



**Innovative pulse and cereal-based food fermentations for human health and sustainable diets**

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## Fermented foods for health- what are the evidences?

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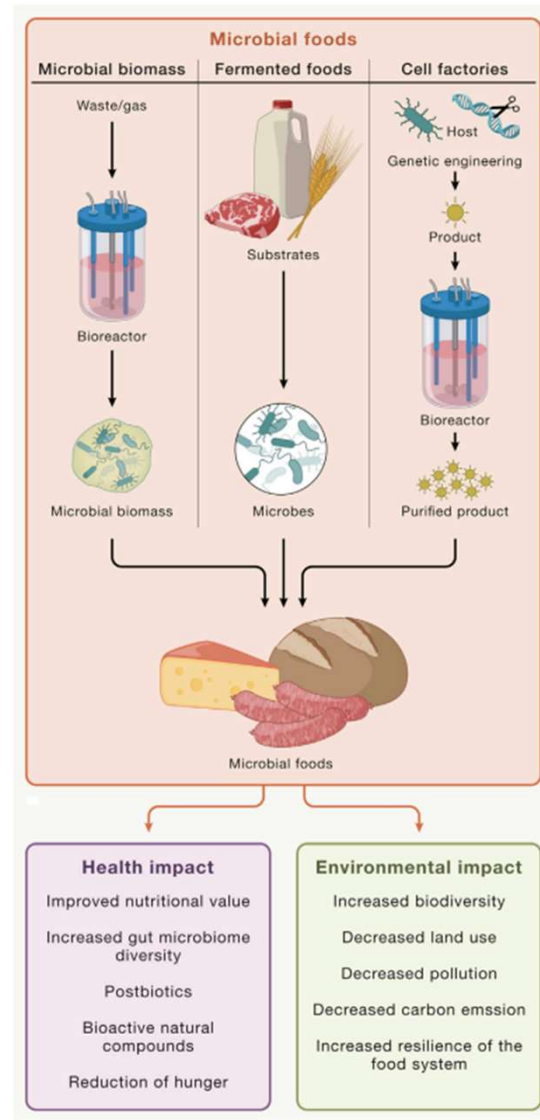
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# Microbioal foods

All types of microbial foods have the potential to positively impact human and planetary health.



**Fermented foods**— traditionally produced from grains, seeds, nuts, legumes, fruit, vegetables, roots, milk, meat, and fish through the controlled transformation by microorganisms.

**Microbial biomass** --- produced from a defined sugar source such as glucose but also possibly from different waste streams or atmospheric gases, followed by the harvesting of microbial biomass and its processing into palatable and safe foods.

**Cell factories** --- defined microorganisms that are selected and (genetically) optimized to produce certain compounds. These compounds are usually purified and used for various applications—such as enzymes for baking.

Jahn et al. (2023) Cell

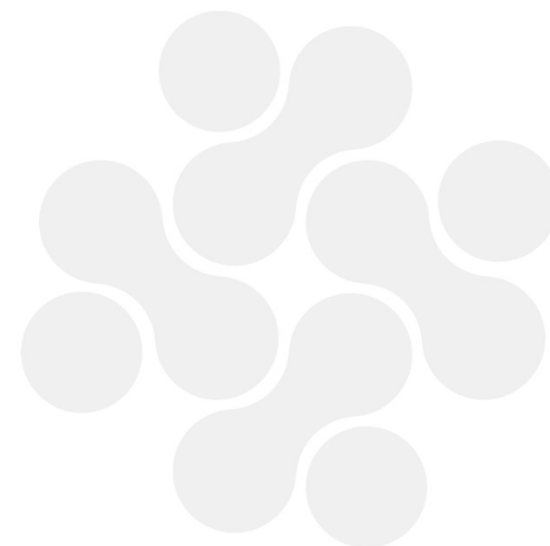
## Fermented foods and beverages

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“Foods made through desired microbial growth and enzymatic conversions of food components”



Marco et al., 2021, The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on fermented foods



## Fermented foods

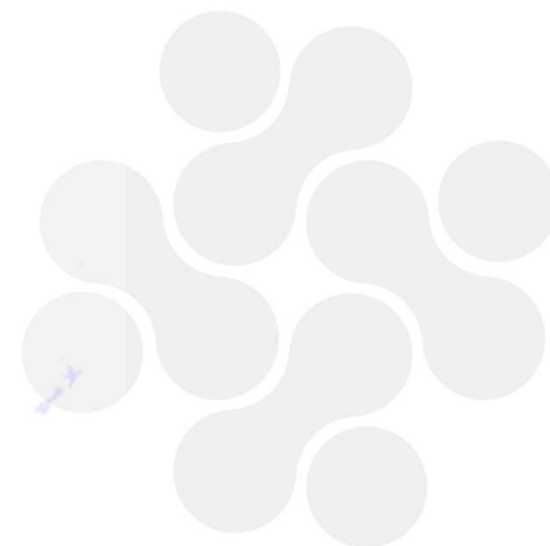
~8000 BC

~1/3 of the world's food consumption

>3500 fermented food products

Milk, cereals, legumes, vegetables,  
the, meat and fish

(Xiang et al., 2019. *Food Science and Human Wellness*)



## Fermented foods

Food stability

Food safety

Sensory characteristics

Perceived health-  
benefits



# Perceived health-benefits of fermented foods

## ARE YOU EATING FERMENTED FOODS?

Target: 4 to 6 servings/day!



**Yogurt**  
(3/4 cup)



**Sauerkraut**  
(2 tablespoons)



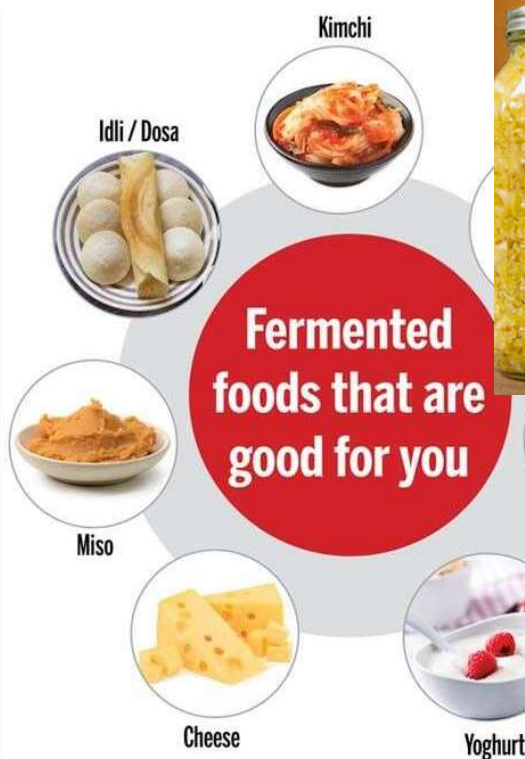
**Kombucha**  
(1 cup)



**Cultured Cottage Cheese**  
(1/2 cup)



**Fermented Veggie**  
(1.5 oz)



## 10 BEST FERMENTED FOODS TO HEAL YOUR GUT

### TOP 10 SUPERFOODS FOR 2018

RDs predict fermented foods like **yogurt, Kefir, Kombucha, sauerkraut, tempeh, pickles, kimchi and miso** will be highly sought by consumers in 2018 because they have **powerful health benefits from boosting gut health**



#1 FERMENTED FOODS



#2 AVOCADO



#3 SEEDS



#4 NUTS



#5 GREEN TEA



#6 ANCIENT GRAINS



#7 KALE



#8 EXOTIC FRUITS



#9 COCONUT PRODUCTS



#10 SALMON

## Recommendations & claims?

- Despite the many ***potential*** benefits of fermented foods, their recommended consumption has not been widely translated to global inclusion in food guides.
- One exception in Asia is the Indian food guide, which stresses the consumption of fermented foods for the public and specifically, for **pregnant women** (“***eat more whole grains, sprouted grams and fermented foods***”)
- Only one claim for beneficial microbes has been approved in the European Union (EU) (yoghurt improves lactose tolerance)

# Description and microbial content of common fermented foods



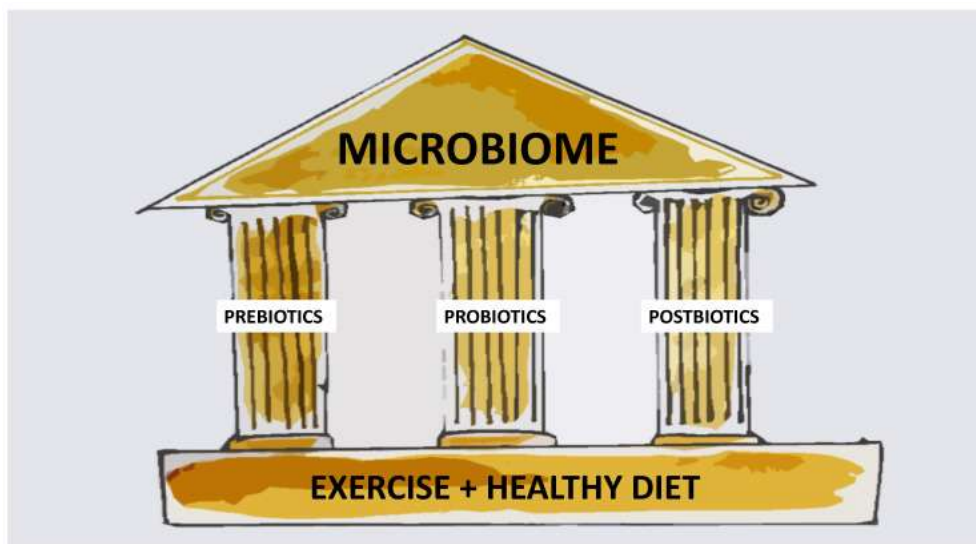
Name	Description	Region of Origin	Source of Microorganisms	Microorganisms Identified in Final Product *
<b>Kefir</b>	Fermented milk beverage	Caucasus	Starter culture	<i>Lactobacillus kefir</i> , <i>Lactobacillus paracasei</i> , <i>Lactobacillus parabuchneri</i> , <i>Lactobacillus casei</i> , <i>Lactobacillus lactis</i> , <i>Lactococcus lactis</i> , <i>Acetobacter lovaniensis</i> , <i>Kluyveromyces Lactis</i> , <i>Saccharomyces cerevisiae</i>
<b>Kombucha</b>	Fermented tea beverage	China	Starter culture	<i>Komagataeibacter xylinus</i> , <i>Saccharomyces cerevisiae</i> , <i>Zygosaccharomyces bailii</i> , <i>Brettanomyces bruxellensis</i> , <i>Acetobacter pasteurianus</i> , <i>Acetobacter aceti</i> , <i>Saccharomyces cerevisiae</i> , <i>Zygosaccharomyces bailii</i> , <i>Brettanomyces bruxellensis</i> , <i>Acetobacter xylinum</i> , <i>Zygosaccharomyces spp.</i> , <i>Acetobacter</i> , <i>Gluconacetobacter</i>
<b>Sauerkraut</b>	Fermented cabbage	China	Spontaneous	<i>Lactobacillus sakei</i> , <i>L. plantarum</i> , <i>Candidatus accumulibacter phosphatis</i> , <i>Thermatoga spp.</i> , <i>Pseudomonas rhizosphaerae</i> , <i>L. hokkaidonensis</i> , <i>L. rhamnosus</i> , <i>Leuconostoc carnosum</i> , <i>Clostridium saccharobutylicum</i> , <i>Rahnella aquatilis</i> , <i>Citrobacter freundii</i> , <i>Enterobacter cloacae</i> , <i>Bifidobacterium dentium</i> , <i>Enterococcus faecalis</i> , <i>Lactobacillus casei</i> , <i>Lactobacillus delbrueckii</i> , <i>Staphylococcus epidermidis</i> , <i>Lactobacillus curvatus</i> , <i>Lactobacillus brevis</i> , <i>Weissella confusa</i> , <i>Lactococcus lactis</i> , <i>Enterobacteriaceae</i> , <i>Leuconostoc spp.</i> , <i>Yarrowia brassicae</i>
<b>Tempeh</b>	Fermented boiled and dehulled soybeans	Indonesia	Starter culture ( <i>Rhizopus oligoporus</i> )	<i>Enterococcus faecium</i> , <i>Rhizopus oryzae</i> , <i>Rhizopus oligoporus</i> , <i>Mucor indicus</i> , <i>Mucor circinelloides</i> , <i>Geotrichum candidum</i> , <i>Aureobasidium pullulans</i> , <i>Alternaria alternata</i> , <i>Cladosporium oxysporum</i> , <i>Trichosporon beigelii</i> , <i>Clavispora lusitaniae</i> , <i>Candida maltosa</i> , <i>Candida intermedia</i> , <i>Yarrowia lipolytica</i> , <i>Lodderomyces elongisporus</i> , <i>Rhodotorula mucilaginosa</i> , <i>Candida sake</i> , <i>Hansenula fabiani</i> , <i>Candida tropicalis</i> , <i>Candida parapsilosis</i> , <i>Pichia membranefaciens</i> , <i>Rhodotorula rubra</i> , <i>Candida rugosa</i> , <i>Candida curvata</i> , <i>Hansenula anomala</i>
<b>Natto</b>	Fermented soybean	Japan	Starter culture ( <i>Bacillus subtilis natto</i> )	Data not available
<b>Miso</b>	Fermented soybean paste	Japan	Starter culture ( <i>Aspergillus oryzae</i> )	<i>Bacillus subtilis</i> , <i>Bacillus amyloliquefaciens</i> , <i>Staphylococcus gallinarum</i> , <i>Staphylococcus kloosii</i> , <i>Lactococcus sp. GM005</i>
<b>Kimchi</b>	Fermented vegetable dish	Korea	Spontaneous, Addedcommercially	<i>Leuconostoc gasicomitatum</i> , <i>Leuconostoc gelidum</i> , <i>Leuconostoc mesenteroides</i> , <i>Weissella koreensis</i> , <i>Weissella confuse</i> , <i>Lactobacillus sakei</i> , <i>Lactobacillus plantarum</i> , <i>Lactobacillus curvatus</i> , <i>Trichosporon domesticum</i> , <i>Trichosporon loubieri</i> , <i>Saccharomyces unisporus</i> , <i>Pichia kluyveri</i>
<b>Sourdough bread</b>	Bread made from longer ferment	Middle East and Europe	Spontaneous or backslopping	Data not available

Dimidi et al. (2019)



## Perceived health-benefits of fermented foods

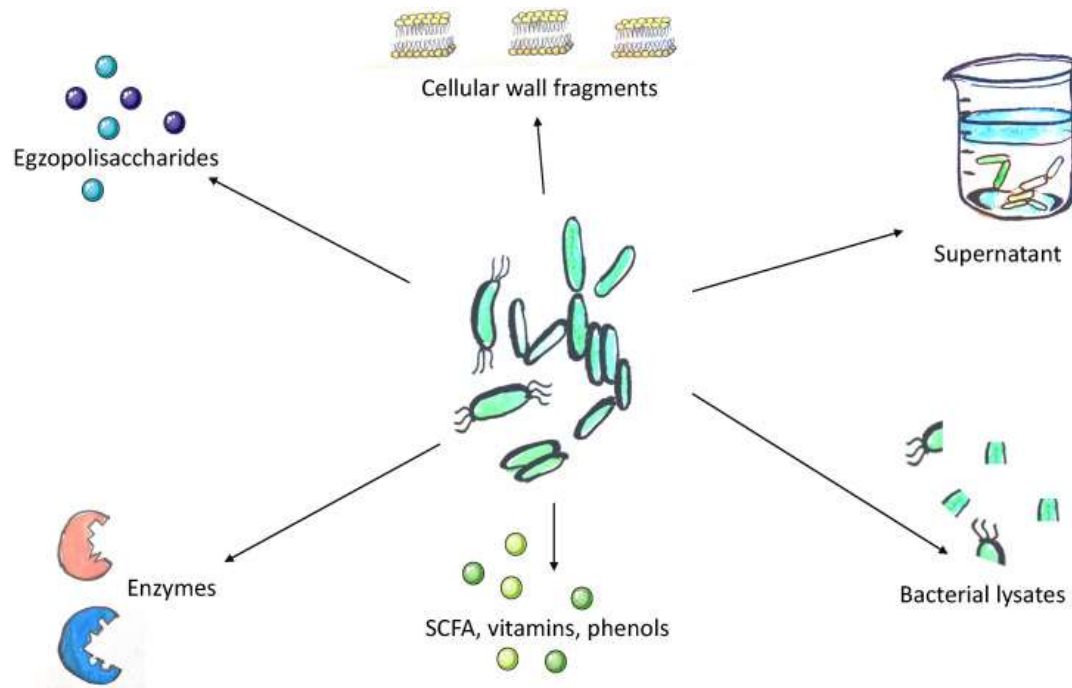
- Little is known
- Observational studies, few intervention trials
- Yoghurt



Żółkiewicz et al. (2020) Nutrients



# Postbiotics



Żółkiewicz et al. (2020) Nutrients

**Postbiotics-** Preparation of inanimate microorganisms and/or their components that confers a health benefit on the host.

Effective postbiotics must contain ***inactivated microbial cells*** or ***cell components***, with or without ***metabolites***, that contribute to observed ***health benefits***

Salminen et al. (2021) Nat Rev Gastroenterol Hepatol.

# Products of gut microbial fermentation of carbohydrates, protein and dietary polyphenols

Mediators of health effects?

Metabolite	Pathway	Genera or species
Acetate	Pyruvate decarboxylation to acetyl-CoA	<i>Akkermansia muciniphila</i> , <i>Bacteroides</i> spp., <i>Bifidobacterium</i> spp., <i>Prevotella</i> spp., <i>Ruminococcus</i> spp. <sup>21,26-28</sup>
	Wood-Ljungdahl pathway	<i>Blautia hydrogenotrophica</i> , <i>Clostridium</i> spp., <i>Streptococcus</i> spp. <sup>21,26-28</sup>
Propionate	Acrylate pathway	<i>Coprococcus catus</i> , <i>Eubacterium hallii</i> , <i>Megasphaera elsdenii</i> , <i>Veillonella</i> spp. <sup>21,26-28</sup>
	Succinate pathway	<i>Bacteroides</i> spp., <i>Dialister</i> spp., <i>Phascolarctobacterium succinatutens</i> , <i>Veillonella</i> spp. <sup>21,26-28</sup>
	Propanediol pathway	<i>Roseburia inulinivorans</i> , <i>Ruminococcus obeum</i> , <i>Salmonella enterica</i> <sup>21,26-28</sup>
Butyrate	Classical pathway via butyrate kinase	<i>Coprococcus comes</i> , <i>Coprococcus eutactus</i> <sup>21,26-28</sup>
	Alternate pathway using exogenous acetate	<i>Anaerostipes</i> spp., <i>C. catus</i> , <i>E. hallii</i> , <i>Eubacterium rectale</i> , <i>Faecalibacterium prausnitzii</i> , <i>Roseburia</i> spp. <sup>21,27,28,35</sup>
Short-chain fatty acids and branched-chain fatty acids	Amino acid fermentation through various dissimilatory proteolytic reactions	<i>Acidaminococcus</i> spp., <i>Acidaminobacter</i> spp., <i>Campylobacter</i> spp., <i>Clostridia</i> spp., <i>Eubacterium</i> spp., <i>Fusobacterium</i> spp., <i>Peptostreptococcus</i> spp. <sup>21,26-28,44</sup>
'Kynurenines' (kynurenine and its derivatives)	Various bacterial enzymes homologous to mammalian enzymes of the kynurenine pathway	<i>Lactobacillus</i> spp., <i>Pseudomonas aeruginosa</i> <sup>49</sup> , <i>Pseudomonas fluorescens</i> <sup>51</sup> Putative: <i>Pseudomonas</i> spp., <i>Xanthomonas</i> spp., <i>Burkholderia</i> spp., <i>Stenotrophomonas</i> spp., <i>Shewanella</i> spp., <i>Bacillus</i> spp., members of <i>Rhodobacteraceae</i> , <i>Micrococcaceae</i> and <i>Halomonadaceae</i> families <sup>45</sup>
Indole	Hydrolytic $\beta$ -elimination of tryptophan to indole (tryptophanase)	<i>Achromobacter liquefaciens</i> , <i>Bacteroides ovatus</i> , <i>Bacteroides thetaiotamicron</i> , <i>Escherichia coli</i> , <i>Paracolobactrum coliforme</i> , <i>Proteus vulgaris</i> <sup>1,3,4</sup>
Indole derivatives	Multiple	<i>Bacteroides</i> spp., <i>Clostridium</i> spp. ( <i>Clostridium sporogenes</i> , <i>Clostridium cadaveris</i> , <i>Clostridium bartlettii</i> ), <i>E. coli</i> , <i>Lactobacillus</i> spp., <i>E. hallii</i> , <i>Parabacteroides distasonis</i> , <i>Peptostreptococcus</i> spp. ( <i>Peptostreptococcus anaerobius</i> ) <sup>5,11,16,167</sup>
Tryptamine	Decarboxylation of tryptophan	<i>C. sporogenes</i> , <i>Ruminococcus gnavus</i> <sup>108</sup>
Serotonin	Induction of host synthesis'	Indigenous spore-forming bacteria, dominated by <i>Clostridium</i> spp. <sup>50</sup> and <i>Turicibacter</i> spp. <sup>103</sup>
Histamine	Decarboxylation of histidine (histidine decarboxylase (HDC))	<i>E. coli</i> , <i>Morganella morganii</i> , <i>Lactobacillus vaginalis</i> <sup>105</sup> Putative: <i>Fusobacterium</i> spp. <sup>103</sup>
Imidazole propionate (ImP)	Non-oxidative deamination of histidine to urocanate followed by reduction of urocanate to ImP by urocanate reductase (UrdA)	<i>Aerococcus urinae</i> , <i>Adlercreutziaae equolifaciens</i> , <i>Anaerococcus prevotii</i> , <i>Brevibacillus laterosporus</i> , <i>Eggerthella lenta</i> , <i>Lactobacillus paraplantarum</i> , <i>Shewanella oneidensis</i> , <i>Streptococcus mutans</i> <sup>106</sup>
Dopamine	Decarboxylation of levodopa (L-DOPA) via tyrosine decarboxylase (TyrDC)	<i>Enterococcus</i> spp. ( <i>Enterococcus faecalis</i> , <i>Enterococcus faecium</i> , 77 human isolates of <i>Enterococcus</i> spp.), <i>Lactobacillus brevis</i> , <i>Helicobacter pylori</i> <sup>103,108</sup>
p-Cresol	From tyrosine or phenylalanine via two pathways: direct cleavage of the Ca-C $\beta$ bond in tyrosine to yield p-cresol by tyrosine lyase; and a series of reactions involving transamination, deamination and decarboxylation of tyrosine or phenylalanine via formation of the cresol precursor phenylacetic acid <sup>5,109</sup>	Assay proven: <i>Blautia hydrogenotrophica</i> , <i>Clostridioides difficile</i> , <i>Olsenella uli</i> , <i>Romboutsia lituseburensis</i> <sup>109</sup> Predicted: <i>Acidaminococcus fermentans</i> , <i>Anaerococcus vaginalis</i> , <i>Anaerostipes</i> spp., <i>Bacteroides</i> spp., <i>Bifidobacterium infantis</i> , <i>Blautia</i> spp., <i>Citrobacter koseri</i> , <i>Clostridium</i> spp., <i>Eubacterium siraeum</i> , <i>Fusobacterium</i> spp., <i>Klebsiella pneumoniae</i> , <i>Lactobacillus</i> spp., <i>M. elsdenii</i> , <i>Roseburia</i> spp., <i>Ruminococcus</i> spp., <i>Veillonella parvula</i> <sup>109</sup>
Phenylacetylglutamine (PAGln) and phenylacetyl glycine (PAGly)	Synthesized during host hepatic phase II metabolism via conjugation of either glutamine or glycine to phenylacetic acid, an intermediate in microbial fermentation of phenylalanine <sup>5,117</sup>	Conjugation of phenylacetic acid to glutamine or glycine occurs in the host liver; see p-cresol (above) for information about its precursor, phenylacetic acid



Krautkrame et al. (2021) Nature Reviews

# Health-benefits of fermented foods - yoghurt



Table 2 Summary of studies

Area studied	Total no. of studies	Study types	No. of positive-quality studies	No. of neutral-quality studies	No. of negative-quality studies	Fermented products studied	Comparators	No. of studies with favorable outcome	No. of studies with no significant effect	No. of studies with unfavorable outcome
Gastrointestinal health and disease	26	RCT=16 RCOT=8 CS=1	19	6	1	Yogurt, fermented milk, fermented milk drinks, pasteurized yogurt, probiotic yogurt, kefir	Dahi, ultra-heat-treated yogurt, non-fermented dairy product, milk, pasteurized yogurt, acidified	20	6	0
Cancer	17	RCT=1 CC=5 CH=11	1	16	0	Yogurt, fermented milk	No yogurt	16	11	1
Diabetes	9	RCT=1 RCOT=2 CS=1 CH=5	2	5	1	Yogurt, probiotic in fermented milk	Sweetened yogurt, skim milk, orange juice, no supplementation, nonfermented milk	19	3	0
Bone health	7	RCT=1 CS=3 CH=3	1	6	0	Yogurt, laban	No yogurt	9	5	3
								7	1	0
								5	2	0

## CONCLUSIONS

Consistent associations exist between **fermented milk consumption** and **reduced risk of breast and colorectal cancer, T2D, improved weight maintenance, and improved cardiovascular, bone, and GI health.**

Associations between yoghurt and reduced risk of:

- Breast and colon cancer
- Type 2 diabetes
- Improved weight management
- Improved inflammatory markers, cardiovascular, bone, and GI health

Savaiano, 2020, *Nutrition Reviews*  
 SaediFard, 2019, *Clinical Nutrition ESPEN*  
 Baruah, 2022, *Journal of Applied Microbiology*

Abbreviations: CC, case-control (study); CH, cohort (study); CS, cross-sectional (study); NRCT, nonrandomized controlled trial; RCOT, randomized crossover trial; RCT, randomized controlled trial.

# Effects of Kefir on gastrointestinal health (intervention studies)



Study	Study Design	Study Population	Intervention	Control	Duration	Gut Microbiota	Other Findings
Ino et al., 2015 [58]	Non-randomised, cross-over controlled intervention	Constipation, <i>n</i> = 11	6 g/day lyophilized kefir. 3 g/day lactose in last 40 day of treatment period	6 g/day powdered milk (baby-formula)	3 months	Not reported	Only three of the 11 participants experienced "more frequent BM without laxative use". Summary descriptive statistics not shown.
Maki et al., 2018 [59]	Non-randomised, cross-over intervention study	Constipation (hospitalised), <i>n</i> = 42	6 g/day of lyophilized kefir	6 g/day powdered milk	12 weeks each period	Not reported	No difference in laxative use between kefir and control groups (7.5 times/3 months vs 8.1 times/3 months; <i>p</i> = 0.35). No difference in number of people who did not require laxatives. No difference in stool consistency/volume.
Turan et al., 2014 [60]	Non-randomised, uncontrolled intervention study	Functional constipation, <i>n</i> = 20	500 mL/day kefir	-	4 weeks	Not reported	Increased stool frequency at follow-up compared to baseline (median 2 BM/week vs 5 BM/week; <i>p</i> < 0.001). Fewer people with hard stools at follow-up compared to baseline (12/20 vs 6/20; <i>p</i> = 0.014). Improvement in bowel satisfaction scores ( <i>p</i> = 0.001). Reduction in gut transit time in participants with slow gut transit time at baseline ( <i>p</i> = 0.013). No change in straining or laxative use. No major adverse events.
Bekar et al., 2011 [61]	Double-blind RCT	Dyspepsia and <i>H. pylori</i> infection, <i>n</i> = 85	500 mL/day kefir	250 mL/day milk	2 weeks	Not reported	Higher <i>H. pylori</i> eradication rate in kefir vs control (78% vs 50%; <i>p</i> = 0.026). Lower occurrence of diarrhoea (relative risk RR = 0.48; <i>p</i> = 0.001), headache (RR=0.17; <i>p</i> = 0.008), nausea (RR = 0.47; <i>p</i> = 0.029), and abdominal pain (RR = 0.38; <i>p</i> < 0.001).
Hertzler et al., 2003 [57]	Cross-over RCT	Lactose malabsorption, <i>n</i> = 15	1) 508 mL/day plain kefir 2) 519 g/day raspberry flavoured kefir (equivalent to 20 g lactose)	3) 407 mL/day low fat cow's milk 4) 378 g/day plain yoghurt (equivalent to 20 g lactose)	Acute 5-day study, each treatment followed by an 8 h breath H <sub>2</sub> test	Not reported	Higher breath H <sub>2</sub> AUC in milk compared with plain kefir ( <i>p</i> = 0.001), plain yogurt ( <i>p</i> = 0.001), or flavoured yogurt ( <i>p</i> = 0.005). Higher breath hydrogen AUC in flavoured kefir compared to plain yogurt ( <i>p</i> = 0.043) or plain kefir ( <i>p</i> = 0.008). No difference in breath hydrogen AUC between flavoured kefir and milk ( <i>p</i> = 0.425) or flavoured yogurt ( <i>p</i> = 0.331). No difference in flatulence severity and frequency, diarrhoea and abdominal pain.

Dimidi et al. (2019) Nutrients

# Effects of sauerkraut, soy products and kimchi in gastrointestinal health and disease (interventions)



Study	Fermented Food	Study Design	Study Population	Intervention	Control	Duration	Gut Microbiota	Other Findings
Fujisawa et al., 2006 [104]	Natto/miso	Uncontrolled open-label study	Healthy, n = 8	200 mL miso soup containing 50 g Natto per day	-	2 weeks	Following natto-containing soup: Higher <i>Bifidobacteria</i> and Bacilli, Lower Enterobacteriaceae, Higher acetic acid and propionic acid (all $p < 0.05$ )	-
Kil et al, 2004 [105]	Kimchi	Non-randomised trial	<i>H. pylori</i> infection, n = 6	300 g of kimchi	60 g of kimchi	4 weeks	Increased <i>Lactobacillus</i> ( $p = 0.0003$ ) and <i>Leuconostoc</i> ( $p = 0.0004$ )	<i>H. pylori</i> not eradicated in any participants ( $p = 0.944$ ). Lower stool pH ( $p = 0.0001$ ), $\beta$ -glucuronidase ( $p = 0.0065$ ) and $\beta$ -glucosidase ( $p = 0.0001$ ) activity
Mitsui et al., 2006 [106]	Natto	Controlled trial	Infrequent bowel movements, n = unknown	50 g/day Natto ( <i>Bacillus subtilis</i> K-2, $3.8 \times 10^9$ CFU)	50 g/day boiled soybeans	2 weeks	Following Natto compared to control: Increased ratio of stool <i>Bifidobacteria</i> :total bacteria	Following Natto compared to control: Higher number of bowel movements. Higher number of days with bowel movements Higher stool quantity
Nielsen et al., 2018 [18]	Sauerkraut	Randomised, double-blind controlled trial	Irritable bowel syndrome, n = 58	75 g/day unpasteurised sauerkraut containing LAB	75 g/day pasteurised sauerkraut	6 weeks	No significant effects of either unpasteurised or pasteurised sauerkraut on microbiota composition	Lower IBS-SSS score following both unpasteurised ( $p = 0.003$ ) and pasteurised ( $p = 0.04$ ) sauerkraut No difference in change in IBS-SSS between groups

LAB, lactic acid bacteria; IBS-SSS Irritable Bowel Syndrome Severity Scoring System.

# Effects of sourdough bread in gastrointestinal health and disease

Study	Study Design	Study Population	Intervention	Control	Duration	Other Findings
Korem et al., 2017 [170]	Randomised crossover trial	Healthy, <i>n</i> = 20	145 g sourdough wholegrain wheat bread	110 g white wheat bread	1 week	Significant interpersonal variability in glycaemic responses Baseline microbiome could predict type of bread that results in lower glycaemic response in each participant
Polese et al., 2018 [171]	Double-blind, cross-over RCT	Healthy, <i>n</i> = 17	2 sourdough croissants	2 brewer's yeast croissants	Single study day	11% decrease in gastric volume AUC 3 h post-consumption ( <i>p</i> = 0.02) 30% lower hydrogen production during the 4 h post-consumption ( <i>p</i> = 0.03) Milder abdominal discomfort ( <i>p</i> = 0.002), bloating ( <i>p</i> = 0.001) and nausea ( <i>p</i> = 0.004)
Raninen et al., 2017 [172]	Randomised cross-over trial	Minor gastrointestinal symptoms, <i>n</i> = 8	6–10 slices/day of sourdough wholegrain rye bread	6–10 slices/day of wheat bread enriched with bioprocessed (fermented) rye bran	4 weeks	Significant difference in exhaled breath volatile organic compound profile between groups in fasting state ( <i>p</i> = 0.026). No difference was shown at 30, 60 and 120 min after a standardised meal
Laatikainen et al., 2016 [11]	Randomised, double-blinded, cross-over trial	Irritable bowel syndrome, <i>n</i> = 87	7–8 slices/day low FODMAP sourdough rye bread	7–8 slices/day traditional sourdough rye bread	4 weeks	Lower breath H <sub>2</sub> in low FODMAP rye bread group compared to traditional rye bread (median AUC 53 ppm vs 73; <i>p</i> = 0.01) Milder flatulence ( <i>p</i> = 0.04), abdominal cramps ( <i>p</i> = 0.01), rumbling ( <i>p</i> = 0.001) and total symptoms ( <i>p</i> = 0.02) No difference in IBS-SSS ( <i>p</i> = 0.40). Lower weight in low FODMAP rye bread compared to traditional rye bread (mean difference –0.5 kg, 95% CI –0.9 –0.0; <i>p</i> = 0.03)
Laatikainen et al., 2017 [164]	Double-blinded RCT	Irritable bowel syndrome with subjective wheat intolerance, <i>n</i> = 26	6 slices/day sourdough wheat bread (fermentation time > 12 h)	6 slices/day yeast-fermented wheat bread (fermentation time approx. 2 h)	7 days	No difference in gastrointestinal symptoms or markers of low-grade inflammation. Worse symptoms of tiredness ( <i>p</i> = 0.01), joint symptoms ( <i>p</i> = 0.03) and “decreased alertness” ( <i>p</i> = 0.003)
Di Cagno et al., 2010 [173]	Non-randomised, uncontrolled study	Coeliac disease, <i>n</i> = 8	200 g/day baked products with sourdough wheat flour (10 g hydrolysed gluten)	None	60 days	All patients had normal IgG and IgA-AGA and IgA-tTG antibodies values at the end of the intervention period
Mandile et al., 2017 [174]	RCT	Coeliac disease, <i>n</i> = 20	Sourdough wheat bread (fermented with lactobacilli and yeast)	Traditional wheat bread	3 days	No increase in INF-γ secretion Mobilisation of INF-γ secreting cells in the blood following traditional wheat bread

IBS-SSS Irritable Bowel Syndrome Severity Scoring System; RCT, randomized controlled trial.

## Fermented foods and gastrointestinal health

### In summary:

- Very limited evidence on the effectiveness of most fermented foods in gastrointestinal health
- Majority of studies being of low quality
- Kefir most studied
  - Lactose malabsorption
  - H Pylori eradication





# Metabolic effects of fermented vs non-fermented rye crisp bread



RESEARCH ARTICLE

## Effects of Unfermented and Fermented Whole Grain Rye Crisp Breads Served as Part of a Standardized Breakfast, on Appetite and Postprandial Glucose and Insulin Responses: A Randomized Cross-over Trial

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### AIMS:

- Difference between fermented and unfermented bread?
  - Appetite
  - Glycemia

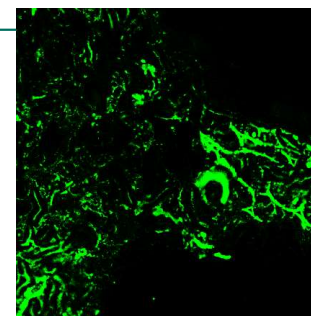
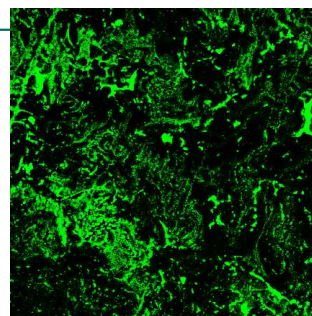
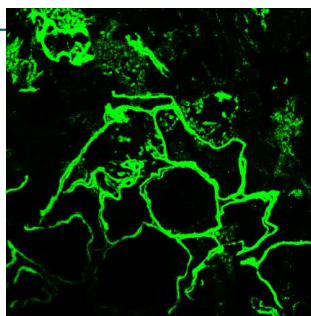


Unfermented whole grain rye  
crisp bread

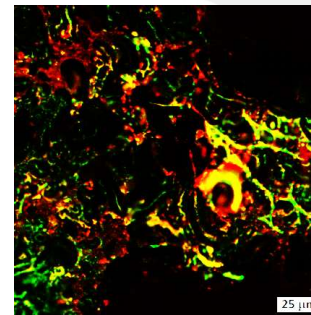
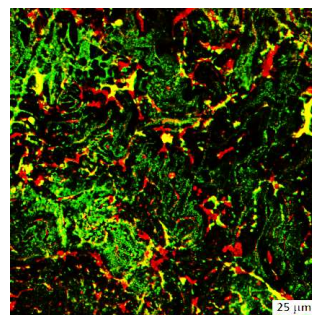
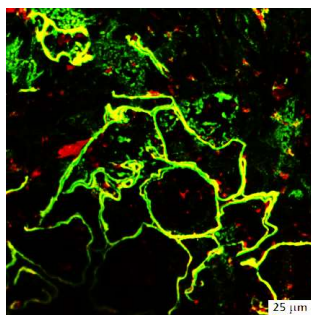
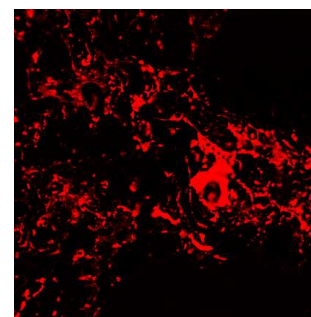
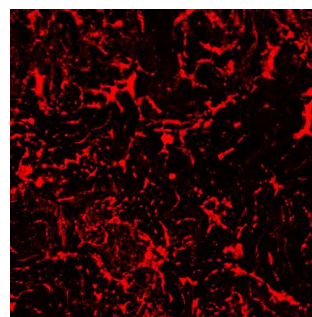
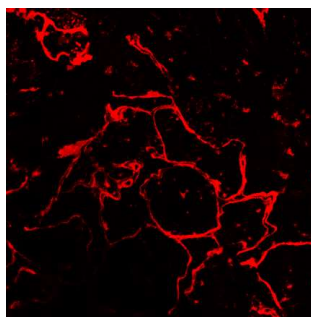
Fermented whole grain rye  
crisp bread

Refined wheat crisp  
bread

1-3,1-4- $\beta$ -D-  
glucans

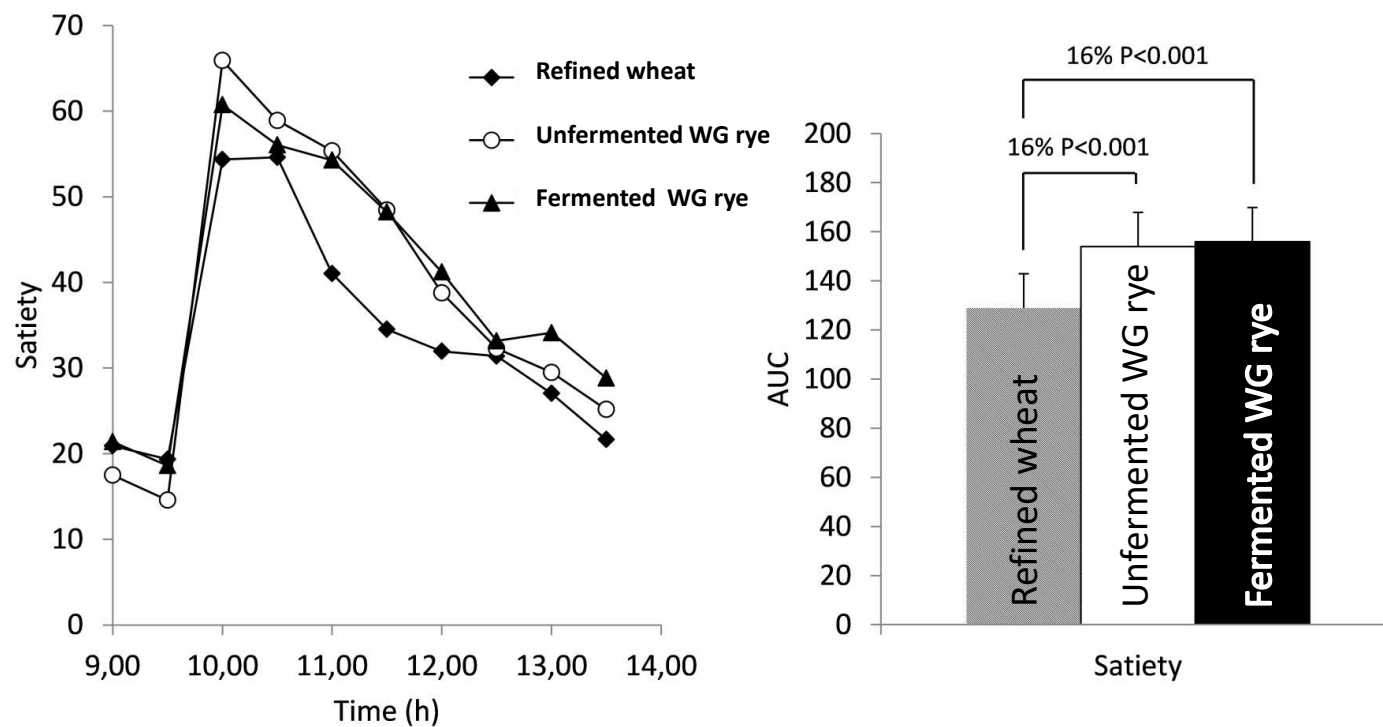


Arabinoxylans  
LM11 antibody



José Luis Vázquez Gutiérrez and Maud Langton

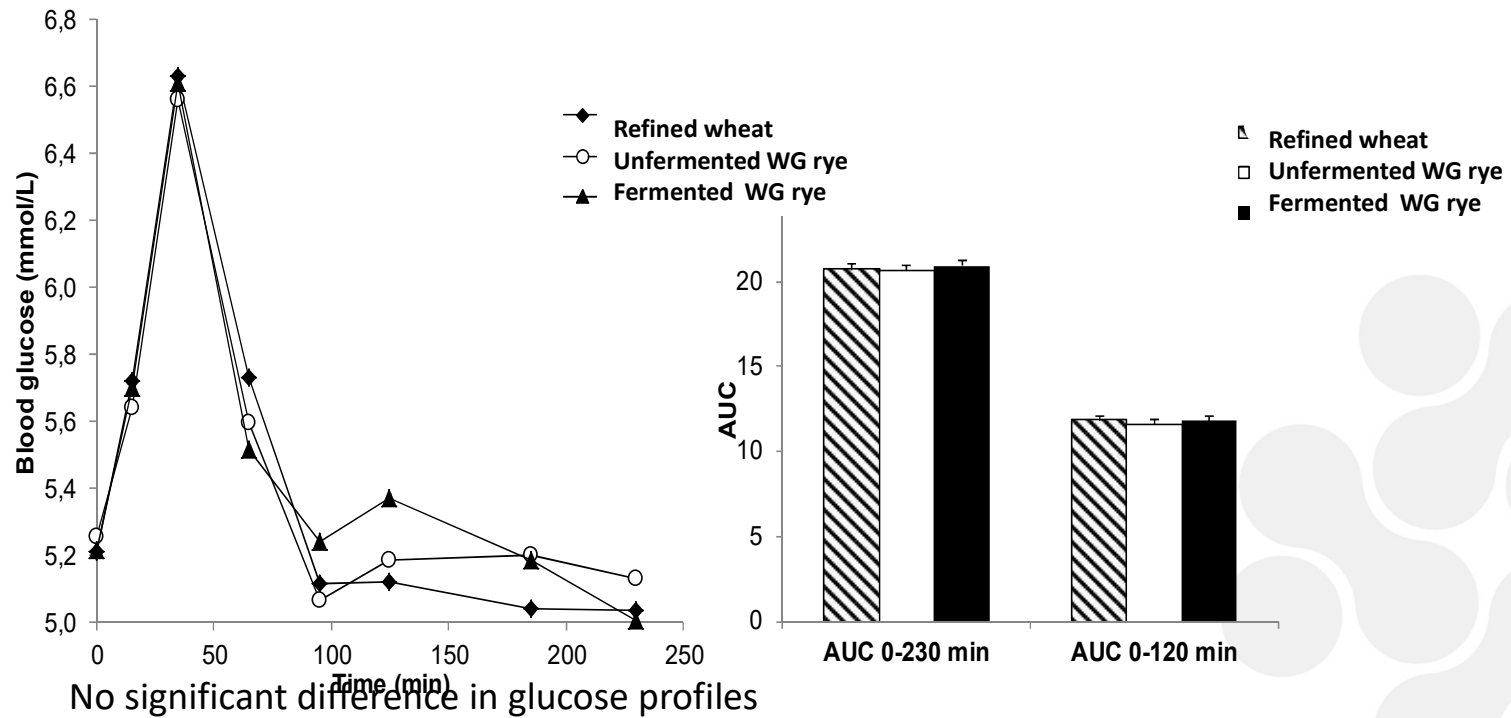
# Results- Satiety



Differences between White- Husman & White- Delikatess (P<0.001)

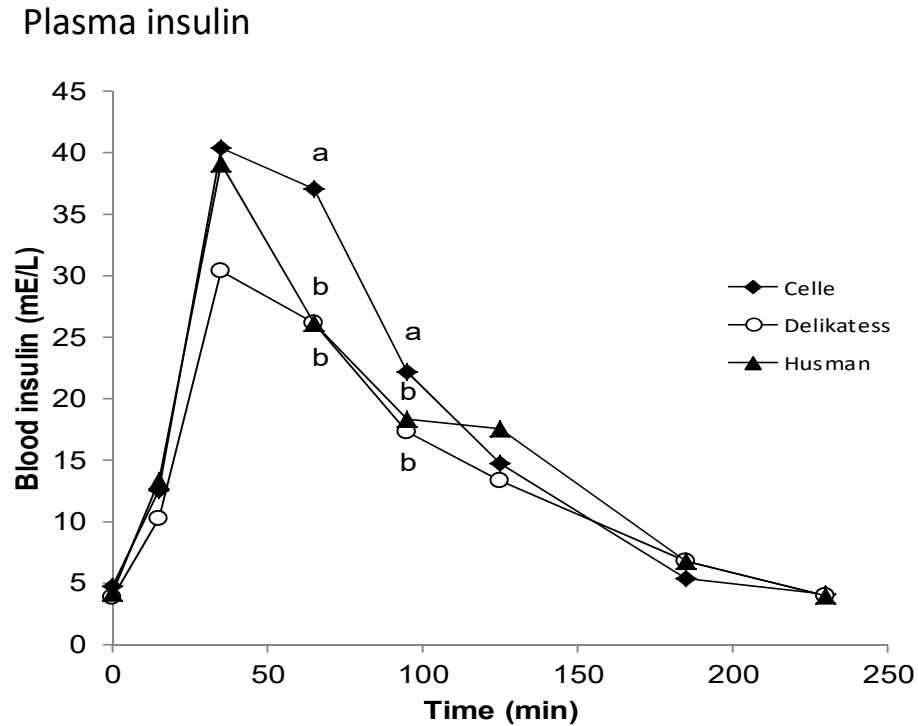
D. Johansson, I Lee, U Risérus, M Langton, R Landberg (2015) PloS One

# Results- Glucose



D. Johansson, I Lee, U Risérus, M Langton, R Landberg (2015) PloS One

# Lower insulin secretion after rye- The "rye factor"-effect



Significant differences at certain time points (treatment x time  $P < 0.05$ )



# Follow-up study "Crisp II"



## AIMs:

- Confirm effects of uRCB on appetite and postprandial insulin responses
- Evaluate the role of sourdough fermented rye crisp bread on appetite and metabolic effects



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doi:10.1017/S000711451700263X

## Impact of sourdough fermentation on appetite and postprandial metabolic responses – a randomised cross-over trial with whole grain rye crispbread

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<sup>1</sup>Department of Molecular Sciences, BioCenter, Swedish University of Agricultural Sciences (SLU), 750 07 Uppsala, Sweden

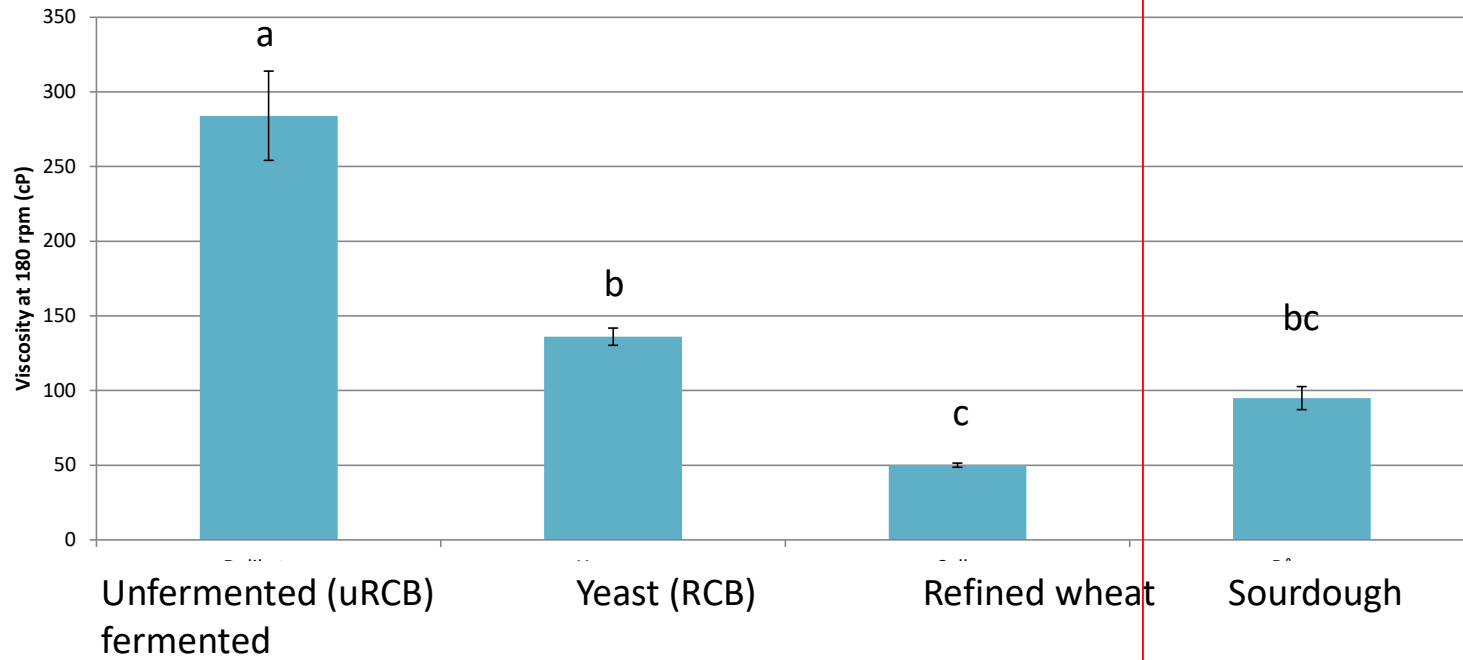
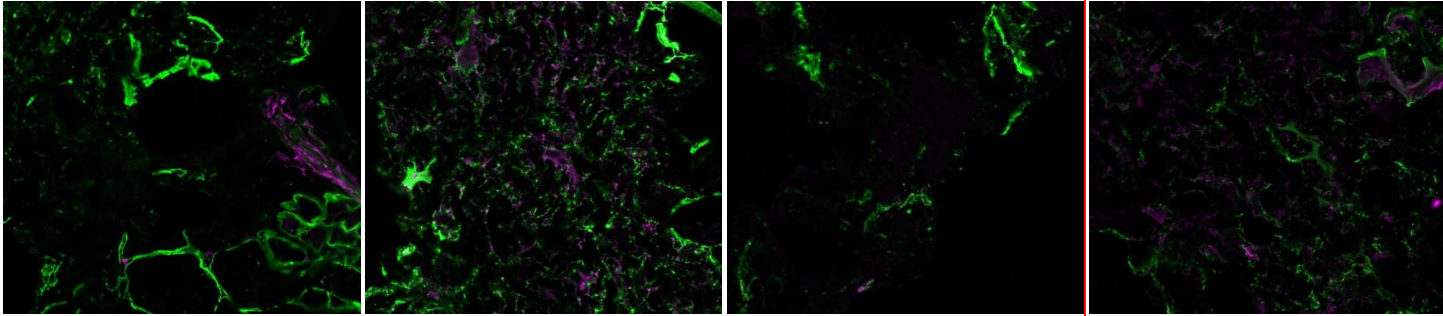
<sup>2</sup>Department of Medical Sciences, Uppsala University, 751 85 Uppsala, Sweden

<sup>3</sup>Unit of Nutritional Epidemiology, Department of Environmental Medicine, Karolinska Institutet, 171 77 Stockholm, Sweden

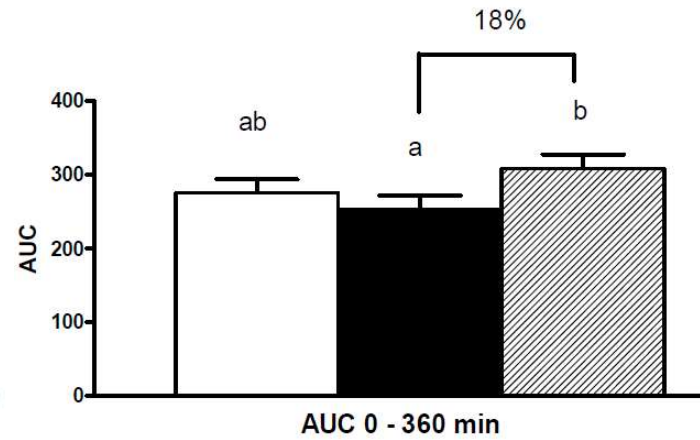
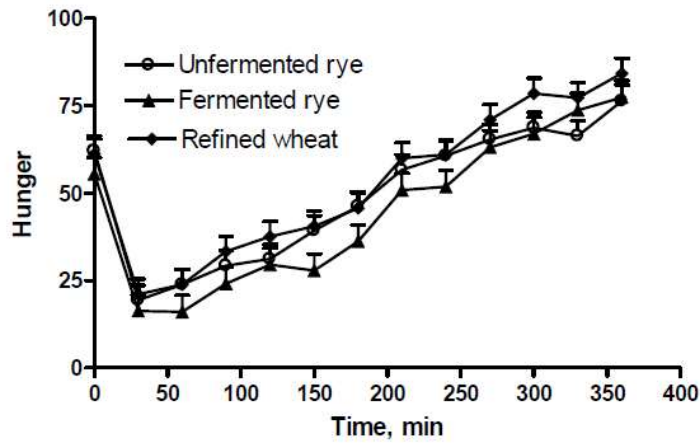
(Submitted 4 January 2017 – Final revision received 10 August 2017 – Accepted 8 September 2017)

Zamaratskaia et al (2017)

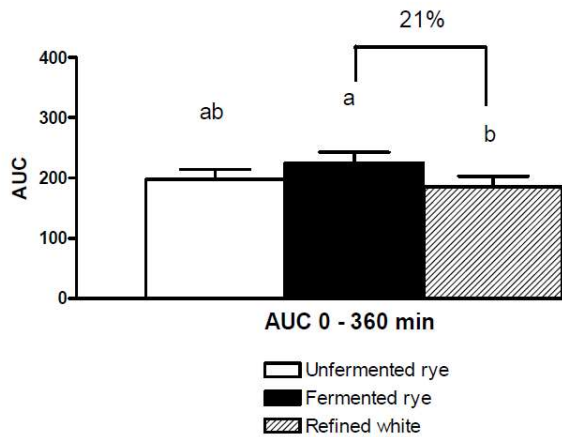
$\beta$ -glucan in green and arabinoxylan in magenta



# Effects on appetite



## Fullness

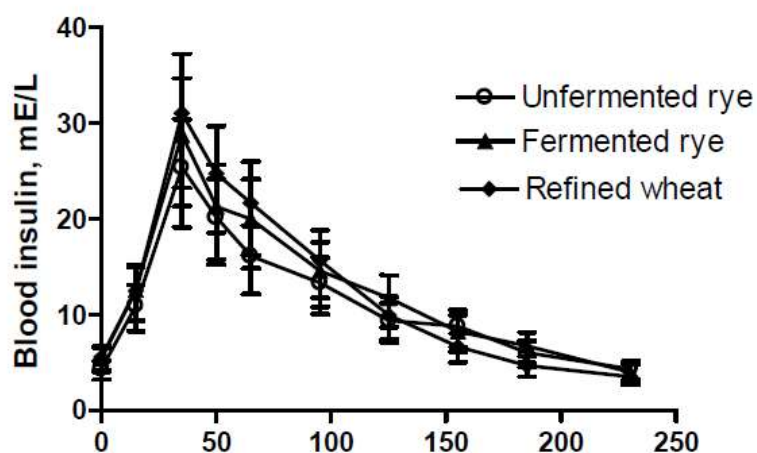


- Unfermented rye differed slightly vs control (borderline significant)
- Sourdough fermented rye about 20% different vs control

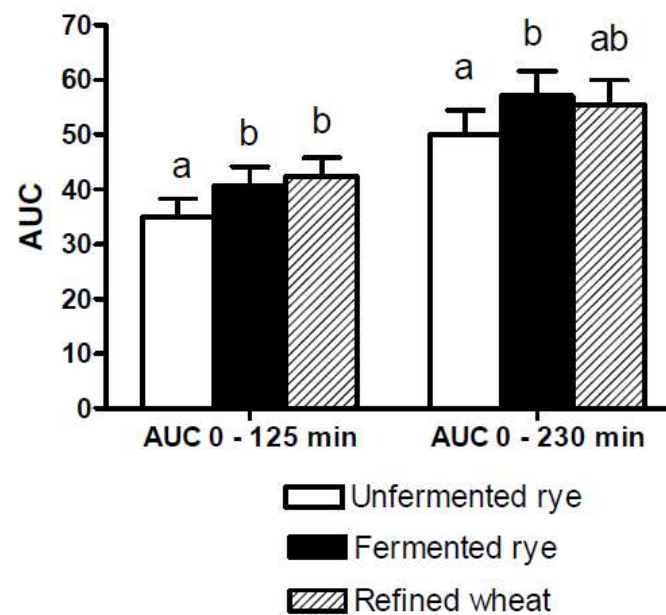
Zamaratskaia et al (2017)



## Effects on insulin



Lower postprandial insulin responses at some time points (significant interaction)



# Effects of rye and sourdough content- A cross-over breakfast study

- 6 armed cross-over design
  - 5 sourdough rye breads
  - 1 refined wheat bread

Appetite records every 30 minutes

7:30  
Breakfast



11:30  
Lunch

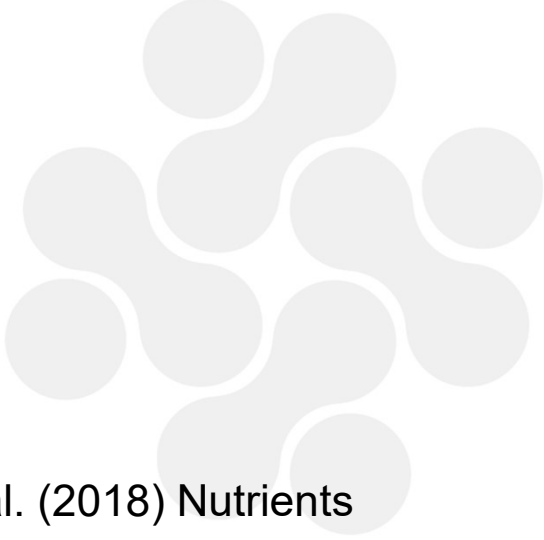


Nöhr-Iversen et al. (2018) Nutrients

# Cross-over breakfast study

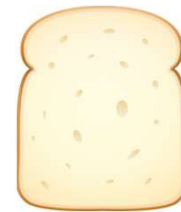
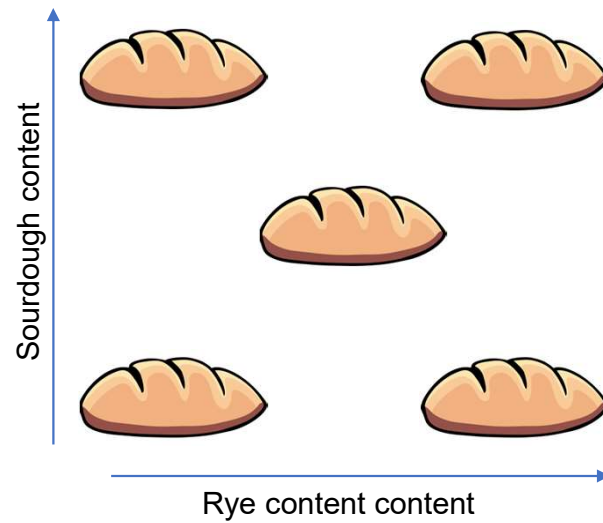
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- 23 healthy volunteers
  - 8 males / 15 females
- 23-63 years old



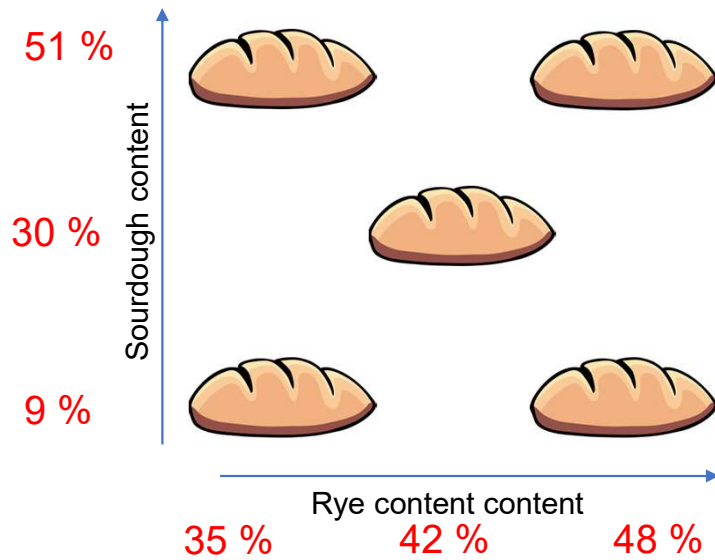
Nöhr-Iversen et al. (2018) *Nutrients*

# Sourdough rye bread



Nöhr-Iversen et al. (2018) Nutrients

# Sourdough rye bread



Nöhr-Iversen et al. (2018) Nutrients

## Table: Rye bread recipes and design

Bread sourdough/rye	R. sourdough <sup>a</sup>	Rye flour	Rye total <sup>b</sup>	Wheat flour	Total water <sup>c</sup>	% Sourdough of total dough	% Rye flour of total flour
1. MS/MR	1250	500	1000	900	1570	30	42
2. HS/LR	2125	0	850	1050	1540	51	35
3. HS/HR	2125	300	1150	750	1540	51	48
4. LS/LR	375	700	850	1050	1600	9	35
5. LS/HR	375	1000	1150	750	1750	9	48

<sup>a</sup> Sourdough consisting of 40:60 whole grain rye flour:water.

<sup>b</sup> Sum of whole grain rye flour added and included in sourdough.

<sup>c</sup> Sum of water added and included in sourdough

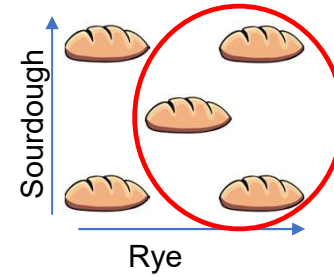
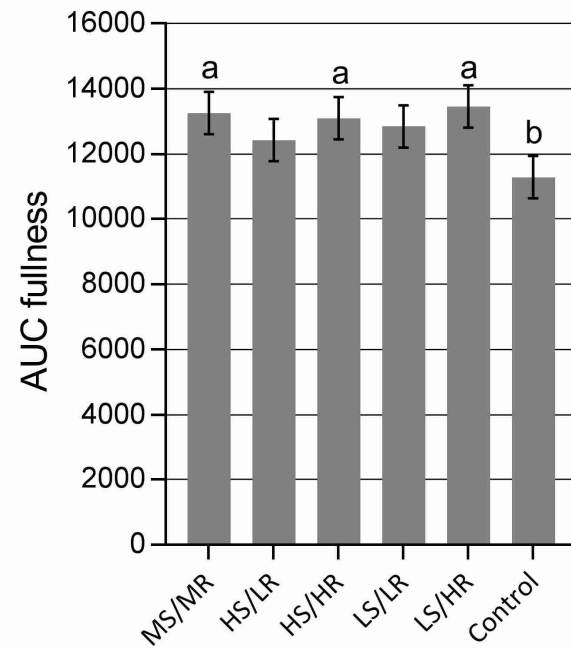
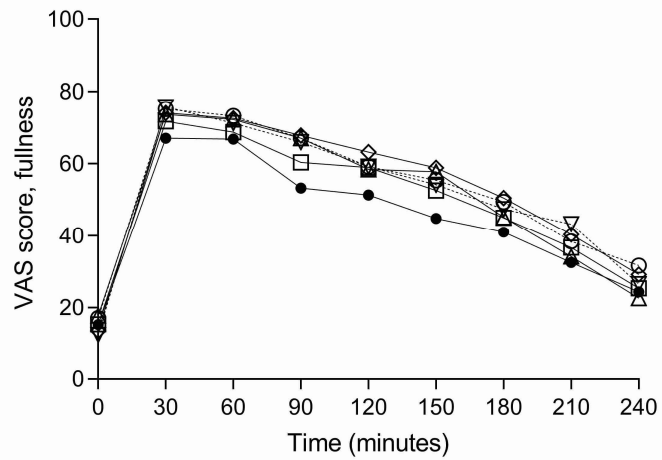
Nöhr-Iversen et al. (2018) Nutrients

**Table: Composition of rye breads (100 g- a serving in the study)**

	MS/MR	HS/LR	HS/HR	LS/LR	LS/HR	Reference
<b>Protein (g)</b>	7.1	7.2	6.9	7.3	6.3	7.5
<b>Fat (g)</b>	2.2	2.2	2.2	2.2	1.9	3.9
<b>Starch (g)</b>	41.2	41.9	39.9	40.4	39.8	41.9
<b>Total fiber<sup>a</sup> (g)</b>	7.0	6.0	7.2	6.8	8.3	3.6
<b>Soluble fiber (g)</b>	2.3	2.0	2.5	2.1	2.7	1.6
<b>Insoluble fiber (g)</b>	4.7	4.0	4.7	4.7	5.5	3.0
<b>Ash (g)</b>	1.7	1.6	1.7	1.7	1.5	1.4
<b>Water (g)</b>	35.0	35.7	36.1	35.8	35.7	38.0
<b>Energy (kJ)<sup>b</sup></b>	959	963	934	946	920	992
<b>pH</b>	4.4	4.2	4.2	5.2	5.3	5.0
<b>Acid equivalents<sup>c</sup></b>	10.3	11.5	12.5	6.3	6.6	4.3
<b>Lactic acid (g)</b>	0.81	0.81	0.89	0.4	0.36	0.27
<b>Acetic acid (g)</b>	0.13	0.14	0.16	0.07	0.04	0.04

Nöhr-Iversen et al. (2018) Nutrients

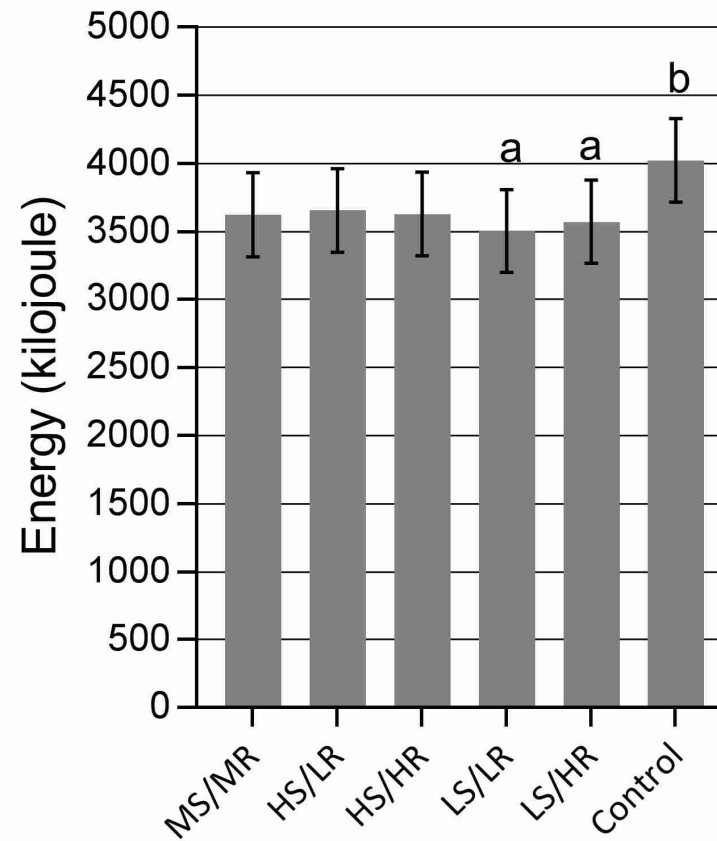
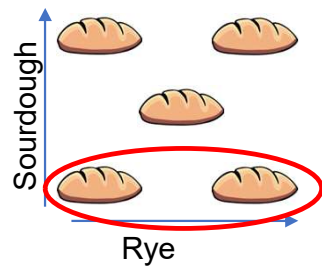
# Fullness



Nöhr-Iversen et al. (2018) Nutrients



## Ad libitum lunch

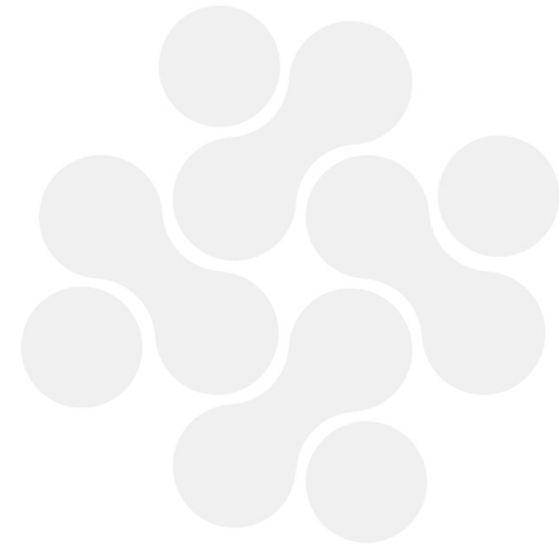


Nöhr-Iversen et al. (2018) Nutrients

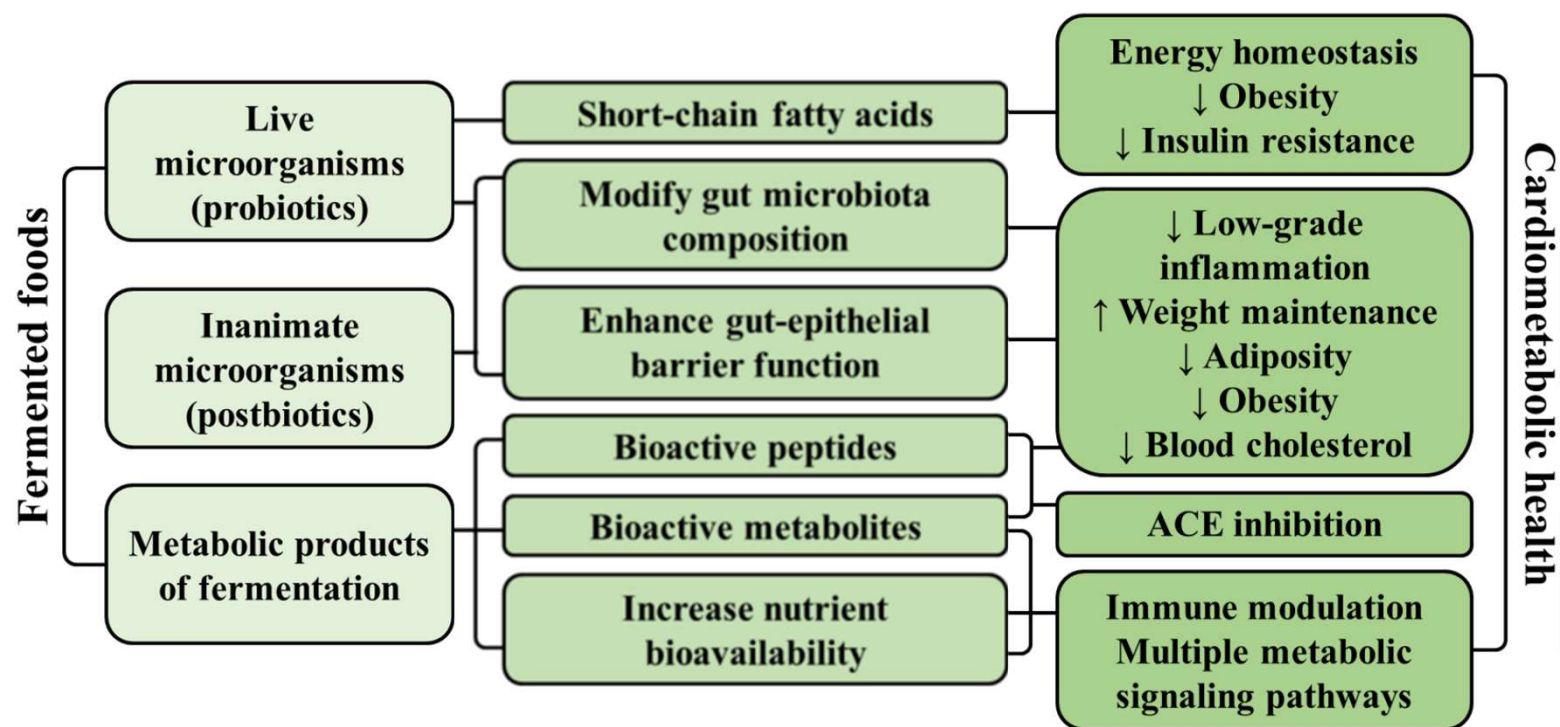
# Conclusion

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- No difference between the sourdough rye breads
- No indication of an effect of increasing sourdough content
  - Despite large difference, 9-51%
- Some indication of an effect of increasing rye content
  - Relatively small difference, 35-48%



## Fermented foods and cardiometabolic health – proposed mechanisms



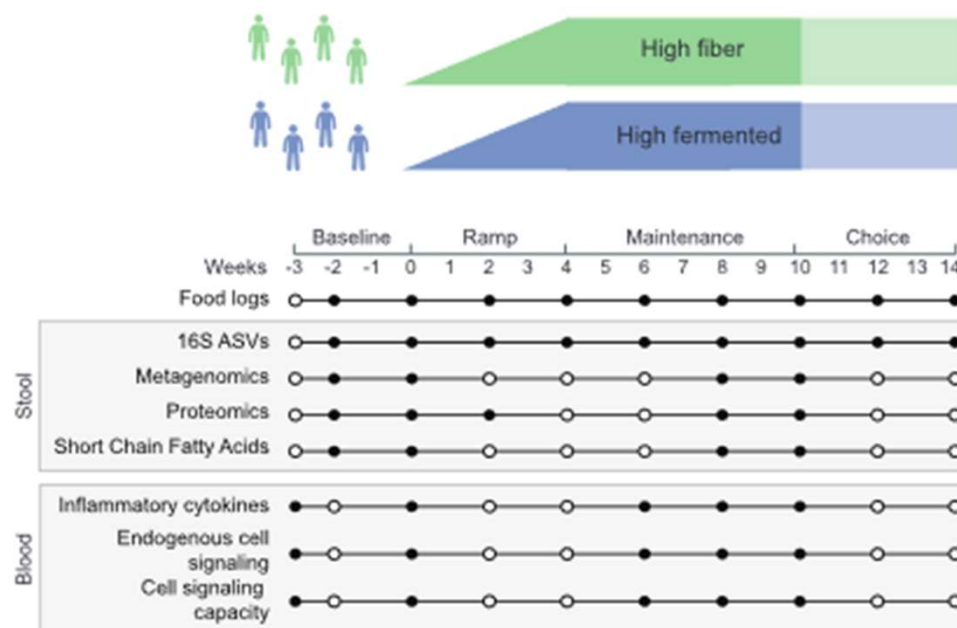
Li, 2022, *Frontiers in Nutrition*

# Health benefits of fermented and high fiber foods – clinical trial

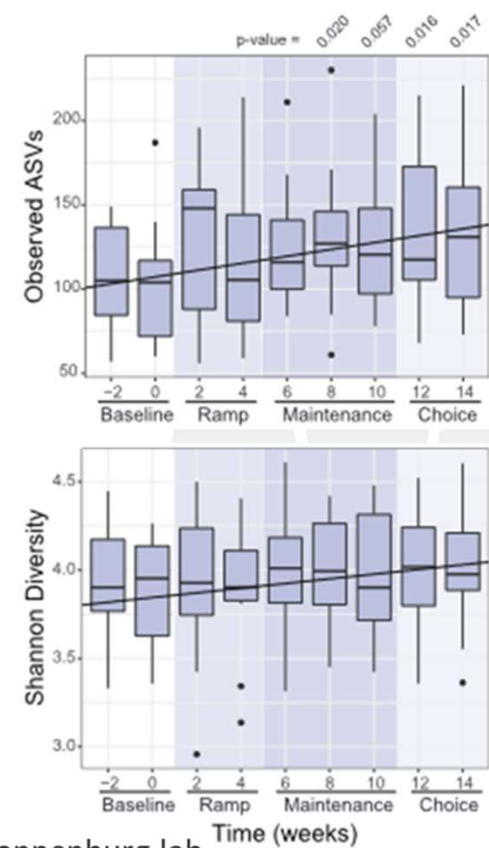
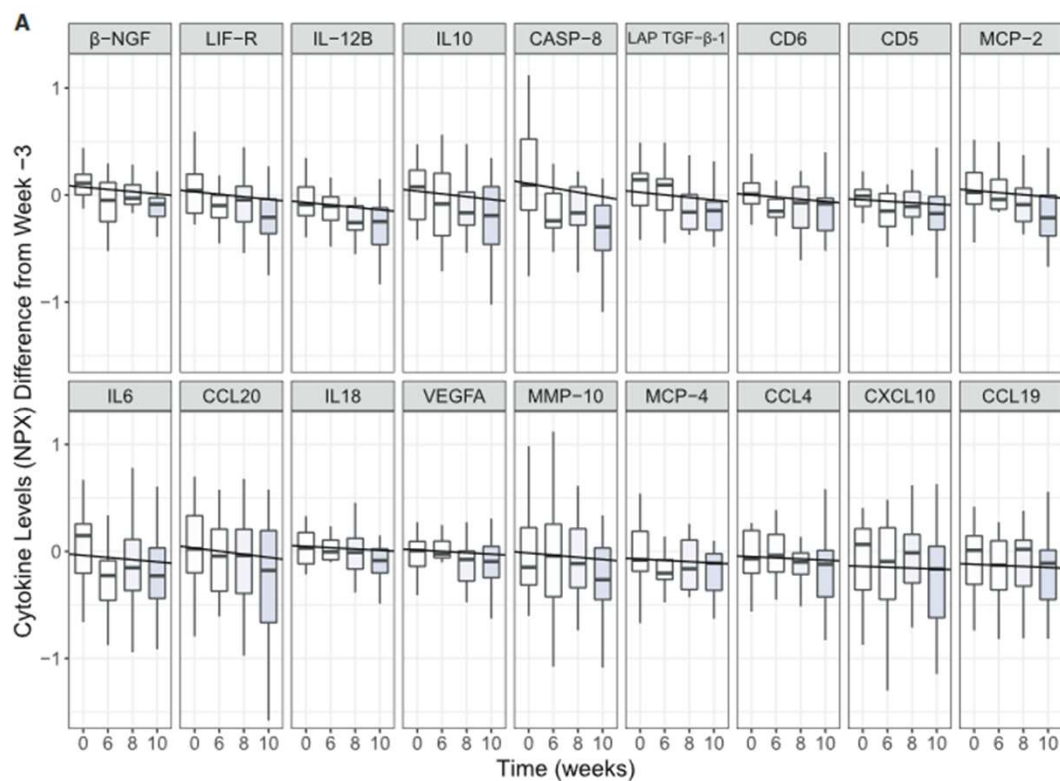
- Parallel study
- Healthy adults, n=18
- Dietary fiber - 20 g/day
- Fermented food - 6 servings/day

Primary aim: Change in Cytokine Response Score

Secondary aims: Effect on microbiota, SCFAs, inflammatory markers, lipid profile

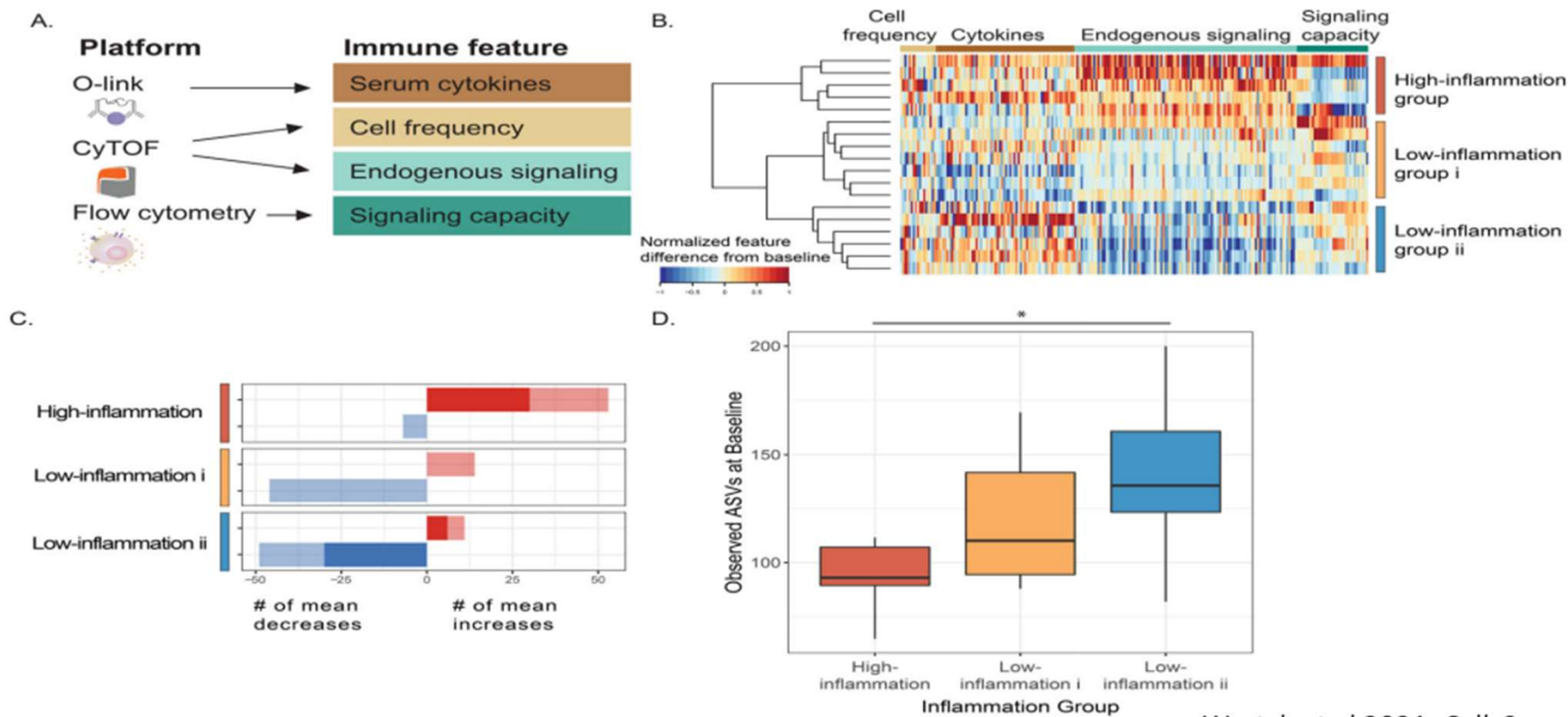


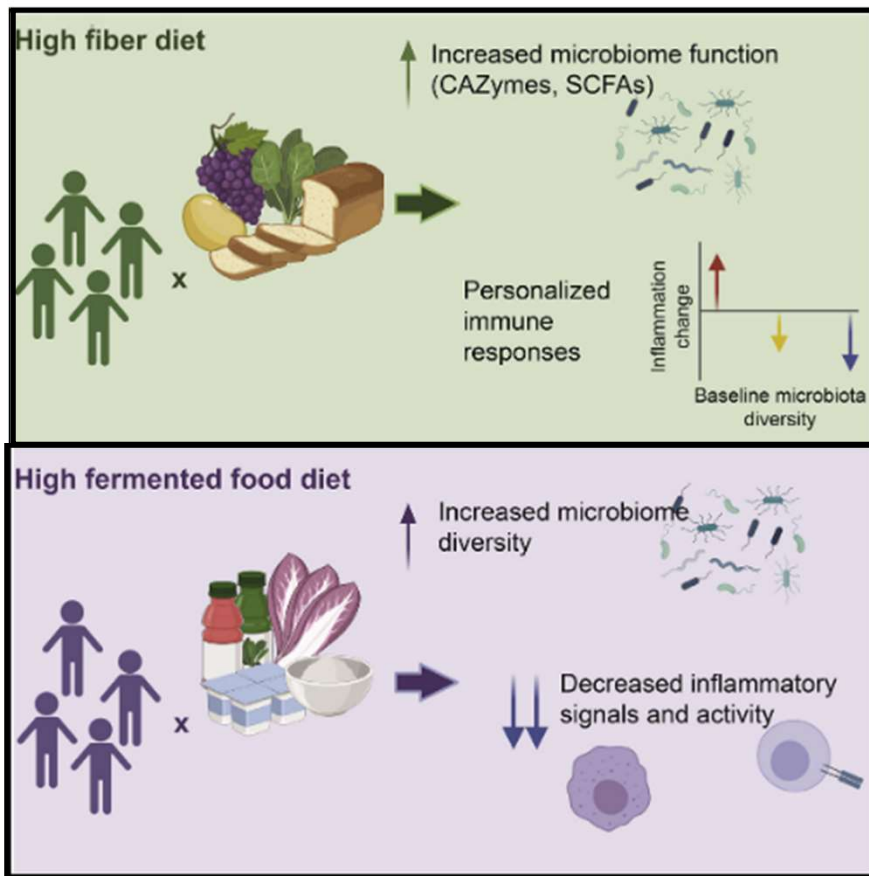
# Health benefits of fermented and high fiber foods – clinical trial



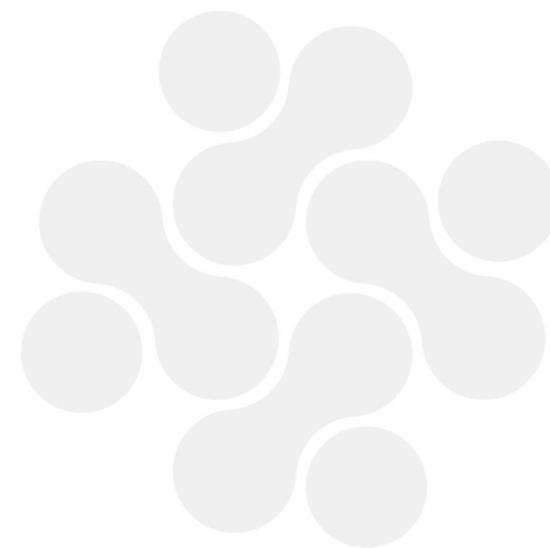
Wastyk et al 2021, *Cell*, Sonnenburg lab

# Inflammation response groups





Wastyk et al 2021, *Cell*, Sonnenburg lab





# HealthFerm

## **Plant-based fermented foods**

**for healthier and more sustainable diets**

HealthFerm is a Horizon Europe research project investigating innovative pulse and cereal-based food fermentations together with the health effects and consumer perception of novel fermented foods.

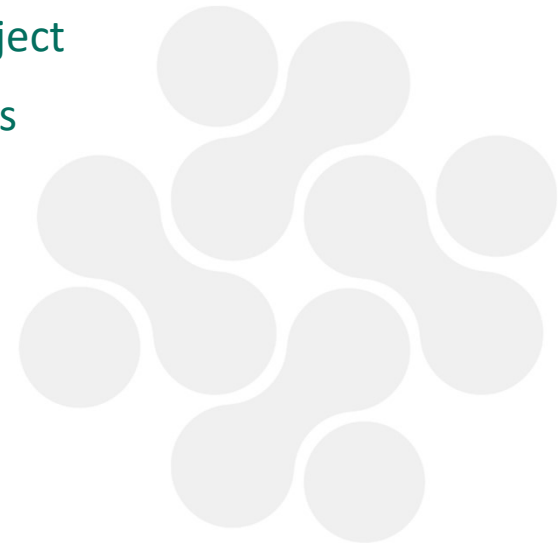


**Funded by  
the European Union**



4-year project

23 partners





## Fermented Plant-based Portfolio Diet 4 Metabolic Health (FermDiHealth)

- Randomized controlled crossover study
- Subjects with metabolic syndrome, n=100

Primary aim: Difference in the inflammatory biomarker(s)

Secondary aims: Lipid profile, glucose and insulin, blood pressure, inflammatory markers, glycaemic variability, microbiota, metabolome, (stratification – Enterotypes)

### FermPlantFoods

#### Fermented foods:

- Yogurt like product
- Meat alternative
- Vegetables
- Kombucha
- Bread

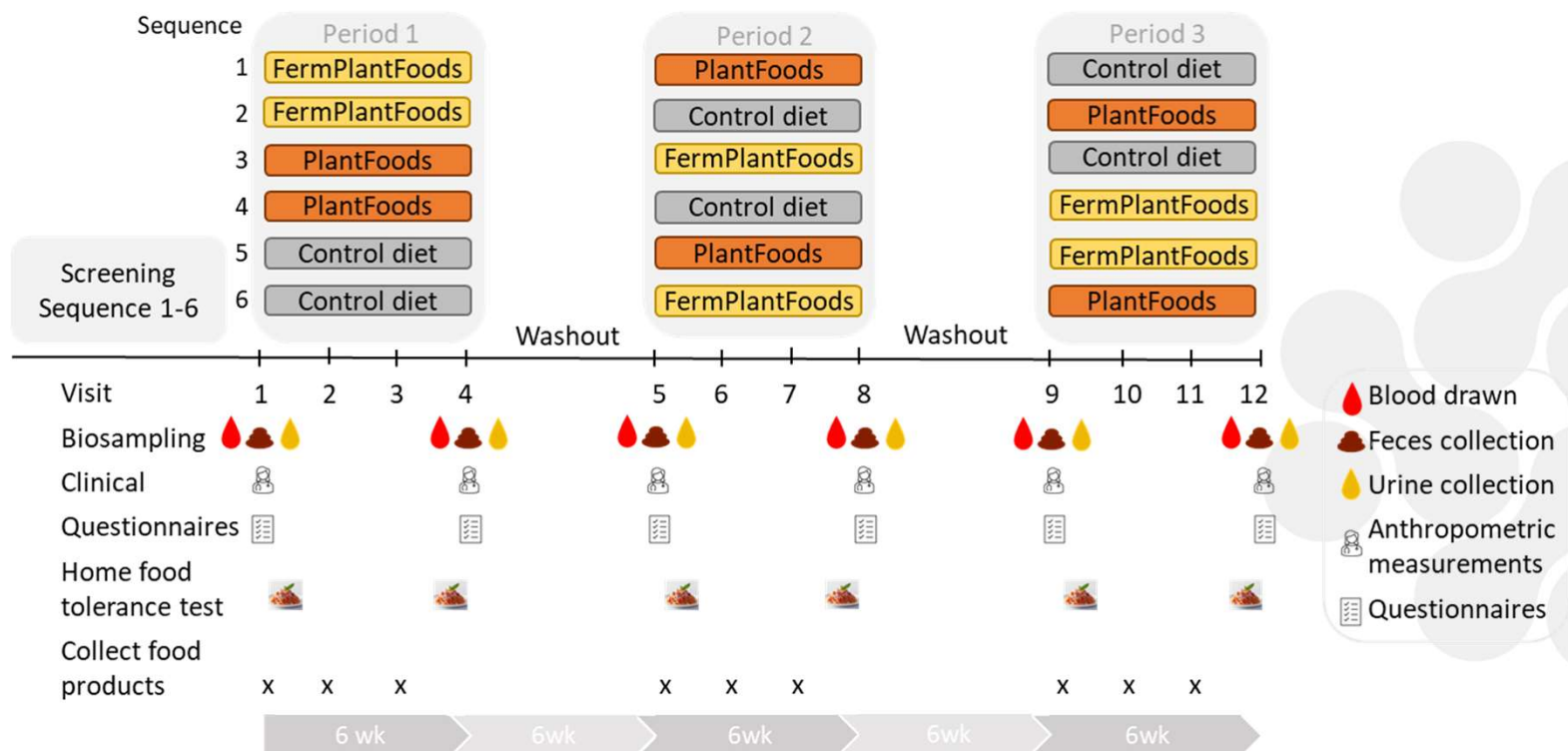
### PlantFoods

Non-fermented counterpart

### Control diet

Average Swedish diet

# Fermented Plant-based Portfolio Diet 4 Metabolic Health (FermDiHealth)



# Food4GutMarKIT



## Literature review

Step 1

Identification of gut microbiota associated with reduction of cardiovascular risk factors

→ *F.prausnitzii*, *Oscillospiraceae*, *Faecalibacterium*

Step 2

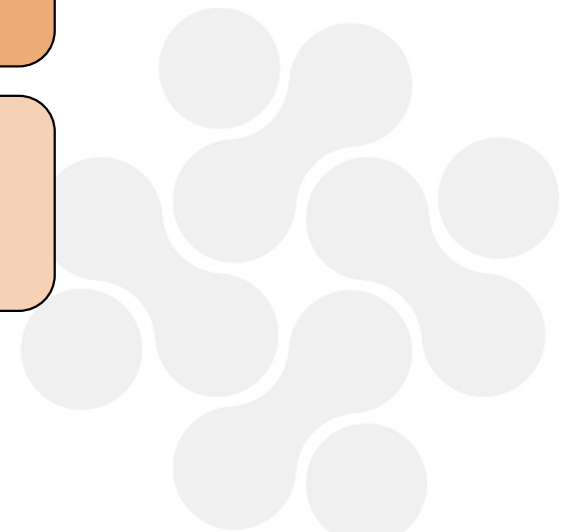
Identified foods shown to increase these bacteria in human intervention trials

→ Rich in fibers and whole grains + fermented foods



### Diet concept

- Rich in fibers and whole grains + fermented foods (4 servings/day)
- Nordic Nutrition Recommendations



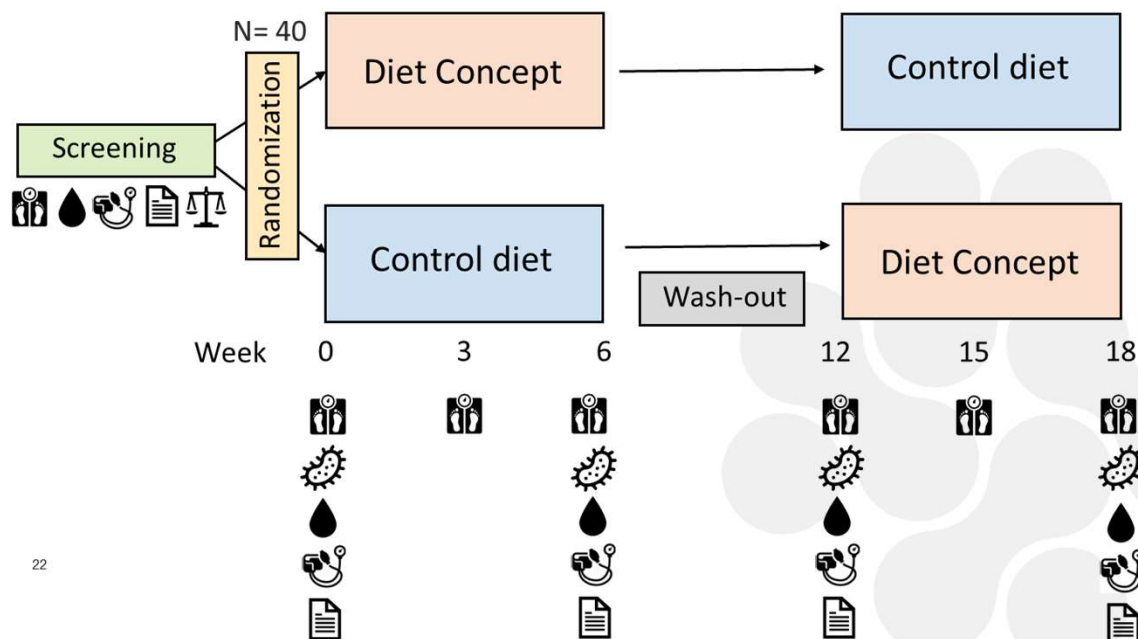
Palmnäs et al *in preparation*

## Food4GutMarKIT – clinical trial

- Randomized controlled cross-over study
- BMI<25, BMI>25
- Completers n=30

Primary aim: Effect on gut microbiota previously shown associated with reduction of cardiovascular risk factors

Secondary aims: Effects on lipids, blood pressure, fasting glucose, CRP and the metabolome.



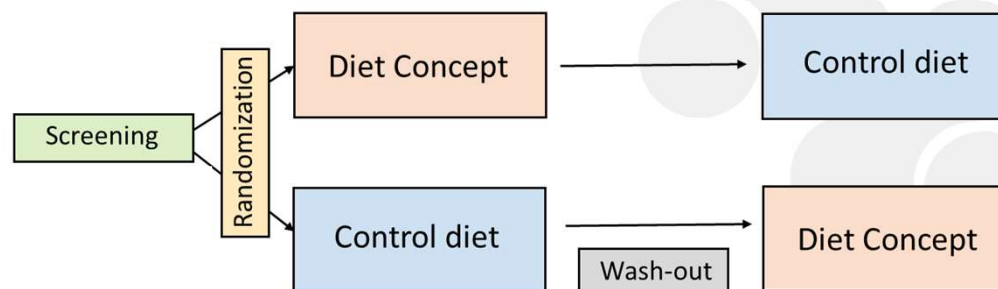
22

## GutMarkIT – clinical trial

### Expected findings

- The intervention diet will alter specific microbes previously shown inversely associated with risk factors for cardiovascular disease
- Affected microbes will be linked with reduction of cardiovascular risk factors
- The effect on microbiota will be mirrored in the metabolome
- Differ between individuals with BMI <25 and BMI >25

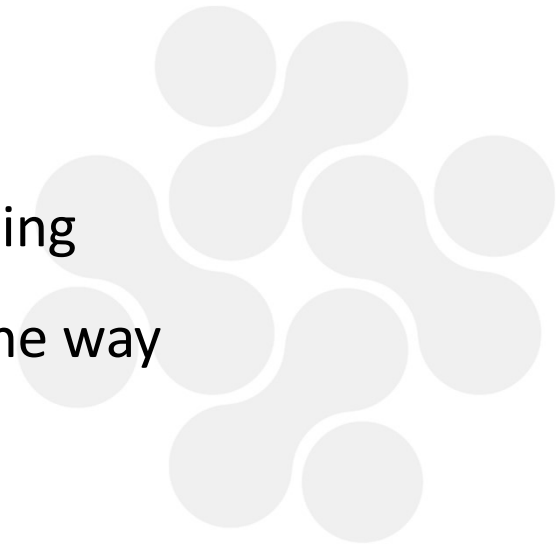
**Stay tuned!**



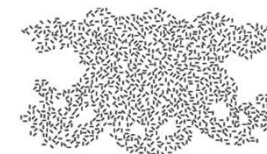
## Take home messages



- Fermented foods is a diverse group! Many different MOs and metabolites formed
- Several mechanisms at play at the same time
- Studies on non-dairy fermented foods and health are lacking
- RCTs on plant based fermented foods and health are on the way



# External collaborators



SVERIGES UNGA AKADEMI



Assist. Prof Qi Sun  
Prof. Frank Hu



Prof. Anne Tjønneland  
Dr. Jytte Halkjær  
Dr. Anja Olsen  
Dr. Cecilie Kyrö



Lantmännen



Prof. Cristina Andres-Lacueva



Prof. Marju Orho-Melander



Prof. Alicja Wolk  
Prof. Agneta Åkesson



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Dr. Kati Hanhineva  
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Dr. Ingvar Bergdahl  
Prof. Bernt Lindahl  
Prof. Olle Rolandsson



Prof. Anna Winkvist  
Prof. Göran Karlsson  
Prof. Fredrik Bäckhed  
Prof. Göran Bergström





**CHALMERS**