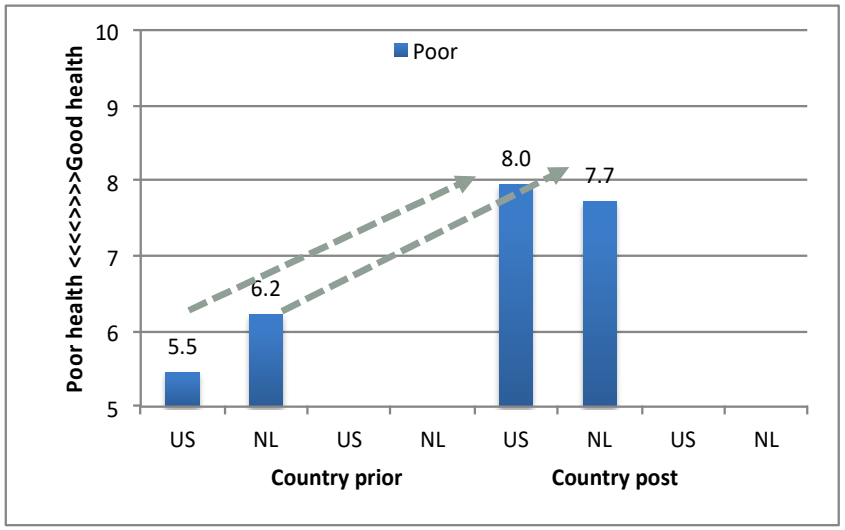
Self evaluation of health changes after RM and RM-kefir consumption

- Questionnaire among 390 NL and 330 US consumers of mainly RM-kefir and RM (Age 54 Y)
- Health score, immunity score, immune status (ISQ), mood, bowel and skin conditions were rated retrospectively based on validated questionnaires.
- Intervention of 2 months
- Participants were in a good health group and poor health based on their perception of health prior to the intervention

Baars et al, Complementary therapies in Medicine2019

Health score after >2 month of RM (US) or Raw milk kefir (NL) consumption





- Adult people, especially those with a poor health status experienced the strongest impact in several parts of their health and mood, after regular consumption of raw and raw fermented drinking milk/kefir.

Baars et al, Complementary therapies in Medicine2019
Baars et al, Nutrition &food science 2019

Conclusion

- Raw cow's milk prevents the development of both asthma and food allergy
  - Observed associations strengthened by causality

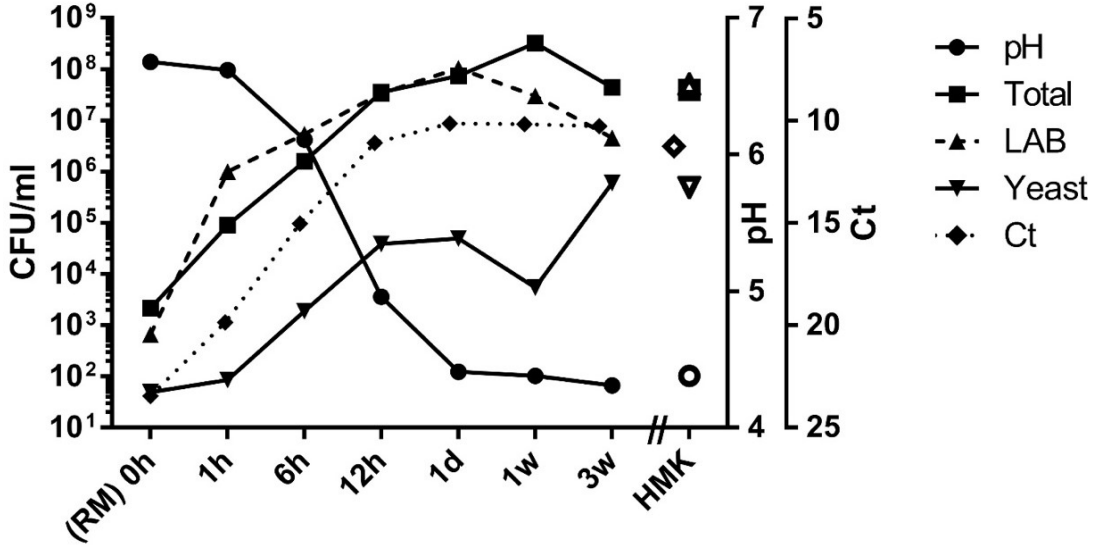
- Protective effect destroyed upon milk processing
  - Heat-treated raw milk showed no asthma-protective effect
  - Commercially available processed milk did not confer protection against food allergic symptoms
  - Heat-sensitive bioactive whey proteins that denature around 65 °C , like alkaline phosphatase and Lactoferrin most likely responsible for the protective effect

→

- Epidemiological evidence confirmed
- We were the first to show the protection against allergic symptoms by raw milk in multiple allergic children
- Improved health by drinking raw milk and raw milk kefir as assessed by validated questionnaires in Adults

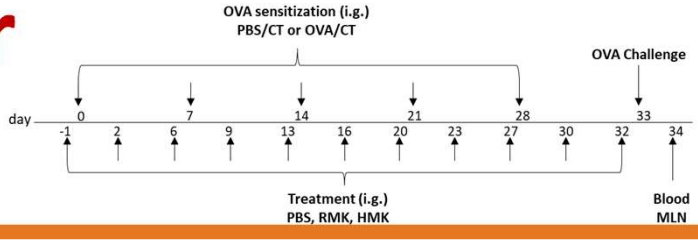
What about health benefits of Raw milk kefir

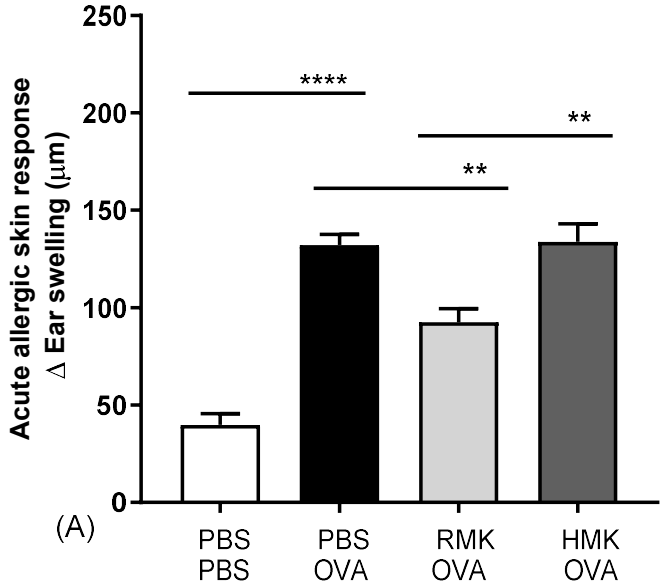
- *To investigate whether raw milk kefir is able to modulate the acute allergic response in a murine ovalbumin (OVA)-induced food allergy model*

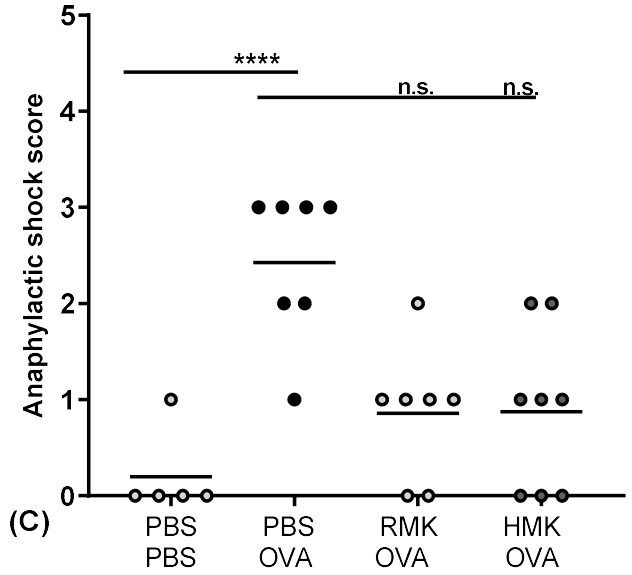


ood&Function (2023)

Effect of raw milk kefir on allergic symptoms

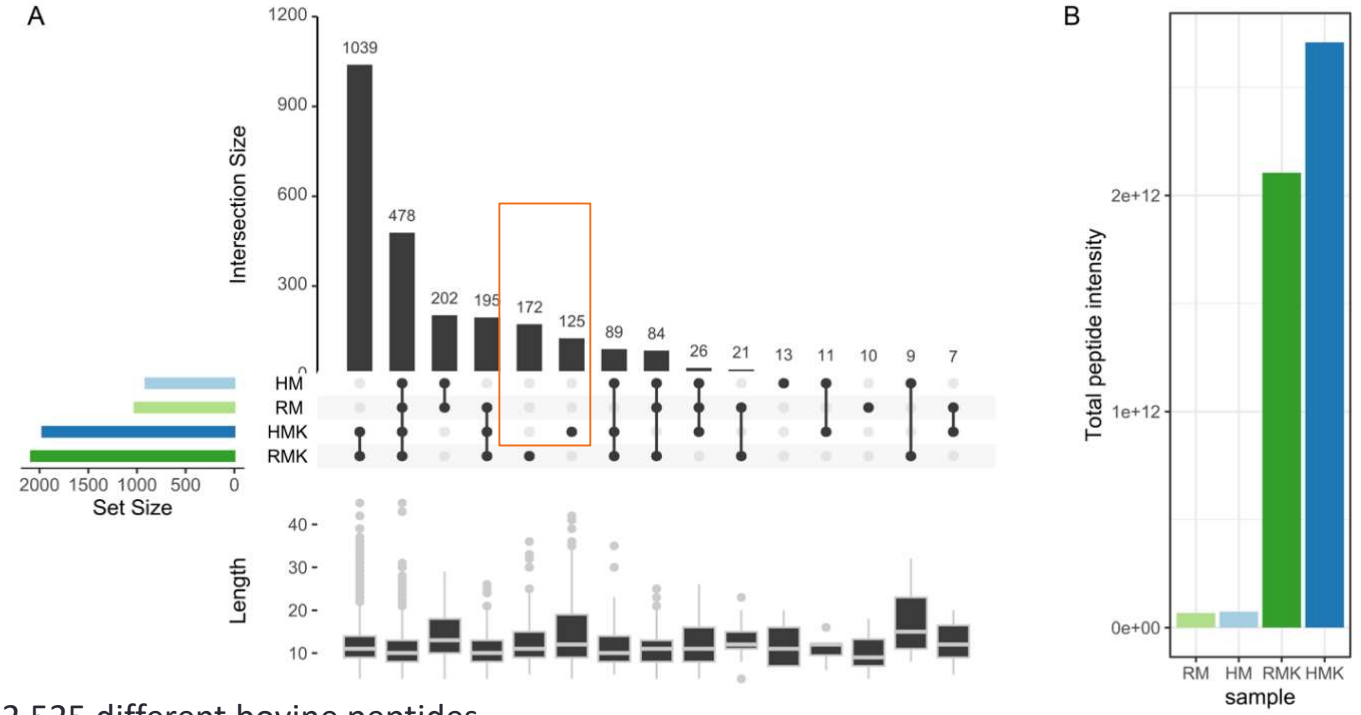






Baars, van Esch et al, Food&Function (2023)

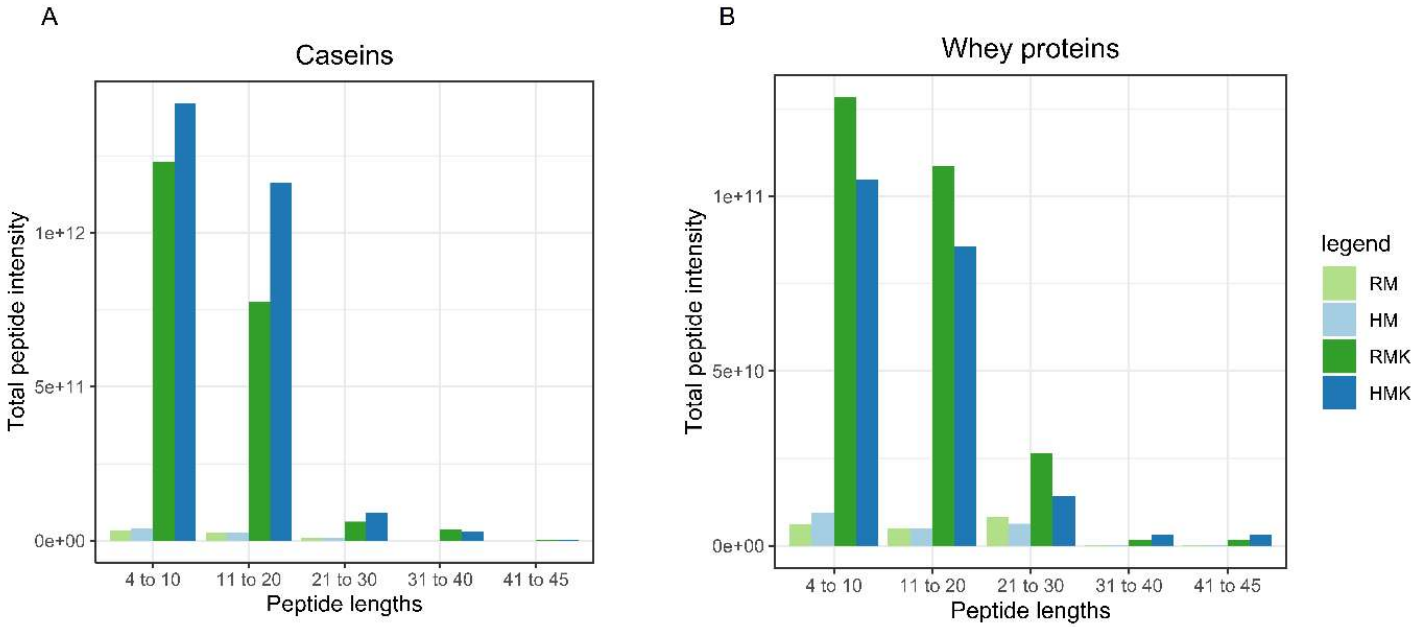
Fermentation of milk increases the number of unique peptides



- 2,525 different bovine peptides
  - 478 peptides were identified in all samples
  - 1,039 peptides were only identified in kefir samples and 202 peptides were only found in milk
  - RMK have a higher number of unique peptides when compared to HMK
  - Nevertheless, the total peptide intensity was higher in HMK than in RMK (Fig B).

Baars, van Esch et al, Food&Function (2023)

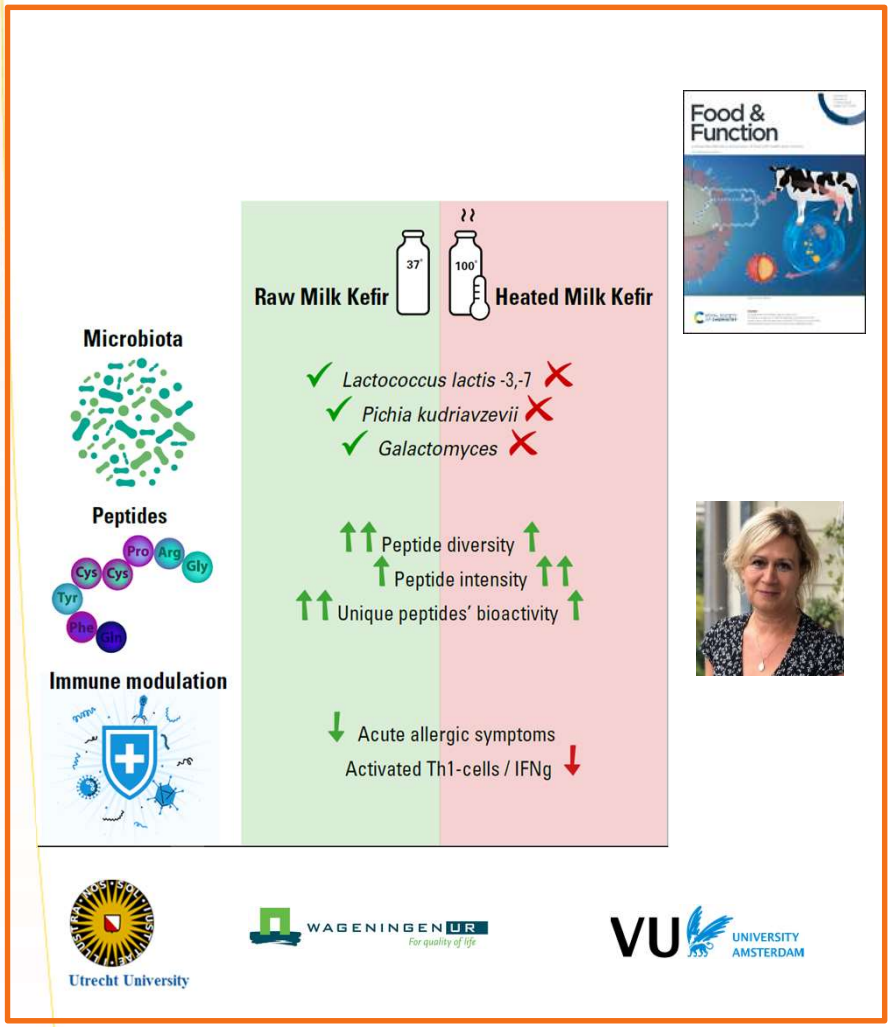
Whey peptides are more abundant in RMK than in HMK



- Whey peptides with a length up to 30 amino acids are more abundant in RMK than in HMK
- The most frequently found bioactivities were ACE-inhibitory, antioxidant, and antimicrobial activity.

Baars, van Esch et al, Food&Function (2023)

Summary raw milk Kefir



- Raw milk kefir reduced acute allergic symptoms
- Raw milk kefir modulated the immune system
- Heated milk kefir showed no effect
- The protective effect on allergic symptoms coincided with increased peptide diversity and microbial diversity

Baars, van Esch et al, Food&Function (2023)

Universiteit Utrecht

Thank you for your attention!

Acknowledgements

Utrecht University

Suzanne Abbring
Johan Garssen
Ton Baars
Pharmacology department

FiBL

Ton Baars

DANONE NUTRICIA RESEARCH | NUTRICIA RESEARCH

Gert Hols
Joseph Thomas Ryan
Sebastien Goeuriot

UNIKASSEL VERSITÄT

Thomas Roos
Daniel Kusche

Philipps Universität Marburg

Daniel Potaczek
Johanna Wolf
Bilal Alashkar Alhamwe
Fahd Alhamdan
Holger Garn
Hani Harb
Harald Renz

WAGENINGEN UNIVERSITY & RESEARCH

Kasper Hettinga
Ling Xiong

Thank you!