



Carbohealth
SP2

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Carbohealth CCC3 – SP2

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Immune effects of selected pre- and probiotics and efficacy in enhancing oral vaccination against *Salmonella* Typhimurium

CCC day 30-11-2017

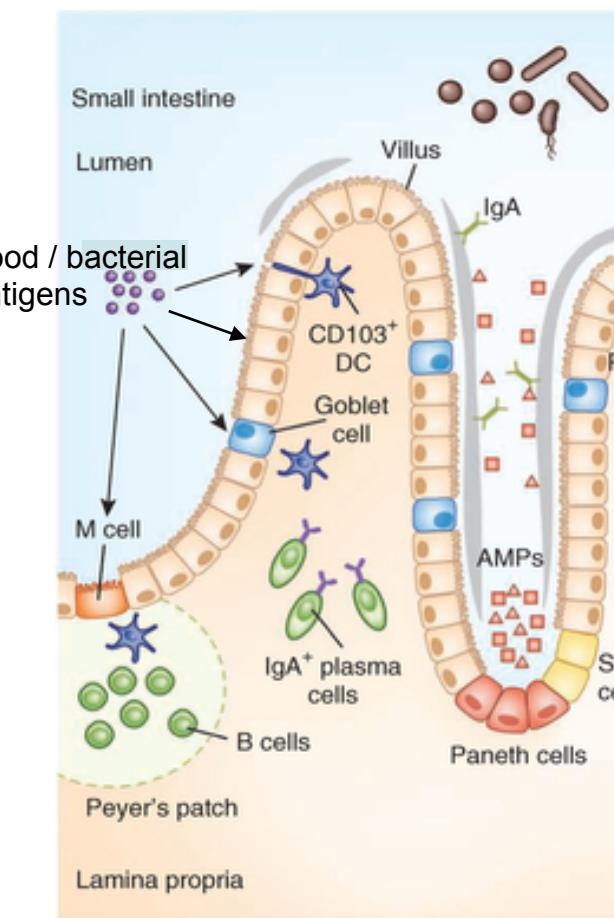
Mucosal immunity

Intestines

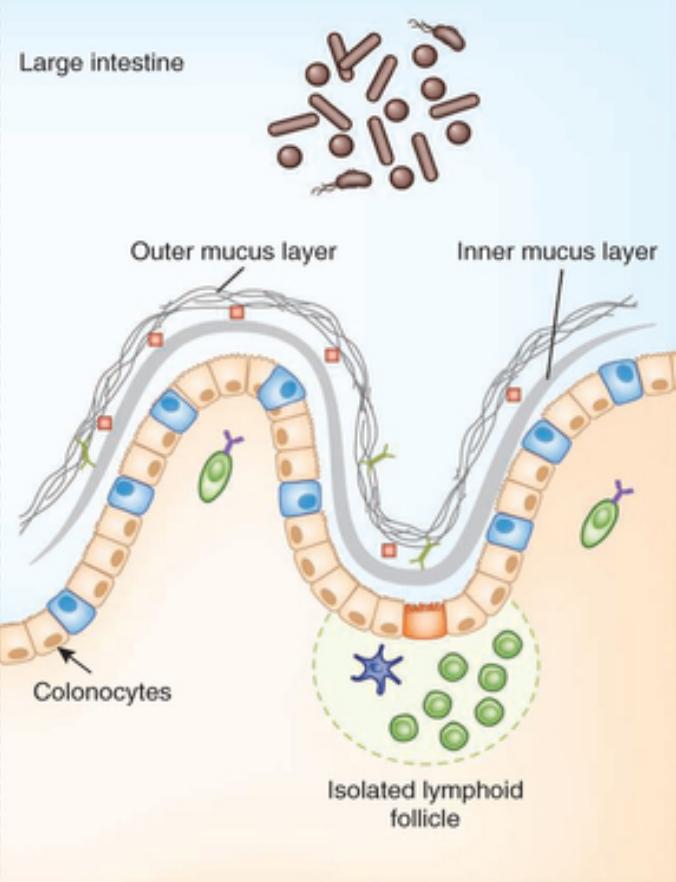


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Direct interactions with immune cells



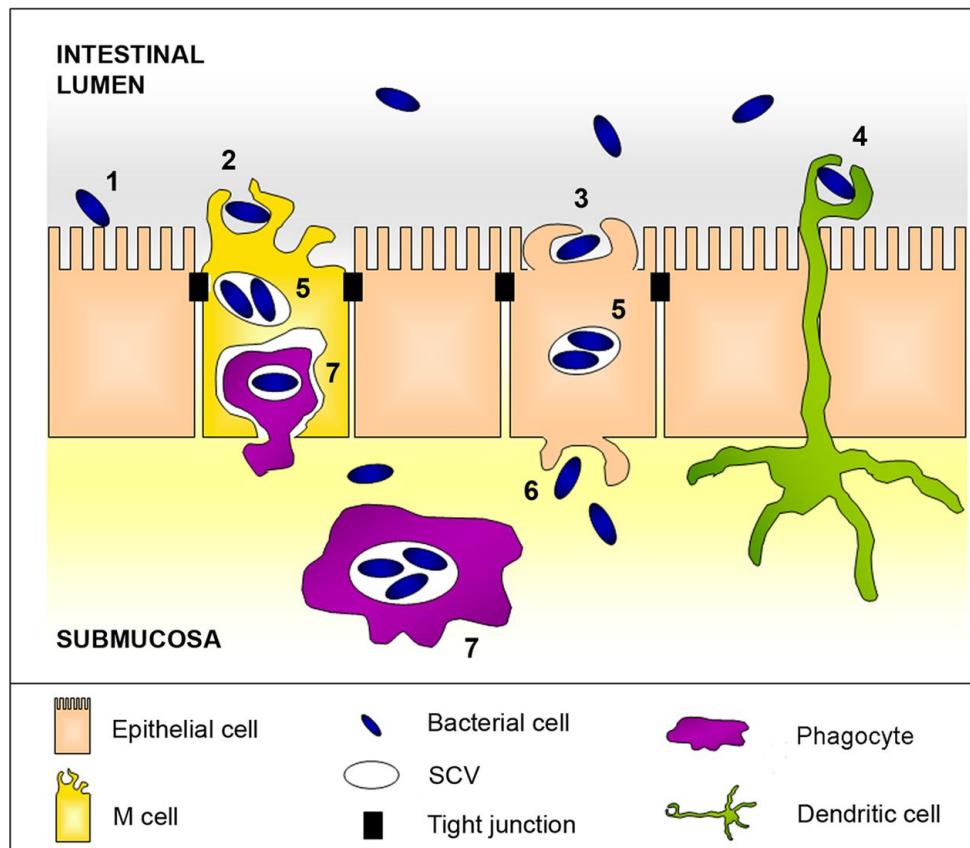
Microbiota driven health effect via fermentation



Enteropathogen *Salmonella*

Oral vaccination has low efficacy

Salmonellosis = 90 million people yearly
12% food poisoning in Europe



Selected pre- and probiotics



Long-chain inulin type fructan

TLR-2 stimulating effect (Vogt, 2014)

Downregulates the Treg function and enhances Th1/Th17 activation (Fransen, 2017)

Enhances hepatitis B vaccination in young adults via Th1 stimulation (Vogt, 2017)

Lactobacilli

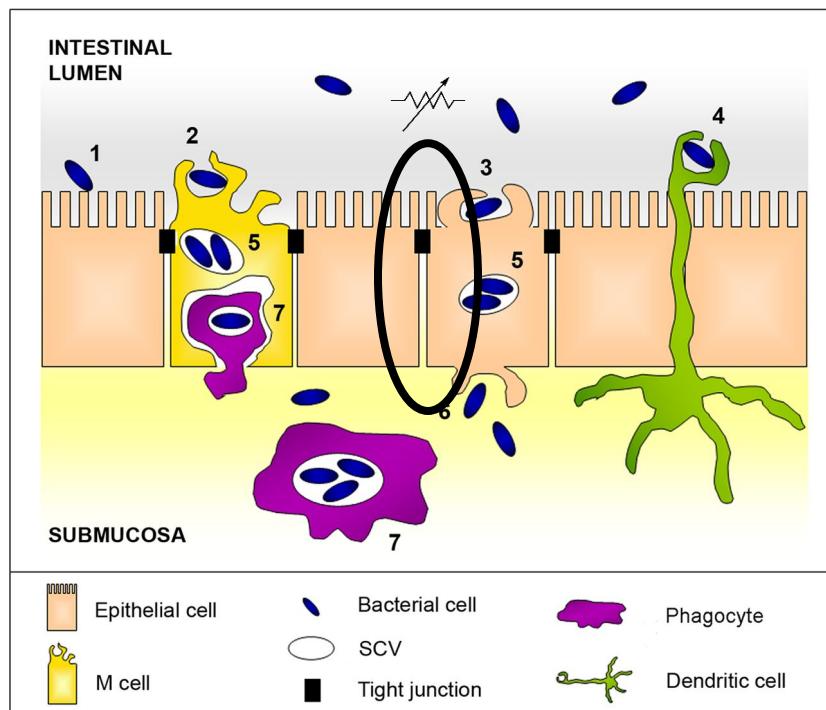
L. brevis W63, L. casei W56, L. acidophilus W37

Active in the ileum

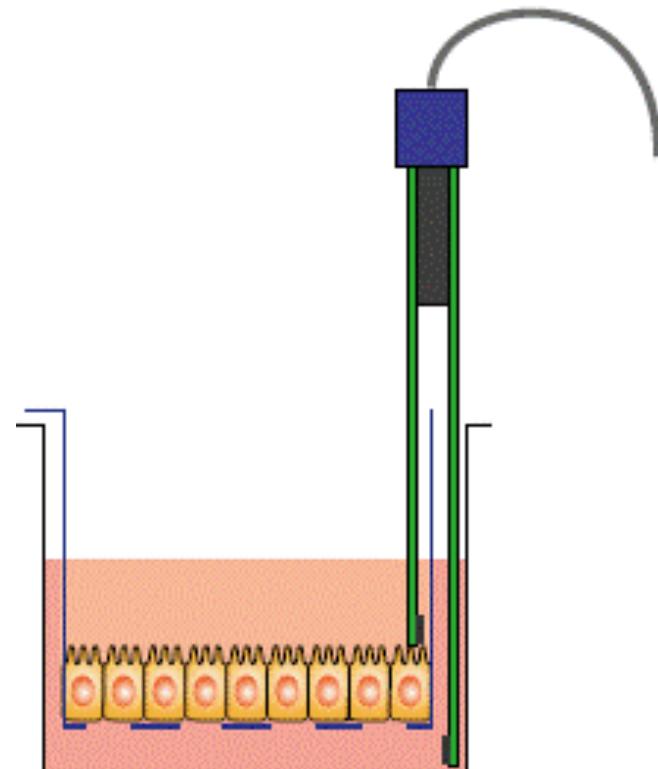
Strain-dependent effects

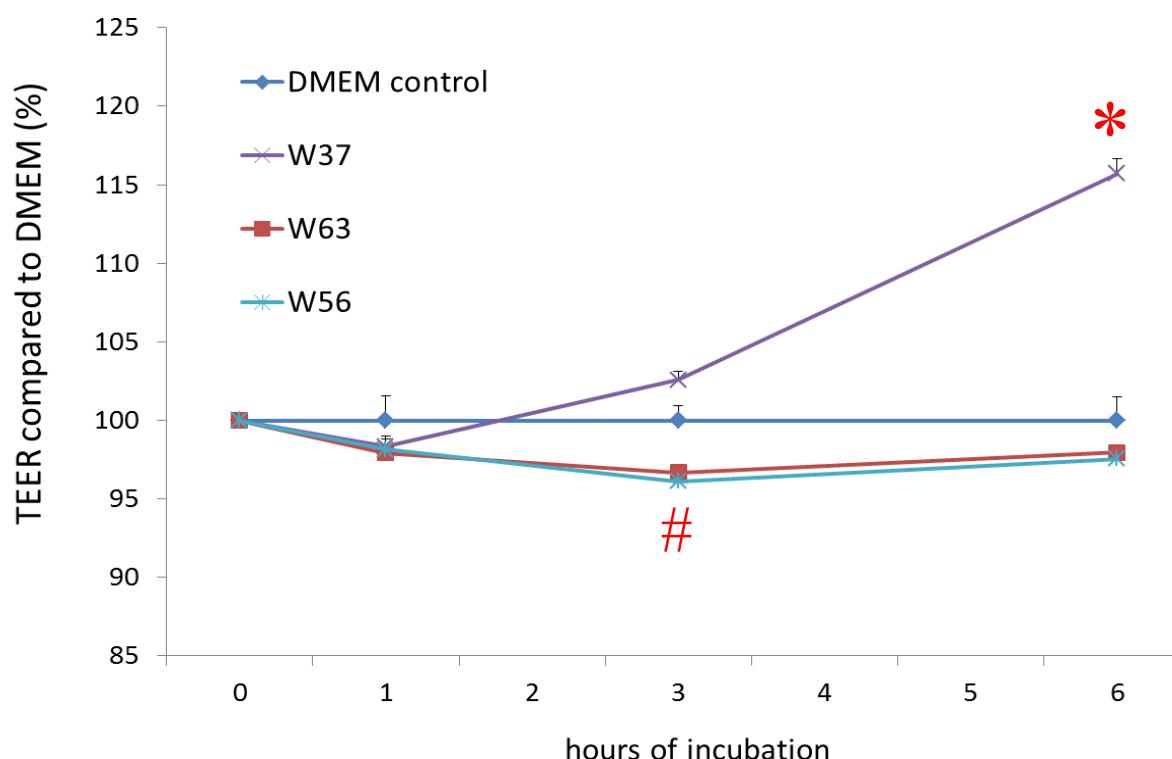
Protects against pathogen adhesion (Perdigon, 2002)

In vitro selection of *Lactobacilli* Comparing effects on gut barrier function



Trans-epithelial electric resistance

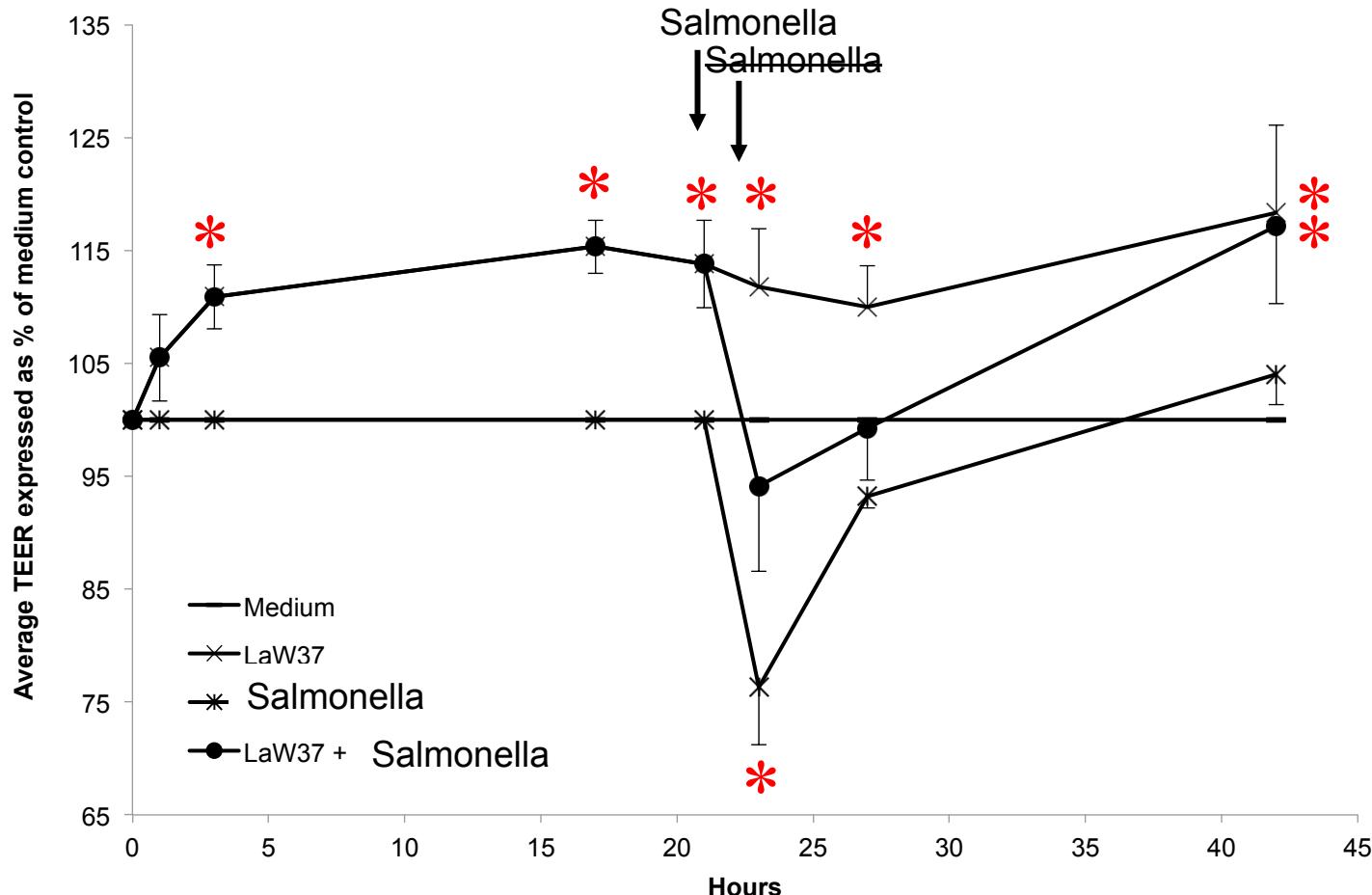




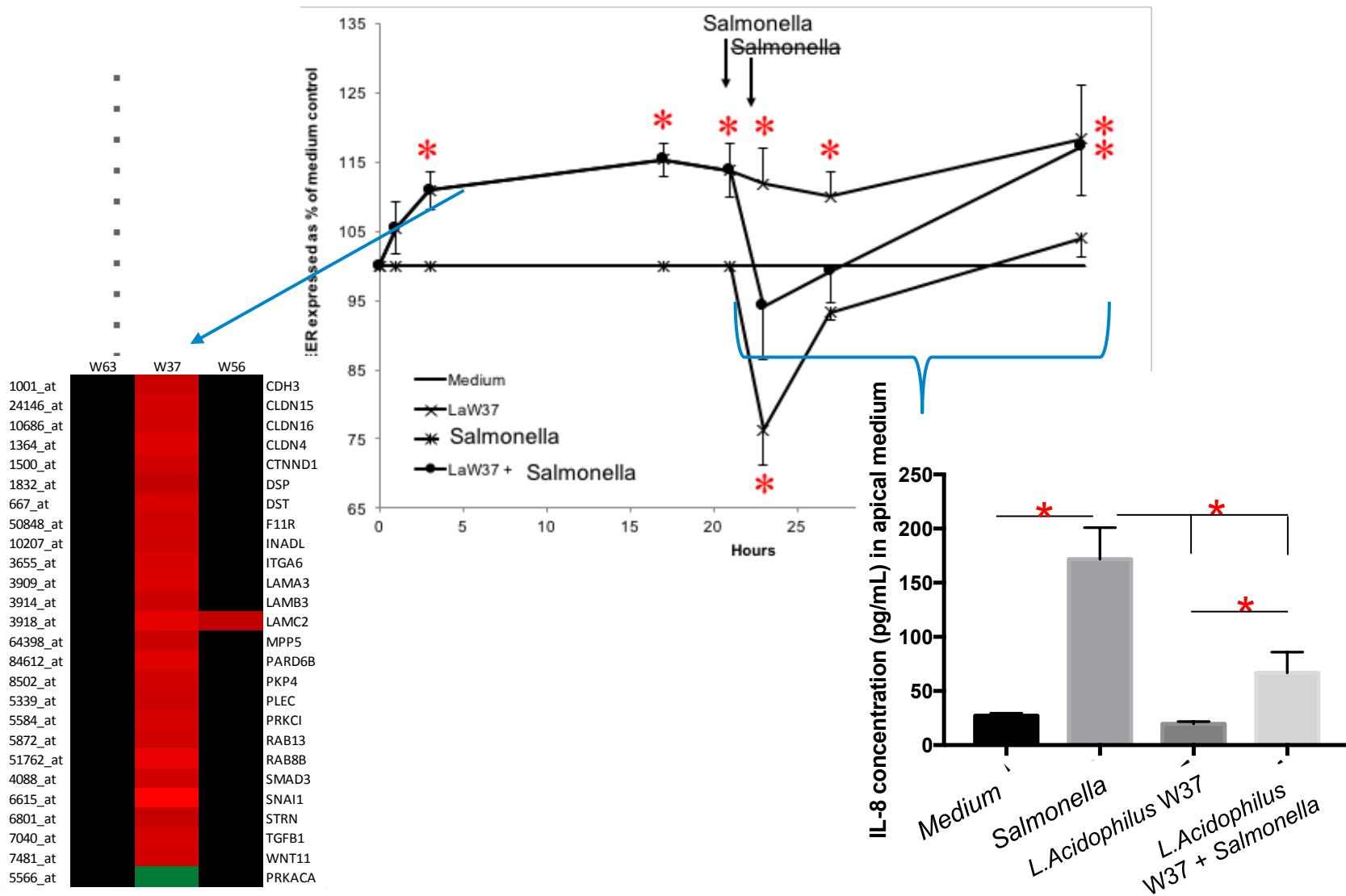
L. acidophilus W37 prevents *Salmonella* induced damage to gut barrier



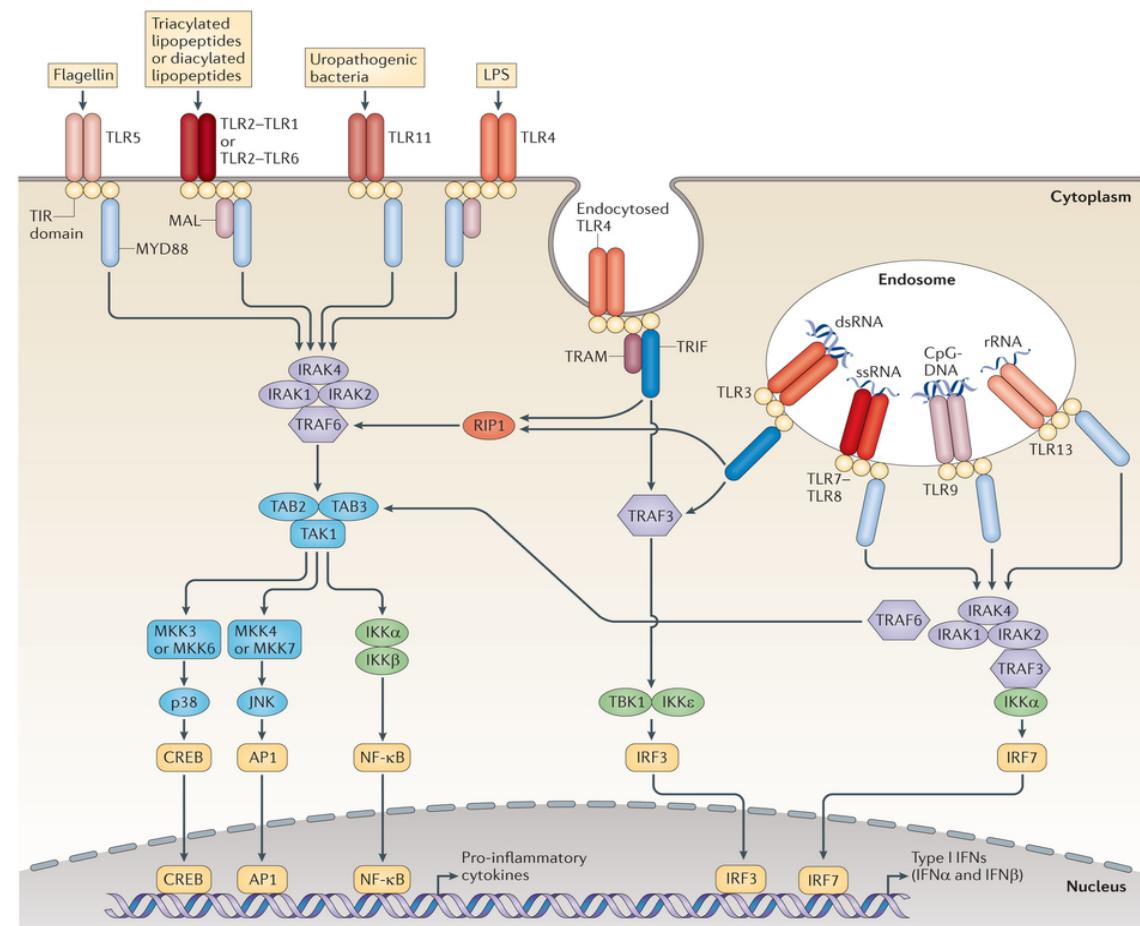
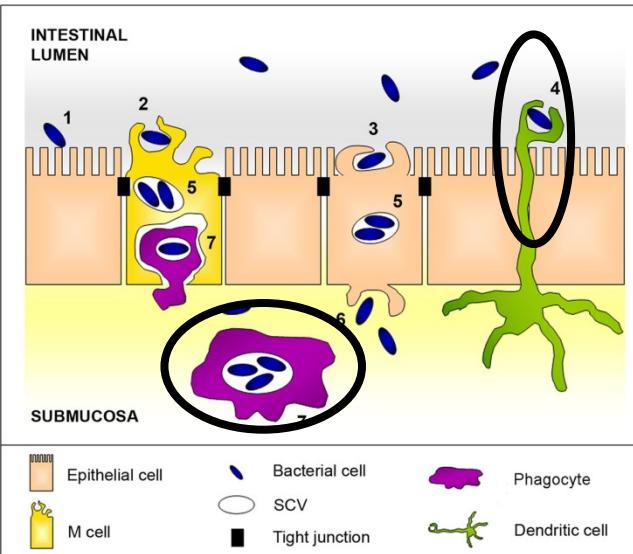
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L. acidophilus W37 reduces pathogenic stress Gut barrier function and signalling



In vitro selection of lactobacilli Immune Toll-like receptors (TLRs)



long-chain inulin/*L. acidophilus* W37 synergistically activate and inhibit Toll-like receptors

Activation	TLR 2	TLR3	TLR4	TLR 5	TLR7	TLR8	TLR 9
<i>L. brevis</i> W63	(+)	(+)	-	-	-	(+)	(+)
<i>L. casei</i> W56			-	-	-	-	-
<i>L. acidophilus</i> W37	++	+	-	-	-	-	-
Long-chain inulin	++	+	(+)	++	(+)	(+)	(+)
Long-chain inulin <i>/L. acidophilus</i> W37	++	++	(+)	+	-	-	-

Inhibition	TLR 2	TLR3	TLR 4	TLR 5	TLR7	TLR8	TLR 9
<i>L. brevis</i> W63	-	-	-	-	-	-	-
<i>L. casei</i> W56	-	-	-	-	-	-	-
<i>L. acidophilus</i> W37	-	-	-	-	-	-	-
Long-chain inulin	++	-	-	-	-	-	-
Long-chain inulin <i>/L. acidophilus</i> W37	++	-	-	++	-	++	-



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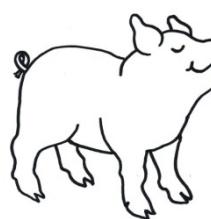
Testing selected ingredients for enhancing vaccination

Salmonella vaccination and challenge

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n = 29

Day 2 after birth
Start daily food intervention

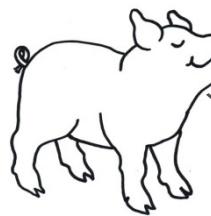


Placebo
Non-vaccinated
control

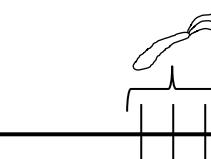
Daily challenge
Salmonella Typhimurium

Day 55
Sacrifice

Day 24
Weaning

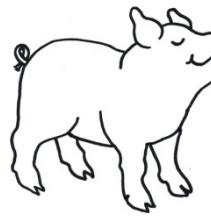


Placebo
Vaccinated control

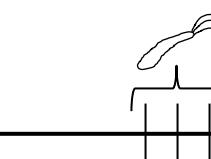


Day 55
Sacrifice

Day 25
Oral vaccination Salmoporc

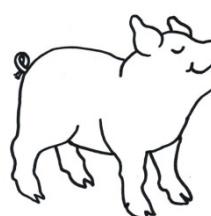


Long-chain inulin
0.114 g/kgBW/day

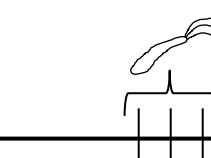


Day 55
Sacrifice

Day 25



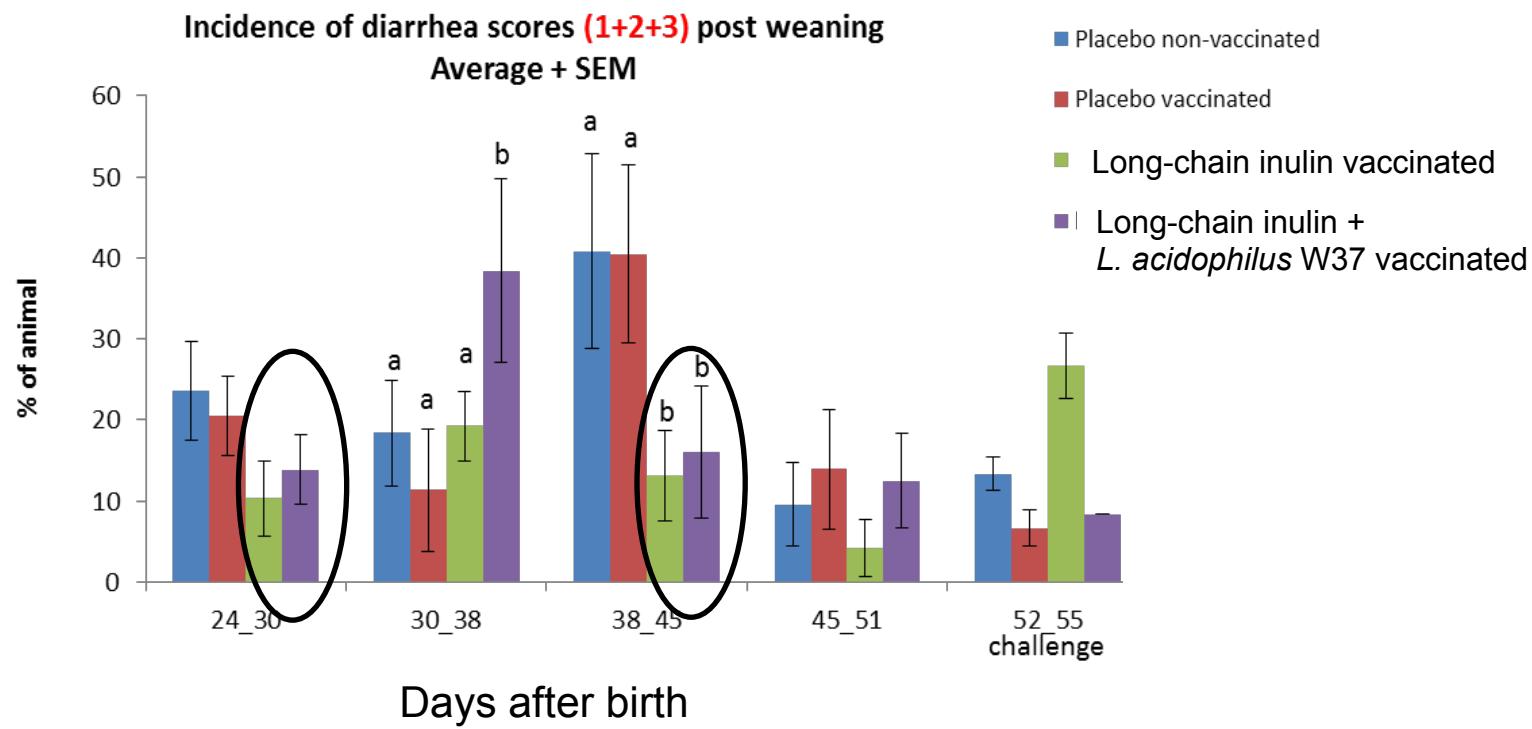
Long-chain inulin
+ L. Acidophilus W37
5.10⁹ CFU/mL



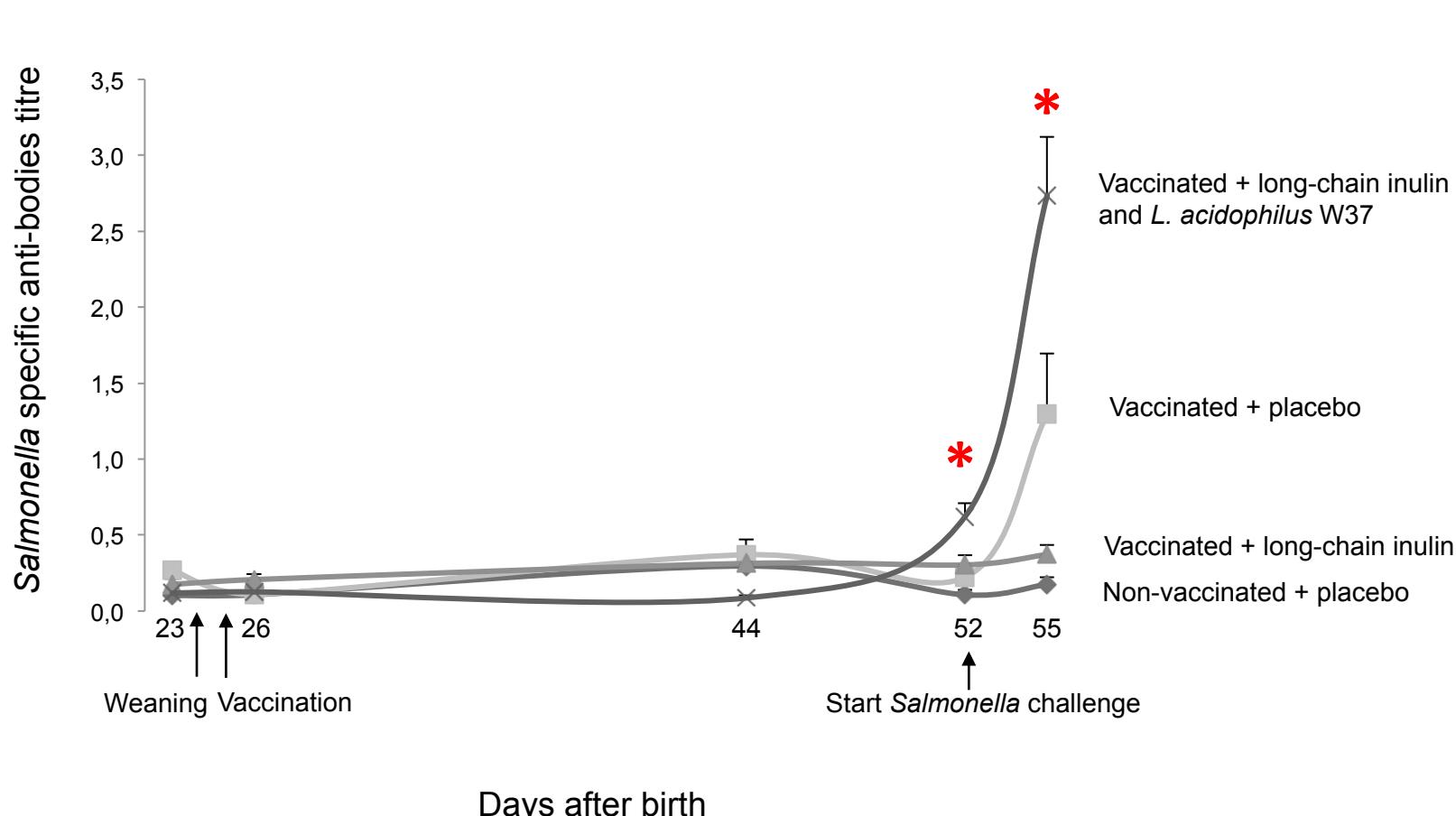
Day 55
Sacrifice

No adverse effects of daily intervention in neonates

Diarrhea post-weaning decreased by inulin



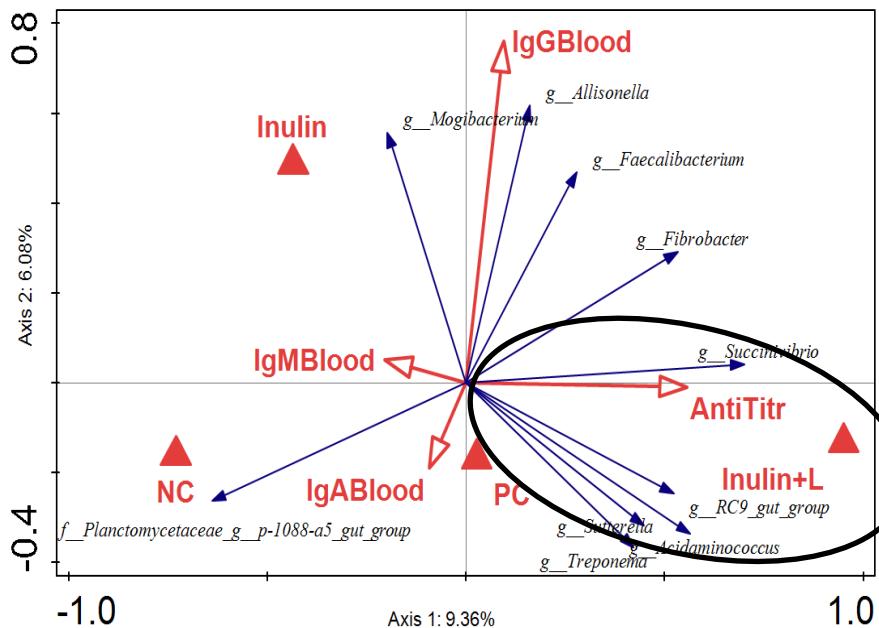
Long-chain inulin/*L. acidophilus* W37 supports oral vaccination efficacy in piglets



Microbiota correlates with enhanced antibody titer in long-chain inulin + *L. acidophilus* W37

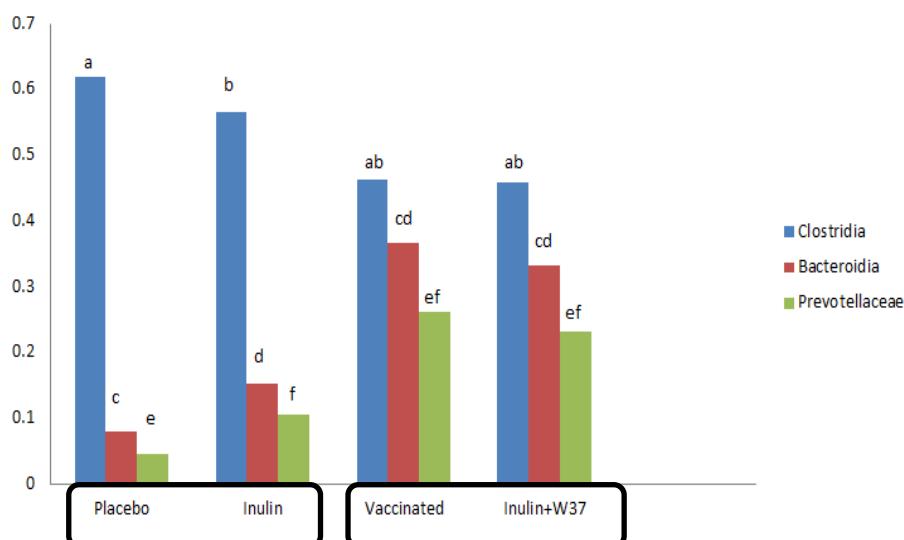


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Conditional Effects

Name	Explains %	pseudo-F	P	P(adj)
Group.Inulin+L.A.W37	8.5	1.8	0.006	0.048
IgG blood	5.3	1.1	0.288	0.84267
IgA blood	5.3	1.1	0.316	0.84267



Pre- and probiotics have very specific effects

Overview of the results



L. acidophilus W37 increased barrier function via upregulation of **tight-junction protein**

L. acidophilus W37 protected epithelial cells against *Salmonella Typhimurium*

Long-chain inulin combined with *L. acidophilus* W37 synergistically activated/inhibited TLRs

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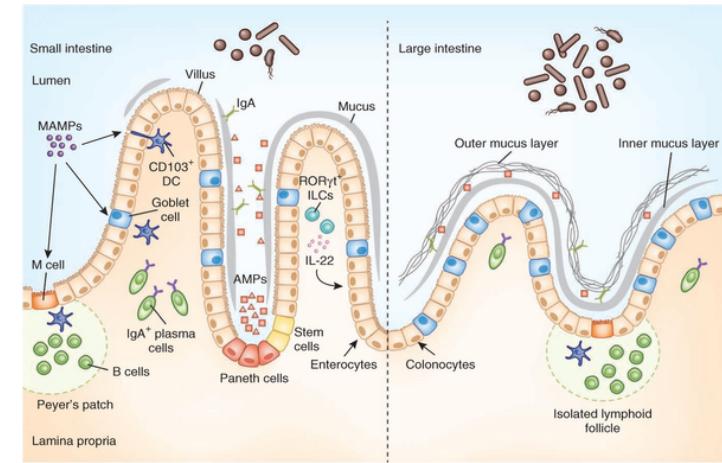
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Long-chain inulin alone increased **feed efficiency**

Long-chain inulin alone and combined with *L. acidophilus* W37 **reduced diarrhea**

Long-chain inulin combined with *L. acidophilus* W37 **supports oral vaccination efficacy** against *Salmonella*



Conclusions

Future perspectives



- Long-chain inulin/*L. acidophilus* W37 improves vaccination
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 - Instrumental in the fight against STM
 -
 - Limit spreading in humans via food consumption.





Thank you for your attention!

