

# Findings from the 'ShinDig' study:

## A human clinical trial comparing the digestibility of sheep and cow milk

Dr Amber Milan PhD

2020 Sheep Milk NZ Conference

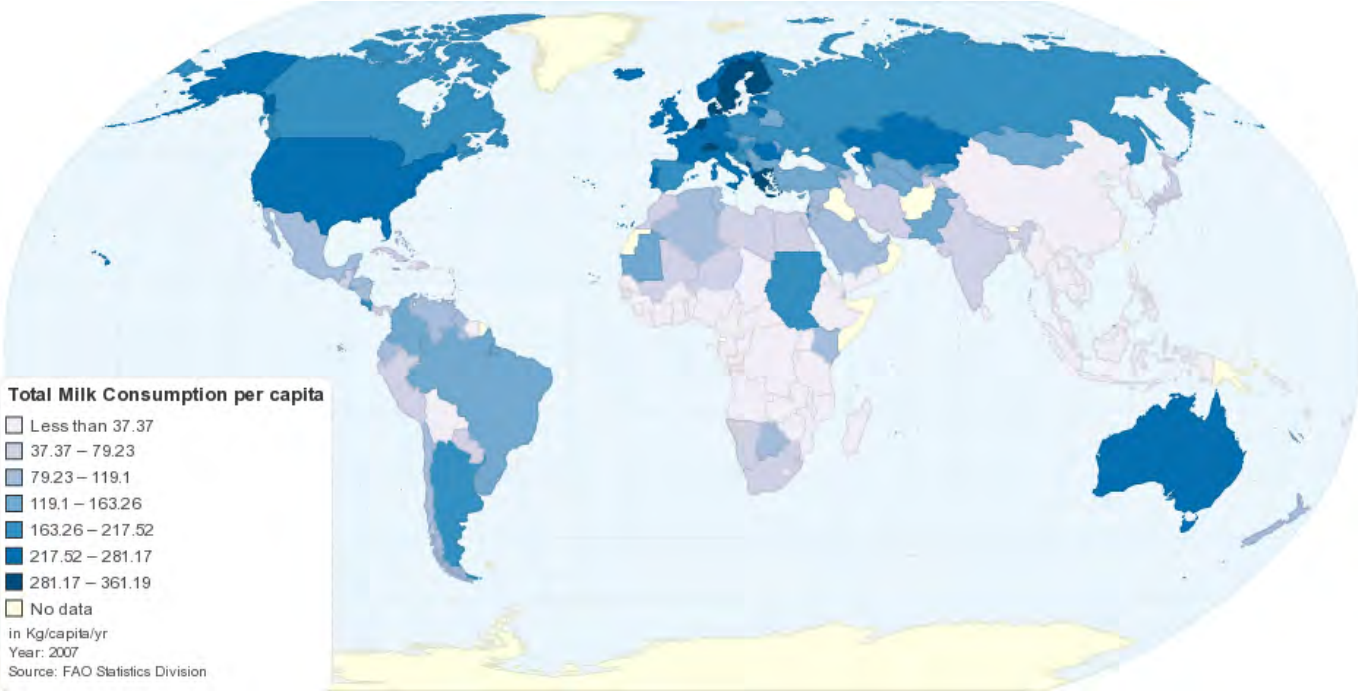
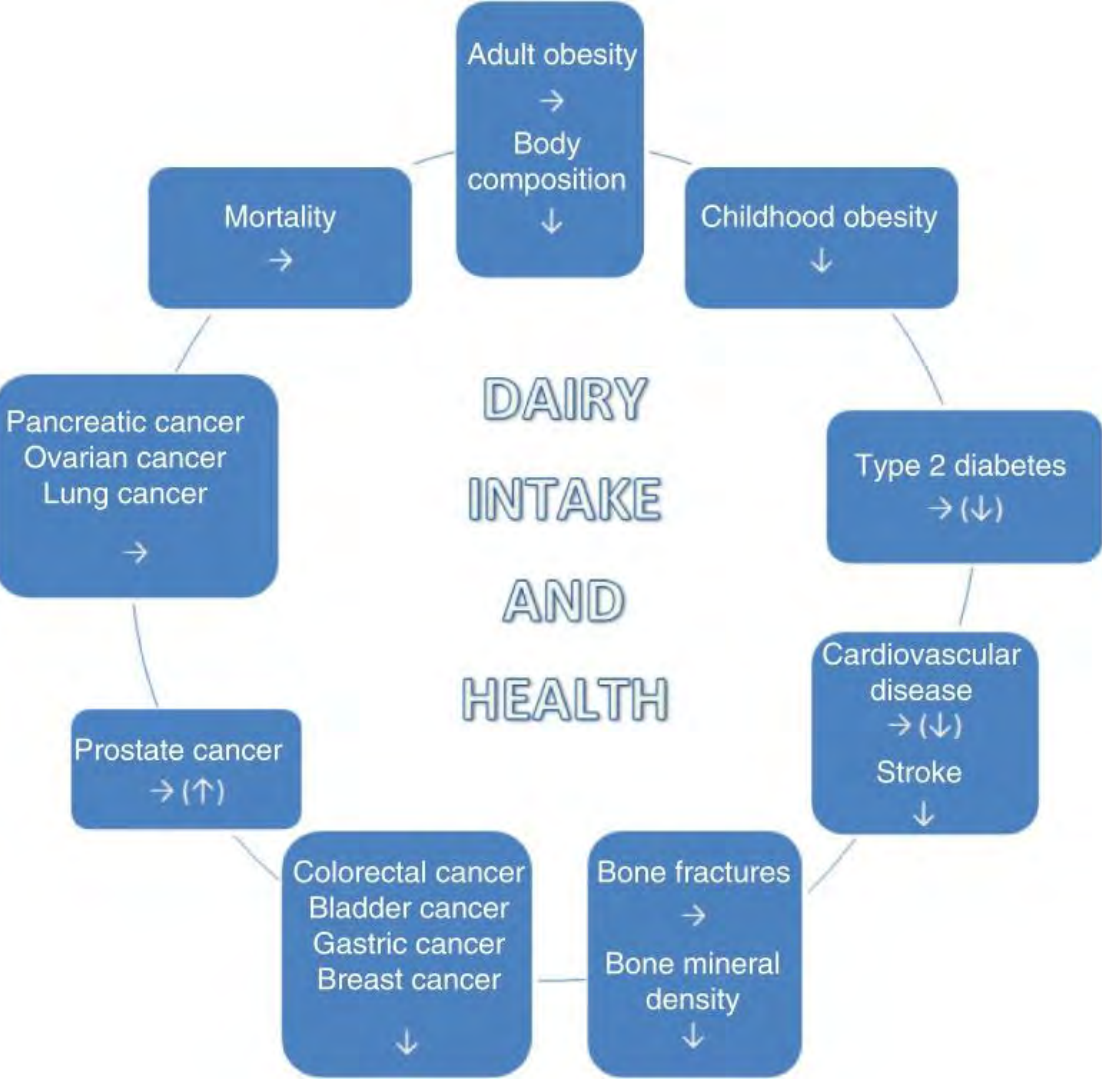
March 31 2020

**ag**research  
*āta mātai, mātai whetū*

## Outline

- *Background*
  - Our relationship with milk
  - Digesting milk – allergy, intolerance, nutrients
- *Research*
  - Different milk, different digestion
    - Nutrients (DiNGo Trial – Goat)
    - Intolerance (aMiGo Trial – a2 Milk™)
  - Sheep Milk Digestion – ShinDig Trial
  - The future: Adaptation and nutrient delivery

# Our relationship with milk: Good days and bad days



ChartsBin statistics collector team 2011, *Current Worldwide Total Milk Consumption per capita*, ChartsBin.com, viewed 18th October, 2017, <<http://chartsbin.com/view/1491>>. Thorning, Tanja Kongerslev et al. "Milk and Dairy Products: Good or Bad for Human Health? An Assessment of the Totality of Scientific Evidence." *Food & Nutrition Research* 60 (2016): 10.3402/fnr.v60.32527. PMC. Web. 18 Oct. 2017.

# Dairy avoidance: Do alternatives make the cut?



“Many individuals with **real or perceived** lactose **intolerance** avoid dairy and ingest inadequate amounts of calcium and vitamin D, which may predispose them to decreased bone accrual, osteoporosis, and other adverse health outcomes.

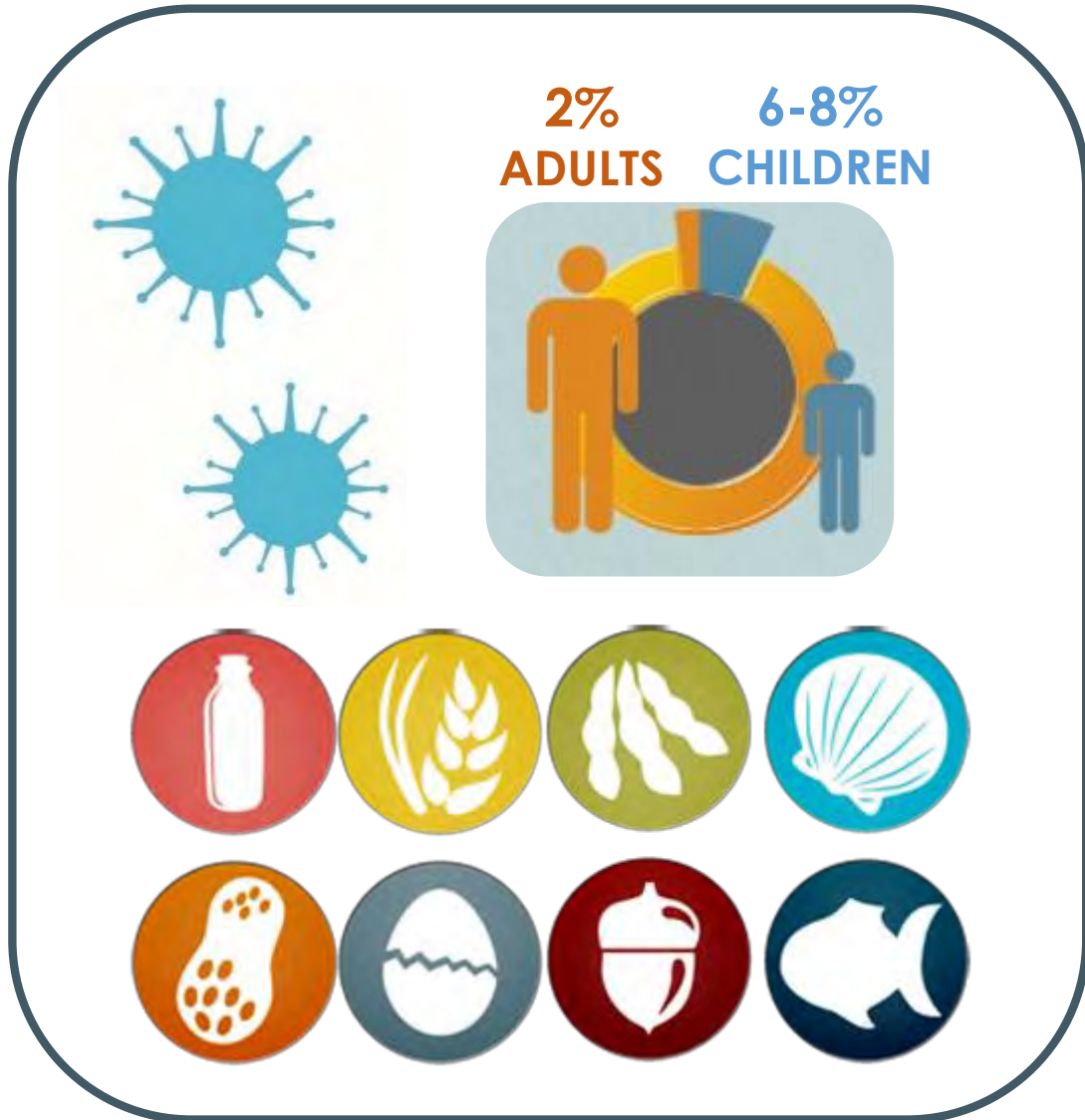
**In most cases, individuals do not need to eliminate dairy consumption completely.”**



# Allergy

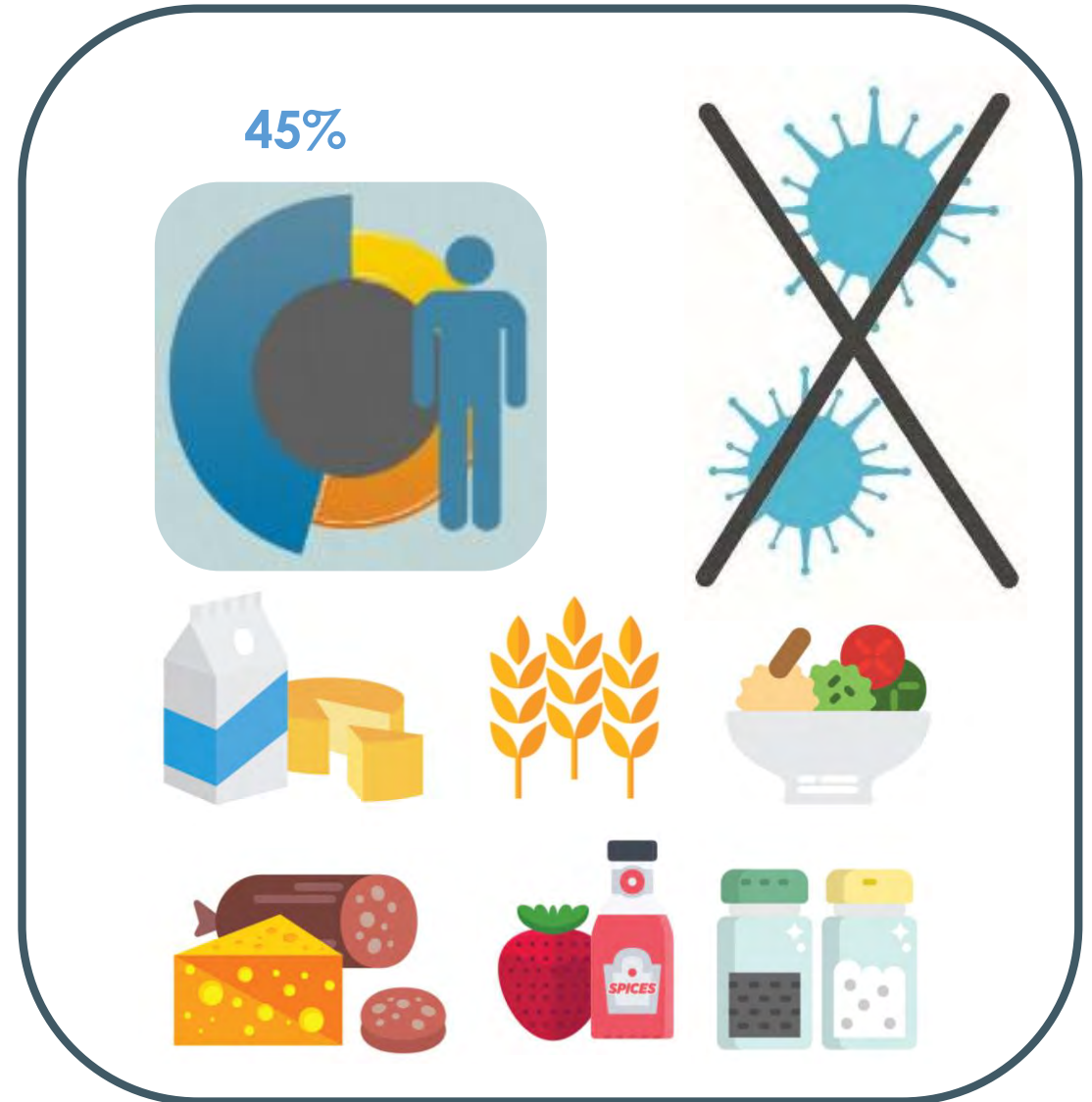
OR

# Intolerance?



2% ADULTS 6-8% CHILDREN

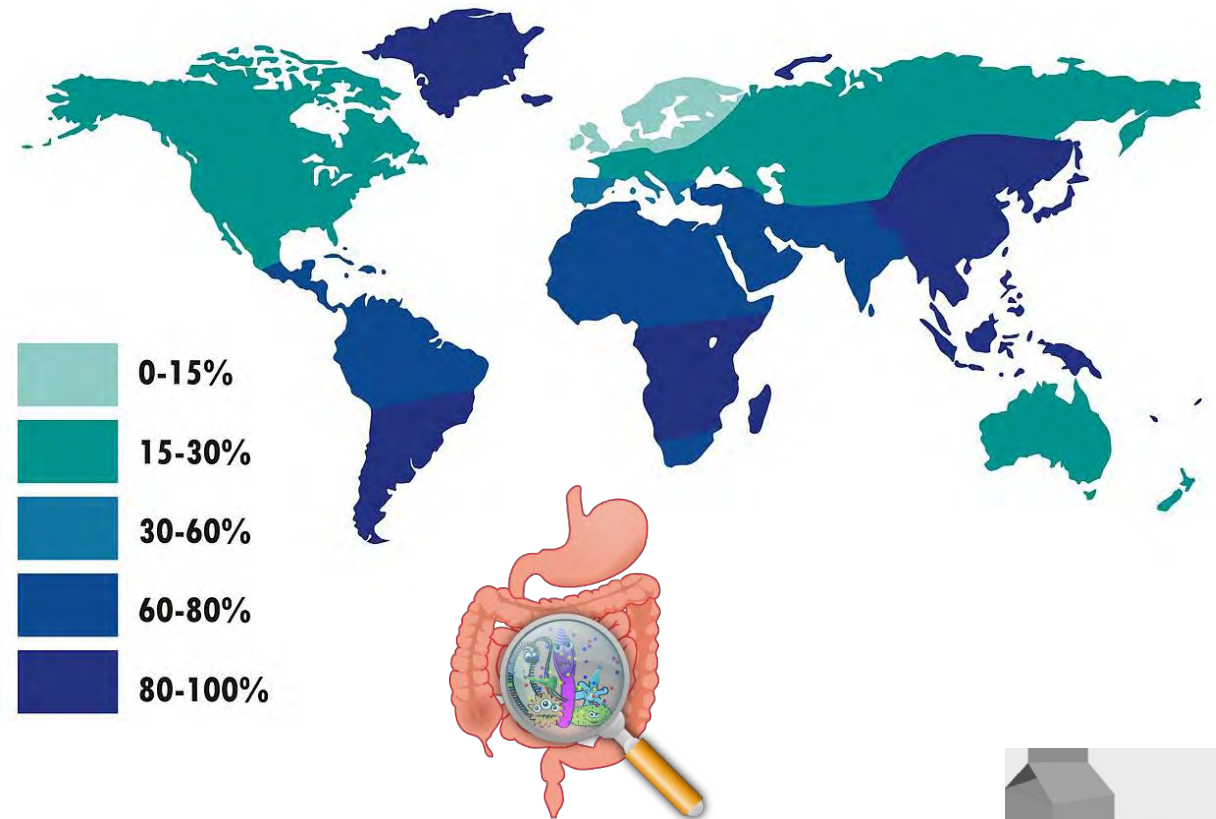
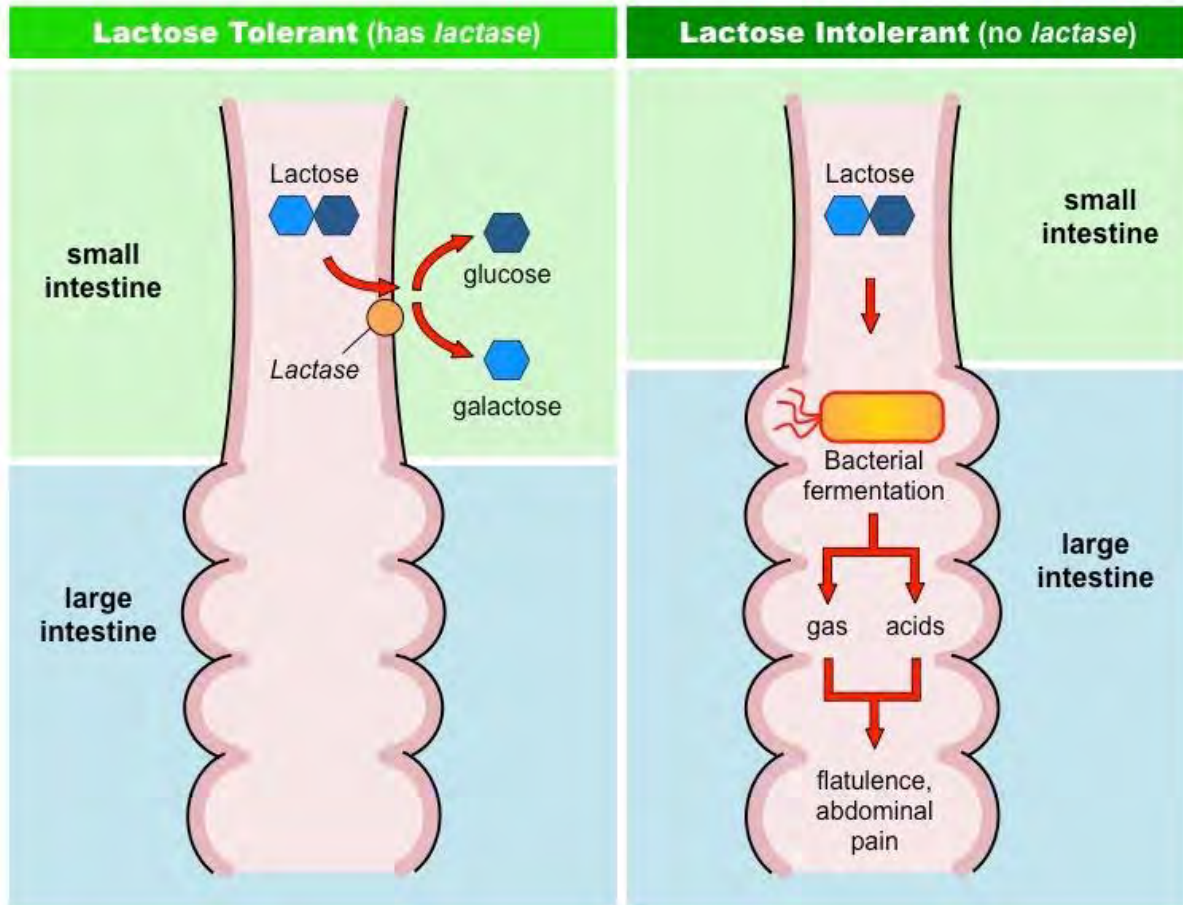
Two blue virus-like icons are shown on the left. In the center, a pie chart is partially filled with orange and blue, with an orange human figure and a blue human figure standing next to it. Below this are two rows of circular icons representing various allergens: a white bottle, wheat stalks, soybeans, a shell, a peanut, an egg, a nut, and a fish.



45%

A pie chart is partially filled with blue and orange, with a blue human figure standing next to it. To the right, two blue virus-like icons are crossed out with a large black 'X'. Below these are three rows of food icons: a carton of milk and cheese, wheat stalks, a bowl of salad, a slice of cheese, a strawberry, a bottle of spices, and two jars of spices.

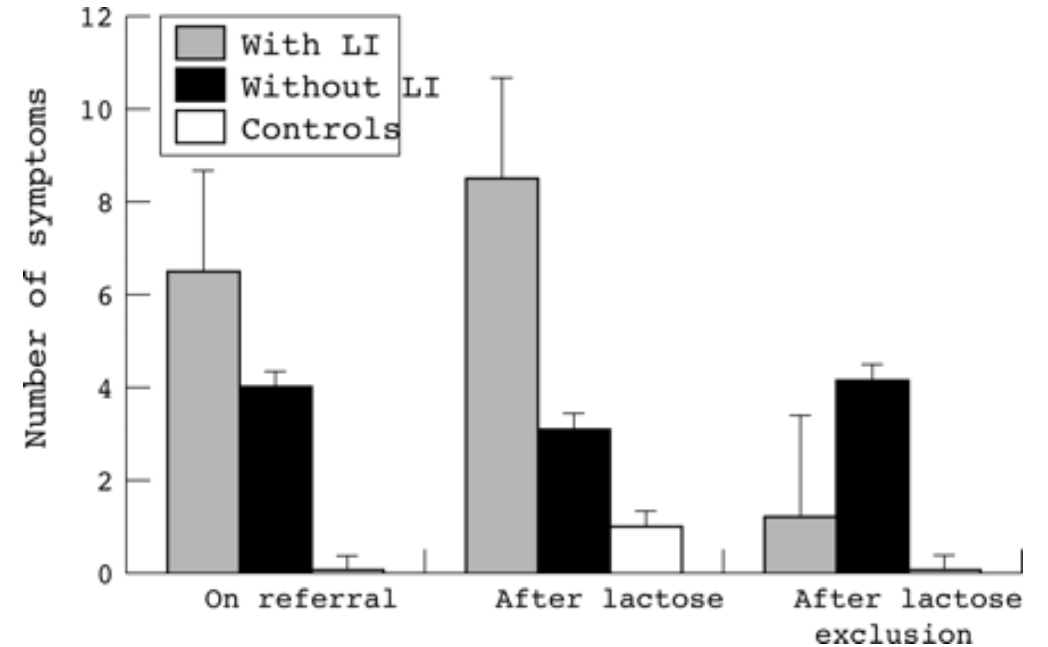
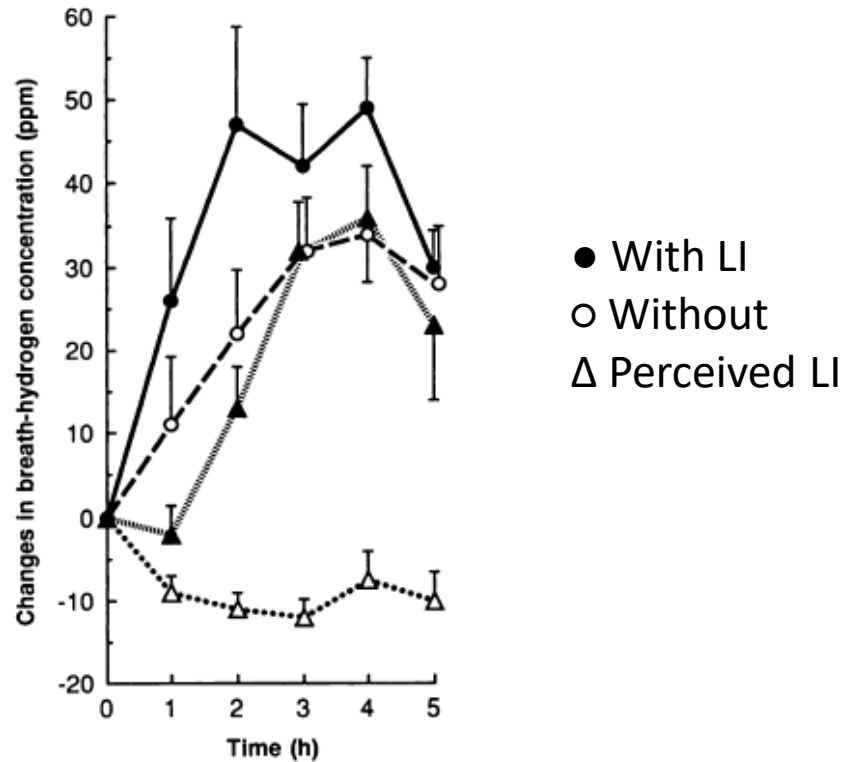
# Lactose Intolerance: A key culprit



“Lactose intolerance is a real and important clinical syndrome, but its true prevalence is not known.”



# When lactose isn't the problem



“Many individuals who think they are lactose intolerant are not lactose malabsorbers.”

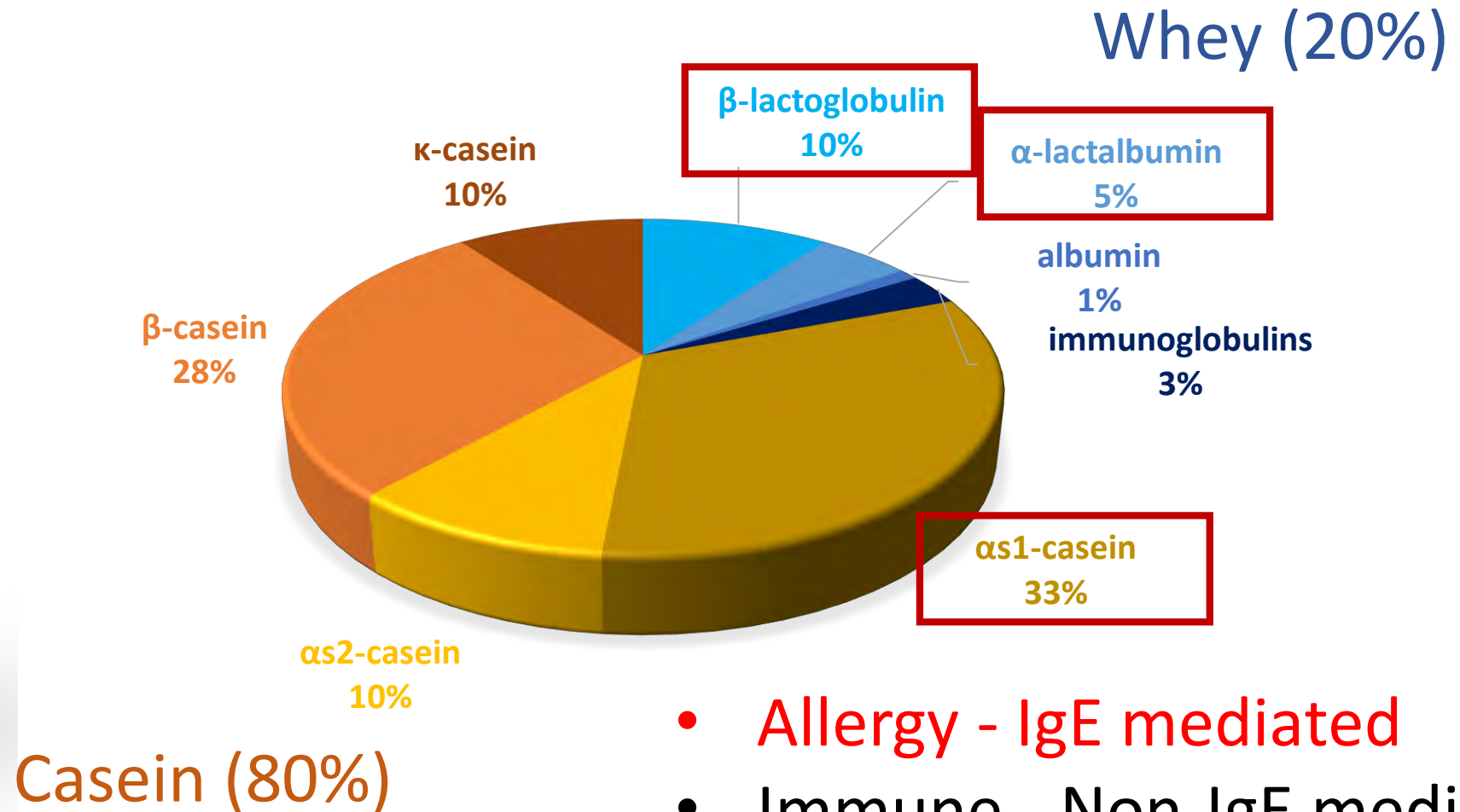
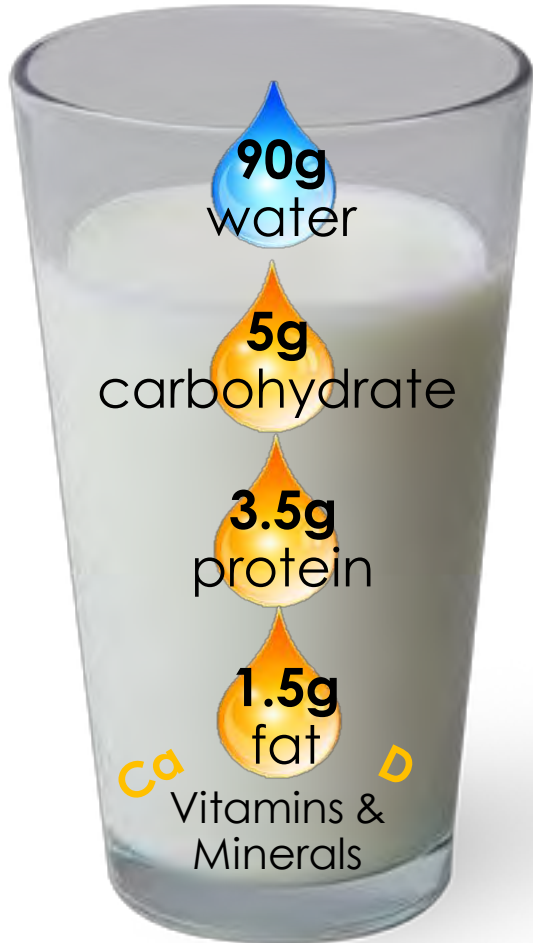


Matthews, Stephanie B., et al. "Systemic lactose intolerance: a new perspective on an old problem." *Postgraduate Medical Journal* 81.953 (2005): 167-173.

Suarez, Fabrizis L., et al. "Tolerance to the daily ingestion of two cups of milk by individuals claiming lactose intolerance." *Am J Clin Nutr* 99.7.65: 1502-6.

Suchy, Frederick J., et al. "NIH consensus development conference statement: lactose intolerance and health." *NIH Consensus and State-of-the-science Statements* 27.2 (2010): 1-27.

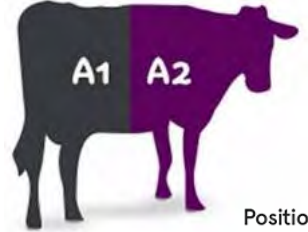
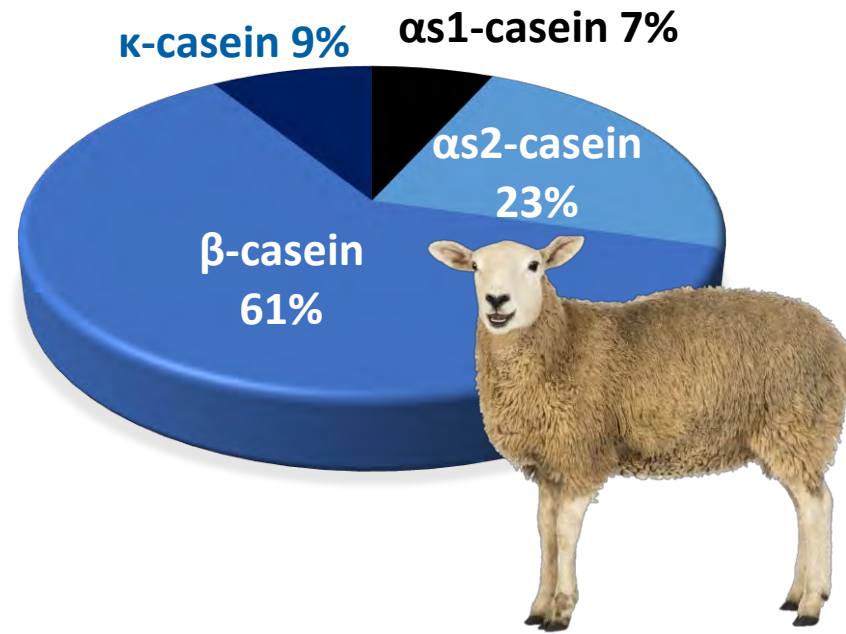
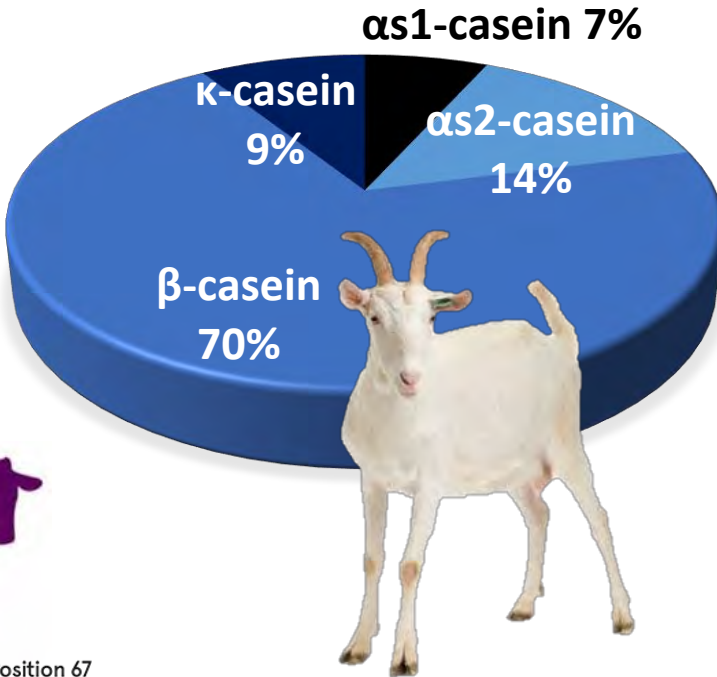
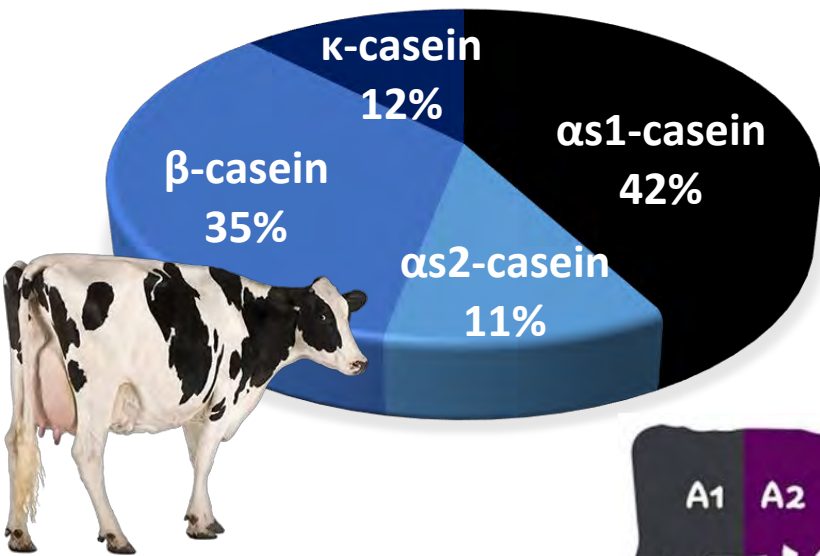
# Dairy proteins – complex and varied



- Allergy - IgE mediated
- Immune - Non-IgE mediated?
- Digestive effects?



# Casein differences – species and individuals

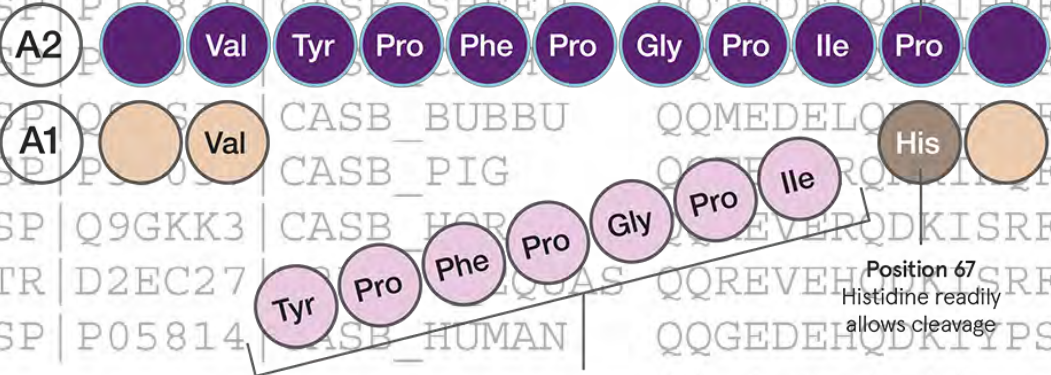


Position 67  
Proline hinders cleavage

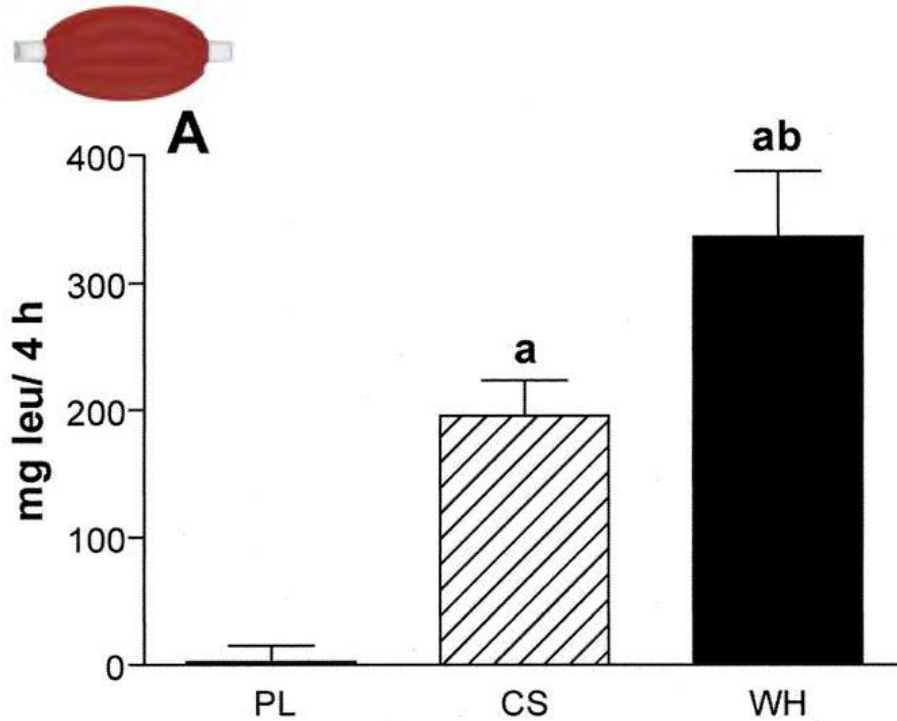
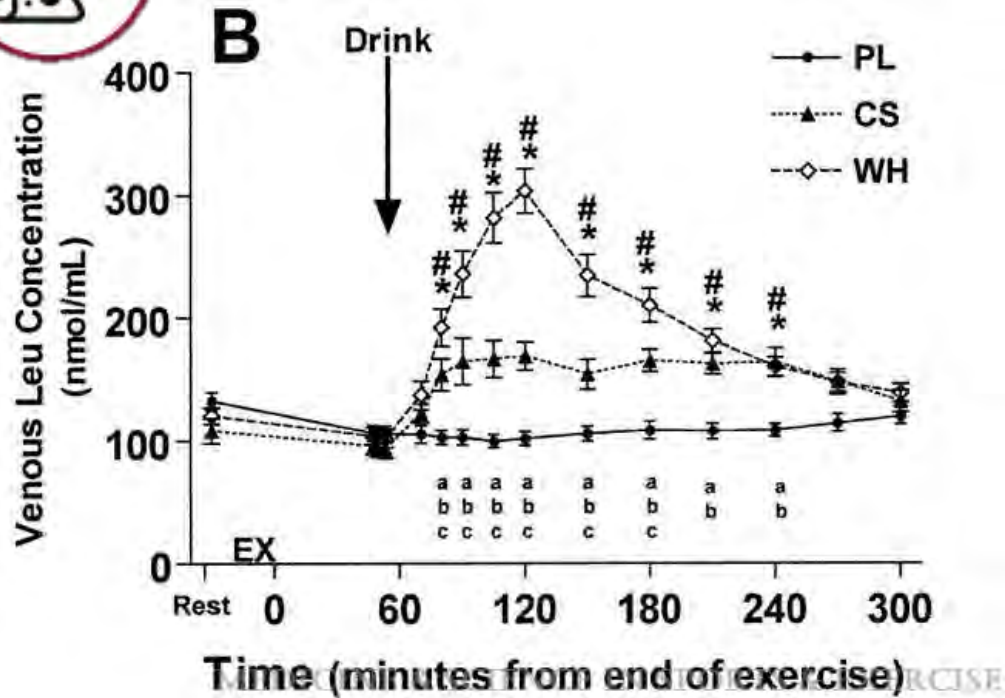
SP	P02666	CASB_BOVIN	QQTEDELQDKIHPFAQTQSLVYPFPGPI	PNS	-LPQ	NIPLLTQTPVVVPPFL	LQPEVMGVSK	112
SP	P11839	CASB_SHEEP	QQTEDELQDKIHPFAQAQSLVYPFTGPI	PNS	-LPQ	NILPLTQTPVVVPPFL	LQPEIMGVSK	112
SP	P00056	CASB_GOAT	FAQAQSLVYPFTGPI	PNS	-LPQ	NILPLTQTPVVVPPFL	LQPEIMGVSK	112
SP	P00056	CASB_BUBBU	QQMEDELQDKIHPFAQTQSLVYPFPGPI	PKS	-LPQ	NIPLLTQTPVVVPPFL	LQPEIMGVSK	112
SP	P01103	CASB_PIG	QQTEDELQDKIHPFAQTQSLVYPFPGPI	PYP	ILPQ	NILPLAQPVVV	-PLLHPEVMKDSK	113
SP	Q9GKK3	CASB_HORSE	QQTEDELQDKIHPFAQTQSLVYPFPGPI	PYP	ILPQ	NILPLAQPVVV	-PLLHPEVMKDSK	113
SP	Q9GKK3	CASB_HORSE	QQREVEHQLKISRFVQPQPVVYPYAEPV	PYAV	VPQS	SILPLAQPPI	--PFLQPEIMEVSQ	118
TR	D2EC27	CASB_HORSE	QQREVEHQLKISRFVQPQPVVYPYAEPV	PYAV	VPQ	NILPLAQPPI	IV--PFLQPEIMEVSQ	118
SP	P05814	CASB_HUMAN	QQGEDEHQLKISRFVQPQPLIYPFVEPI	PYGF	LPQ	NILPLAQP	AVVL-PVPQPEIMEVSK	103

Position 67  
Histidine readily allows cleavage

Beta-casomorphin-7 \* \* \* \* \*



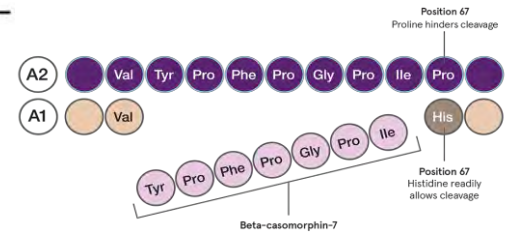
# Digestion: protein impacts rate



PL: placebo  
CS: casein  
WH: whey

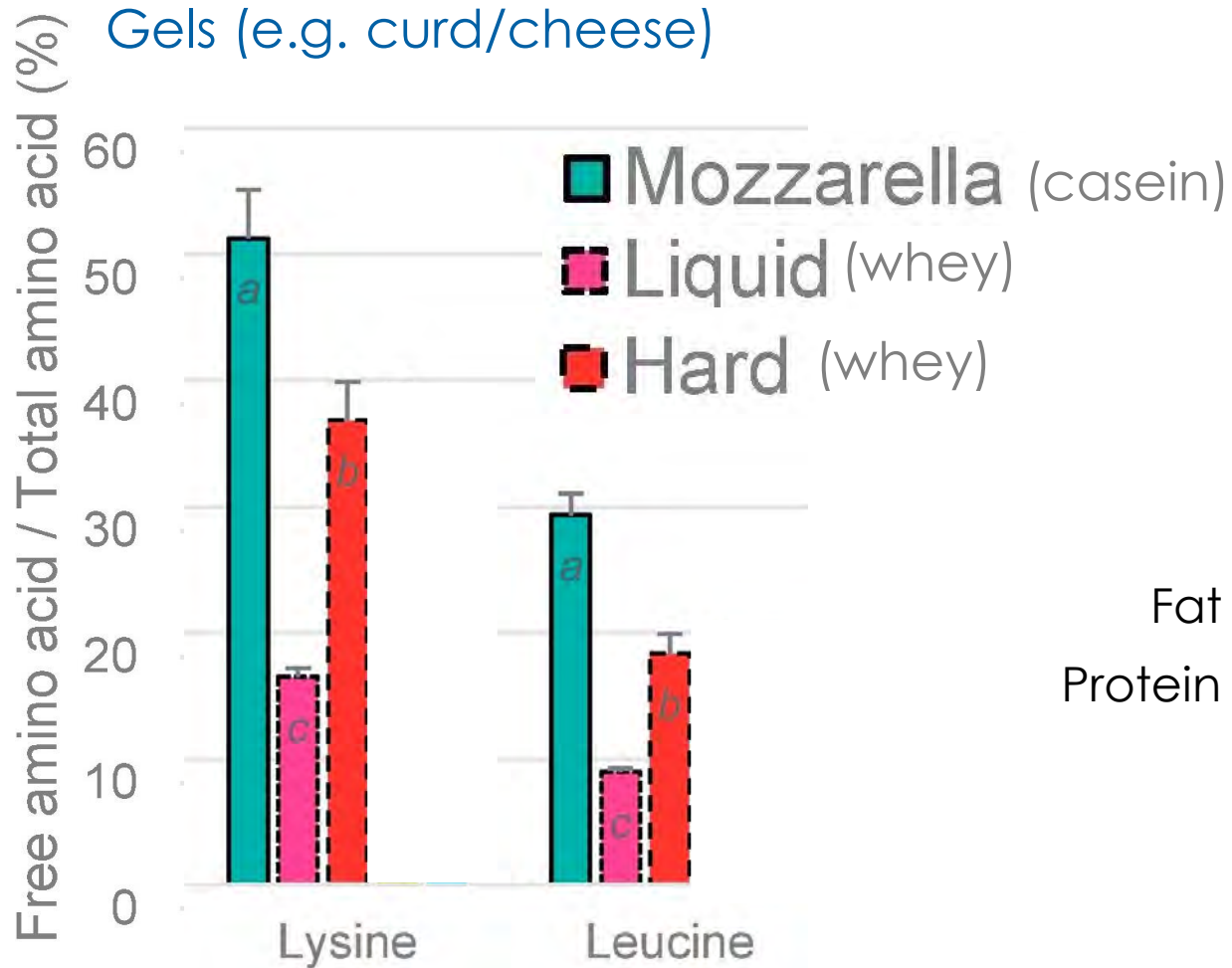


?

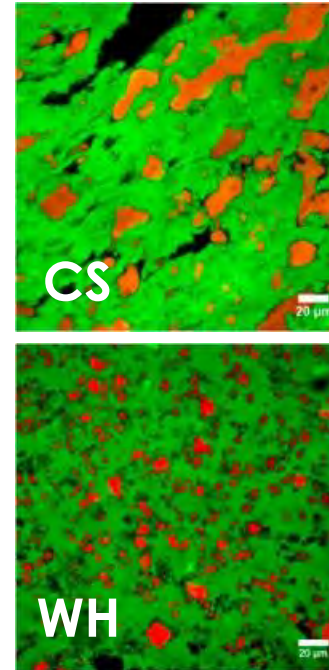


Fast protein → greater amino acid in blood → greater muscle response

# Digestion: structure impacts release

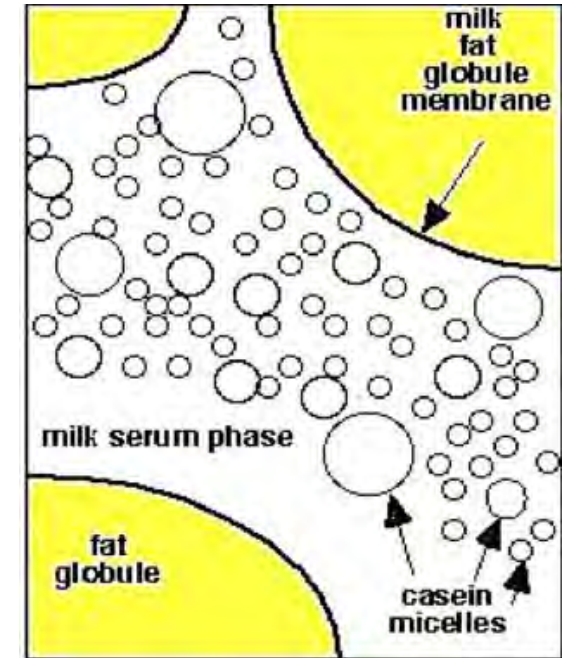


Curd/gel structure



Fat ■  
 Protein ■

Milk structure



- Complex milk structures
- Interactions with fats

# Different milk, different digestion

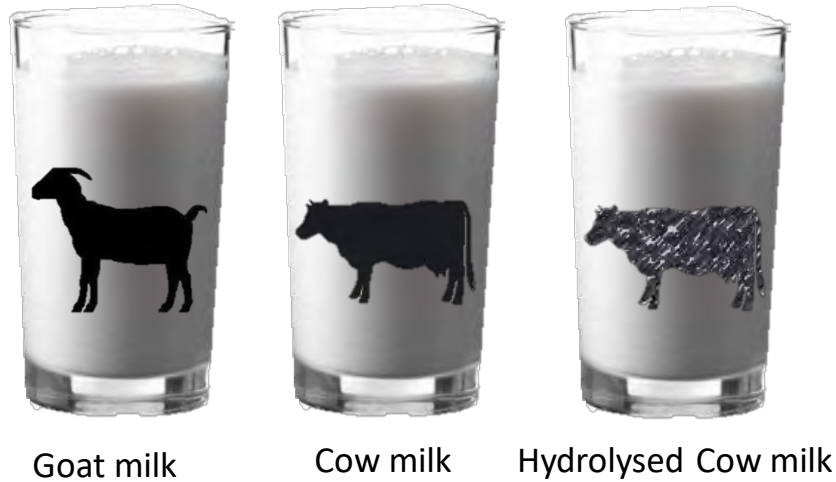
DiNGo Trial: cow and **goat milk** – nutrient availability

aMiGo Trial: a2 Milk™ for Gut Comfort – dairy intolerance

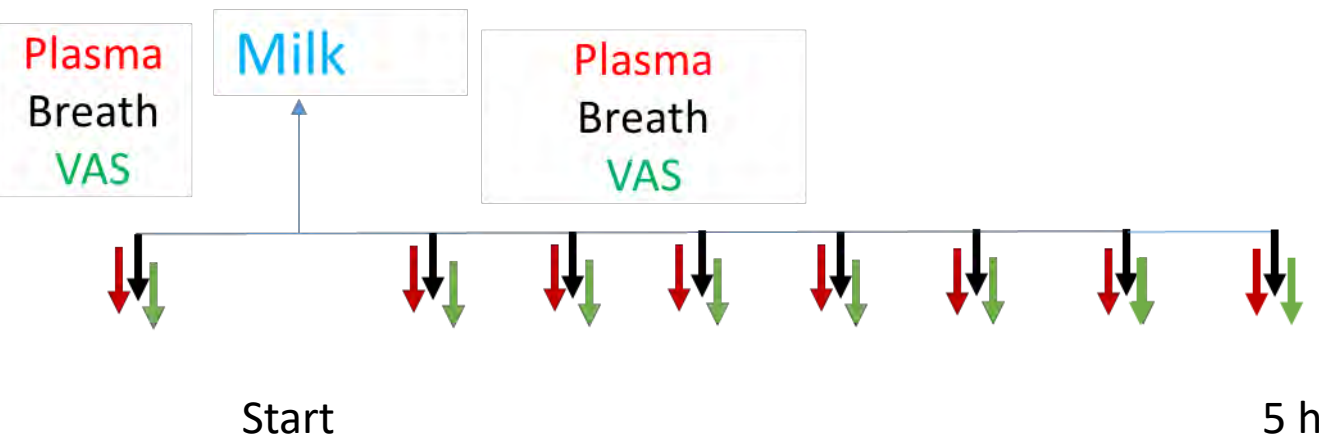
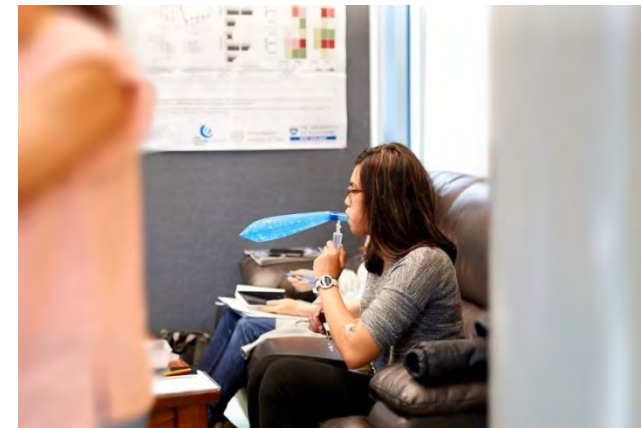
# DiNGo Trial

## Digestive and Nutrient Bioavailability Benefits of Goat Milk Formula

Is protein digestion similar between goat and cow milk?

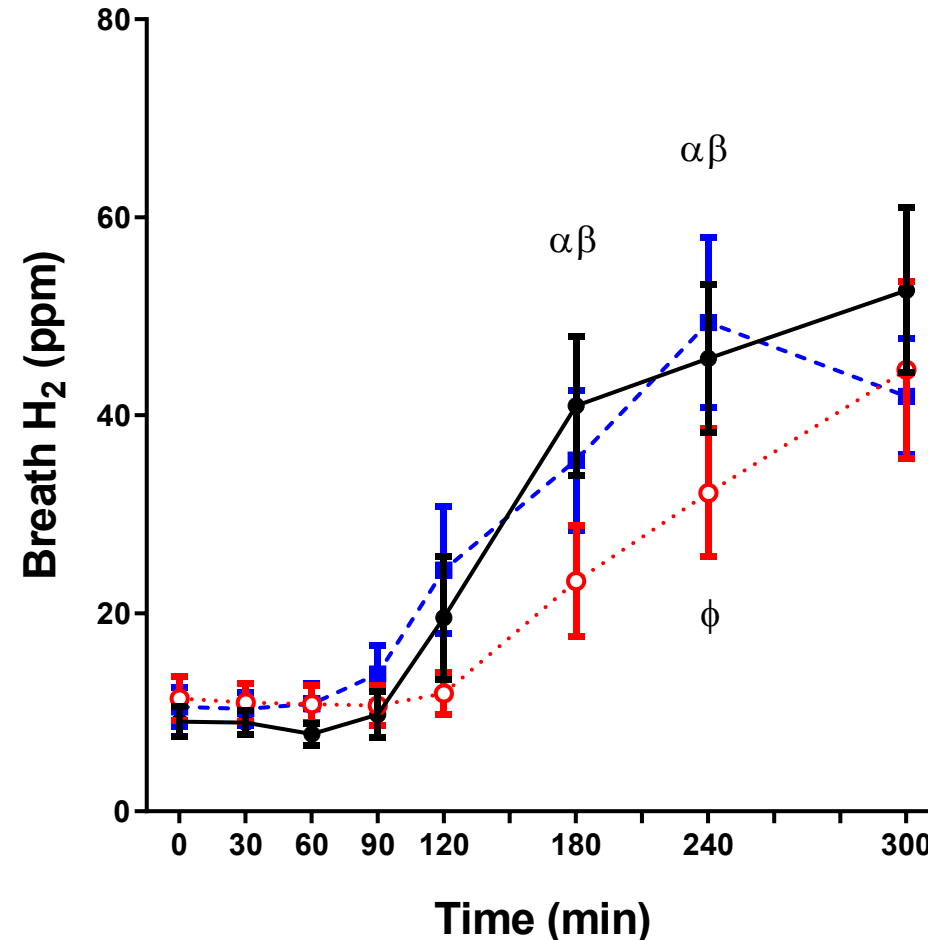
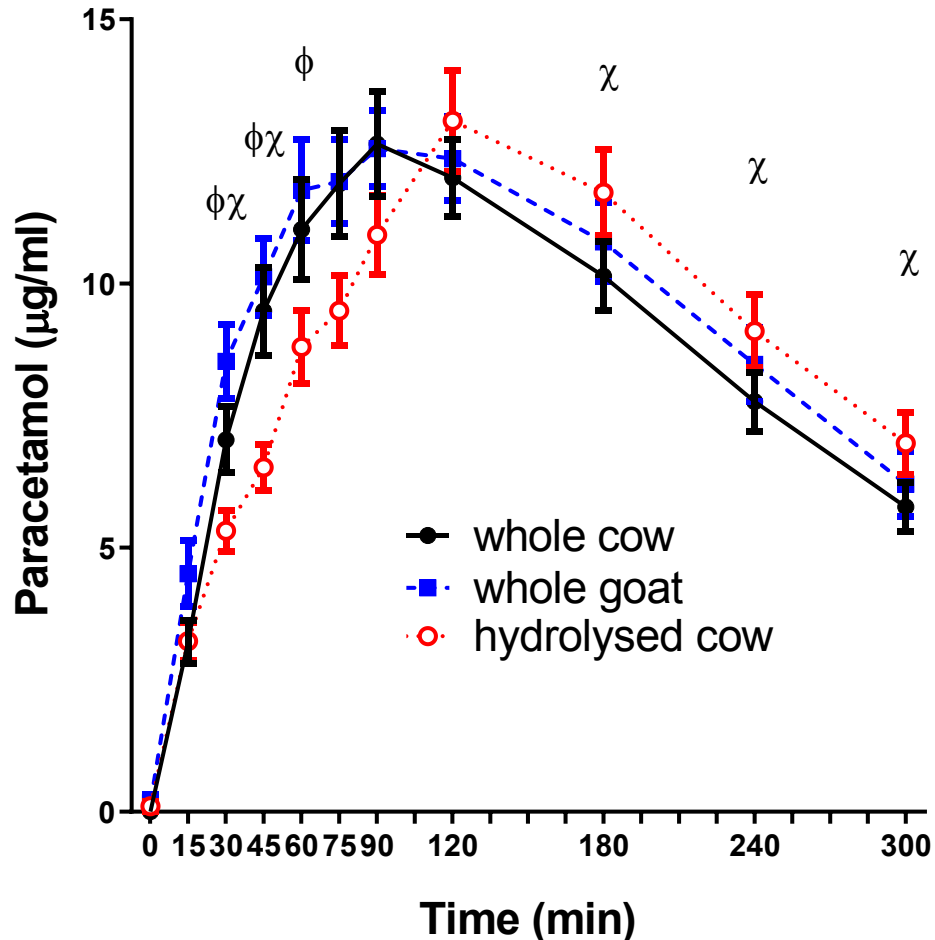


Dose: 11ml/kg body weight



# DiNGo Trial

## Goat and cow milk digestion similar



Goat and Cow:

- Similar digestive comfort
- Similar digestion speed

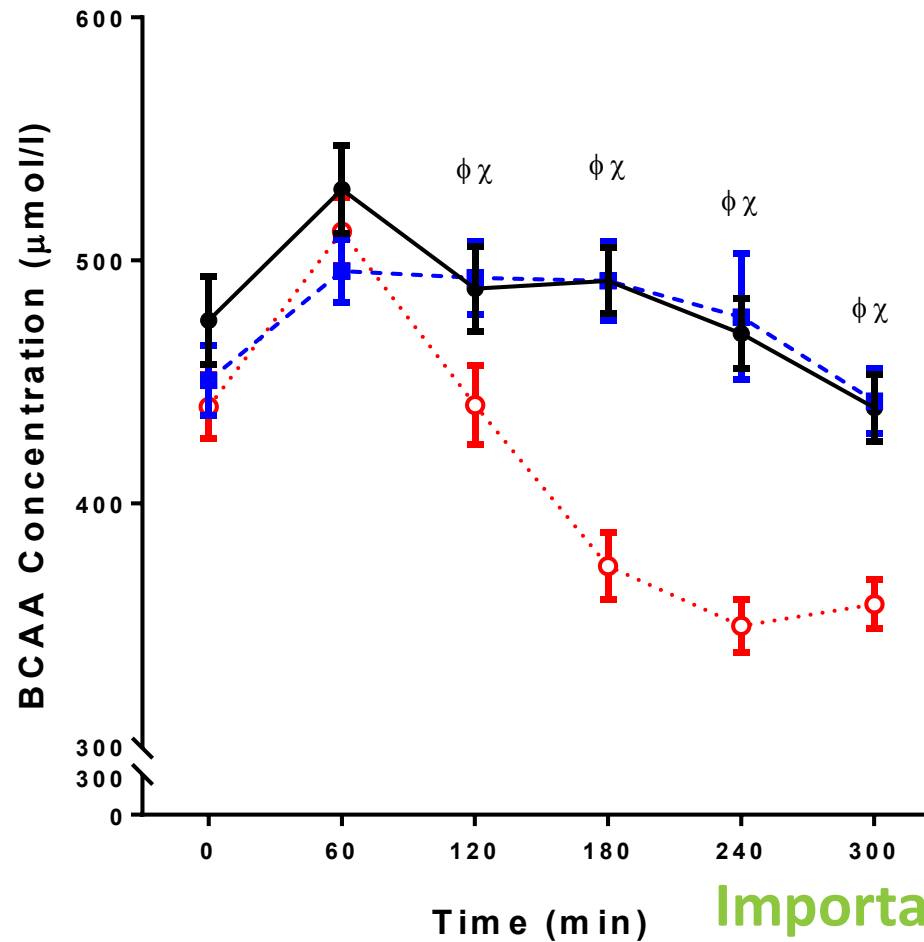
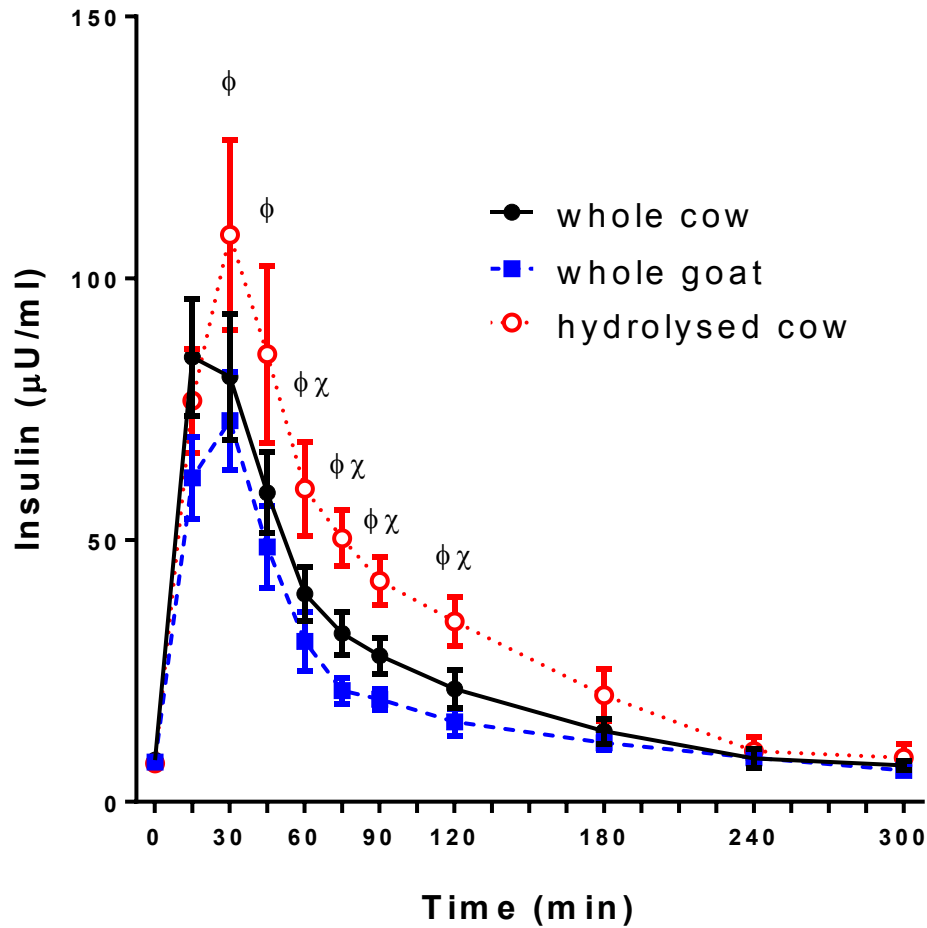
Hydrolysed Cow:

- Delayed emptying
- Delayed malabsorption

φ denotes statistical significance  $p < 0.05$ , hydrolysed cow vs. goat, and χ hydrolysed cow vs. cow, respectively. α increase with cow, β increase with goat.

# DiNGo Trial

## Hydrolysed proteins alter insulin and protein metabolism



Goat and Cow:

- Similar metabolism

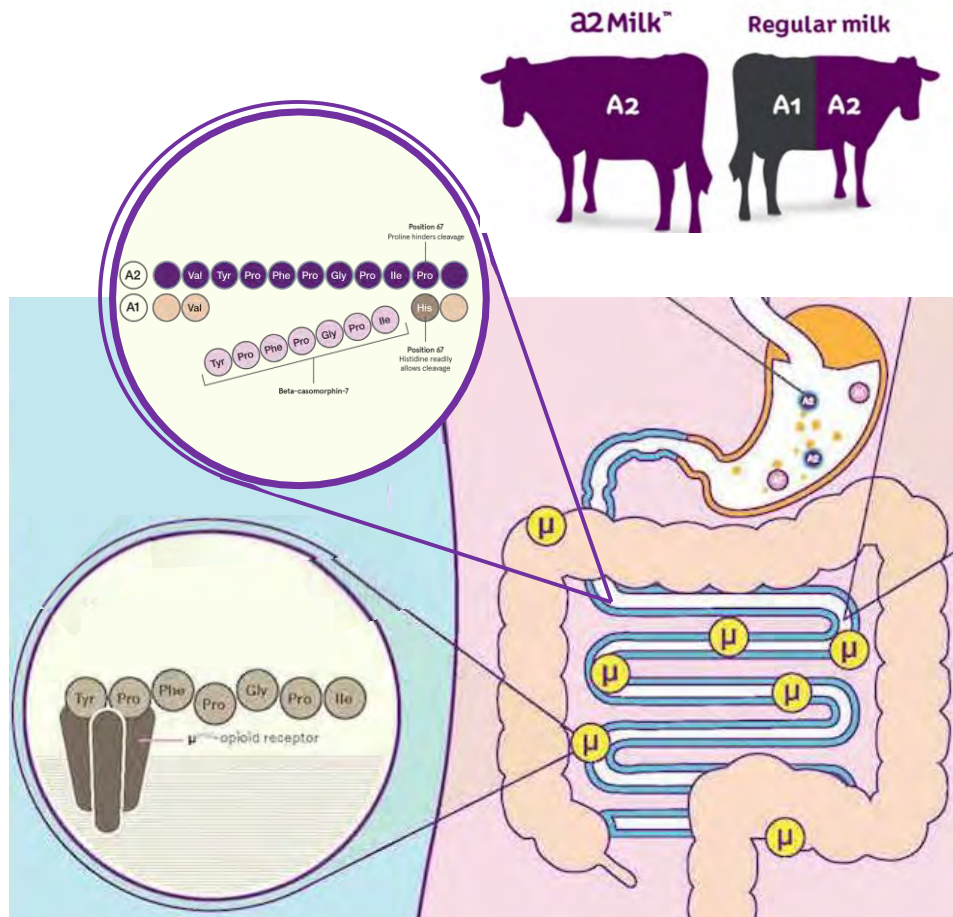
Hydrolysed Cow:

- Exaggerated insulin
- Rapid amino acid clearance

Importance of protein structure

φ denotes statistical significance  $p < 0.05$ , hydrolysed cow vs. goat, and χ hydrolysed cow vs. cow, respectively.

# The aMiGo Trial: a2 Milk™ for Gut Comfort

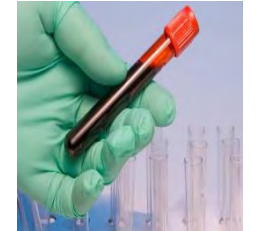
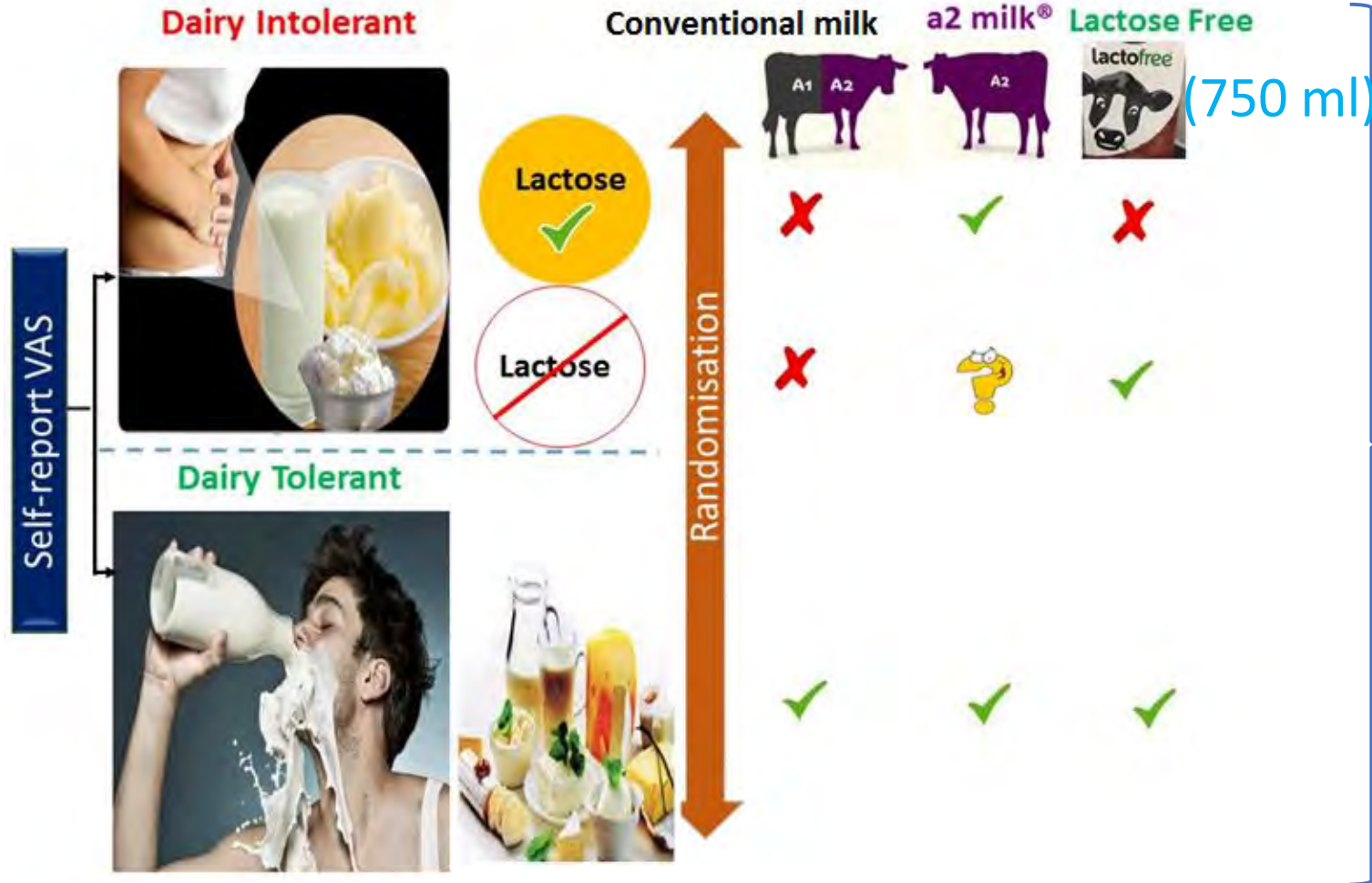


- Non-Lactose Dairy Intolerance
  - Known that a proportion of **self-reported** lactose intolerant are **not lactose malabsorbers**
  - **Protein-mediated** effects of milk intolerance may be **independent** of lactose malabsorption
  - **Symptoms** and identification of protein-mediated milk intolerance are **undescribed**
- Digestive tolerance of a2 Milk
  - Lactose-mediated versus **protein-mediated**



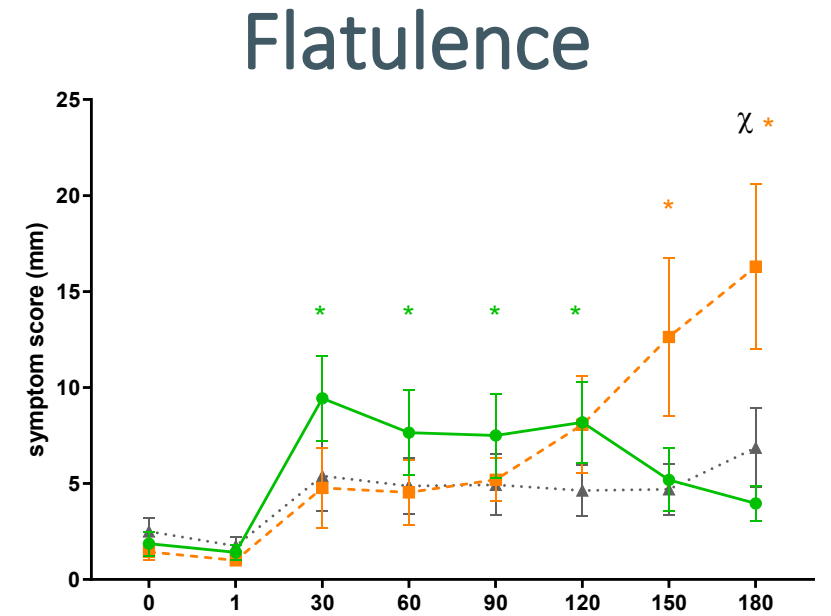
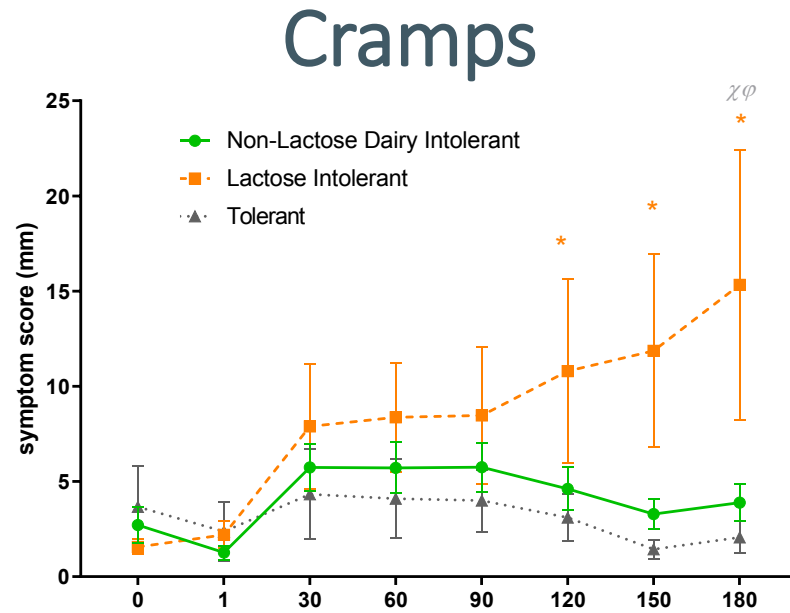
# The aMiGo Trial: a2 Milk™ for Gut Comfort Design

## Hypothesis



# Lactose Intolerance

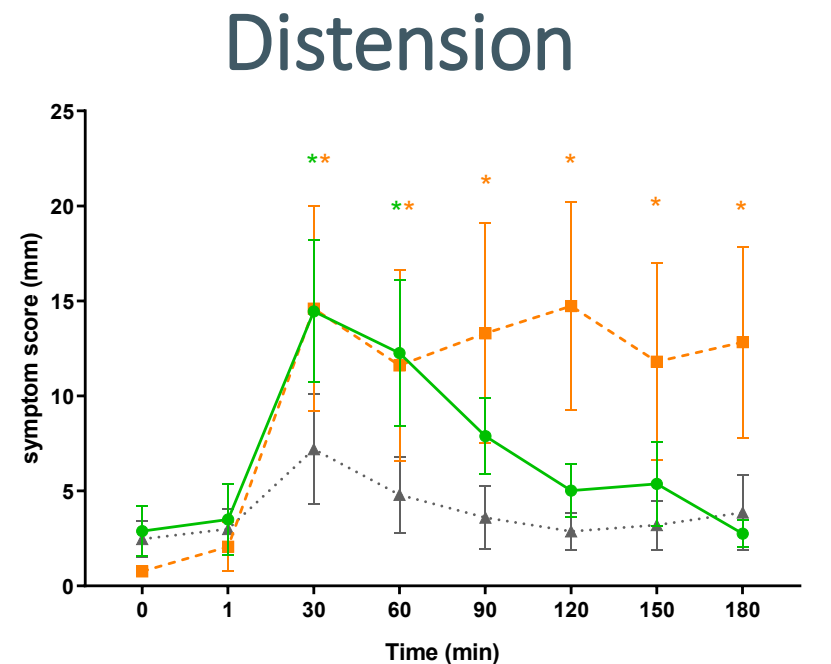
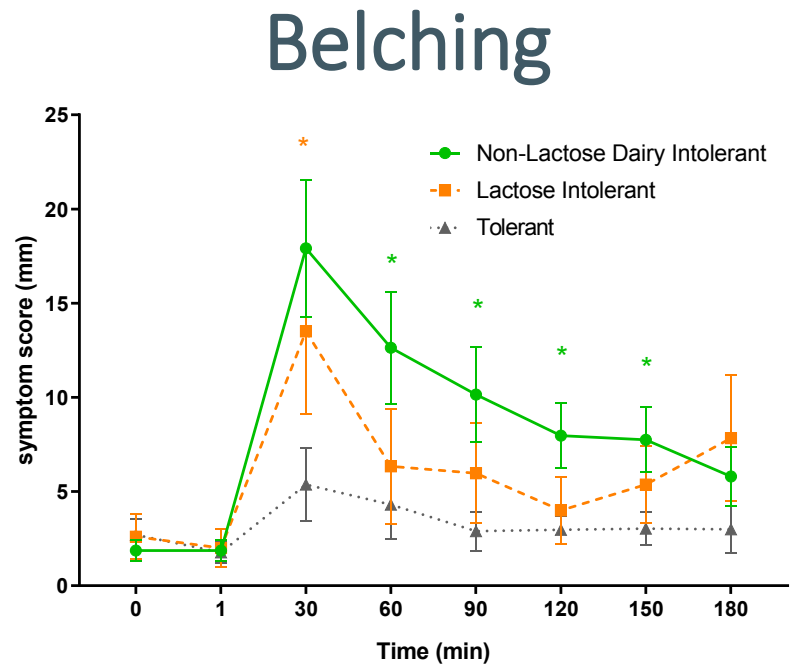
Lower GI  
Delayed (90 min+)



# Non-Lactose Dairy Intolerance

Upper GI; Distension  
Rapid (30-90 min)

**Different mechanism?**



# The aMiGo Trial:

Lactose and dairy intolerant subjects respond differently to  $\beta$ -casein variants

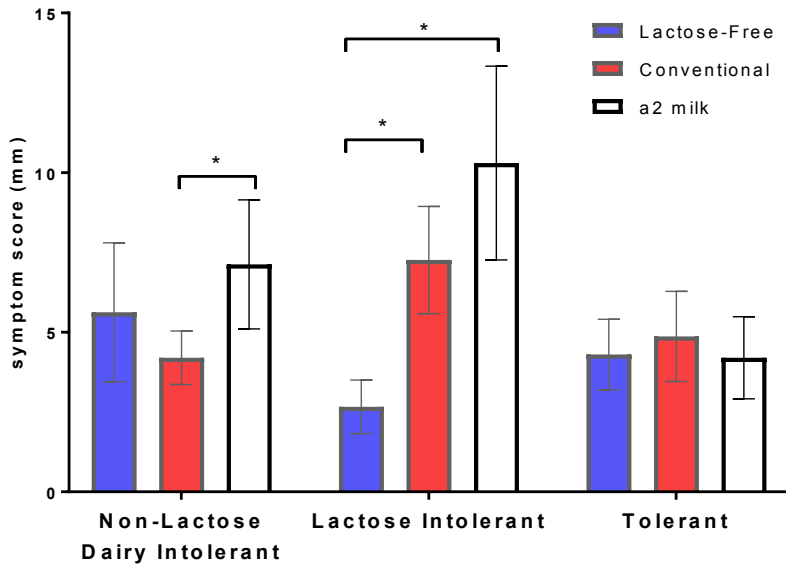


HIGH-VALUE NUTRITION

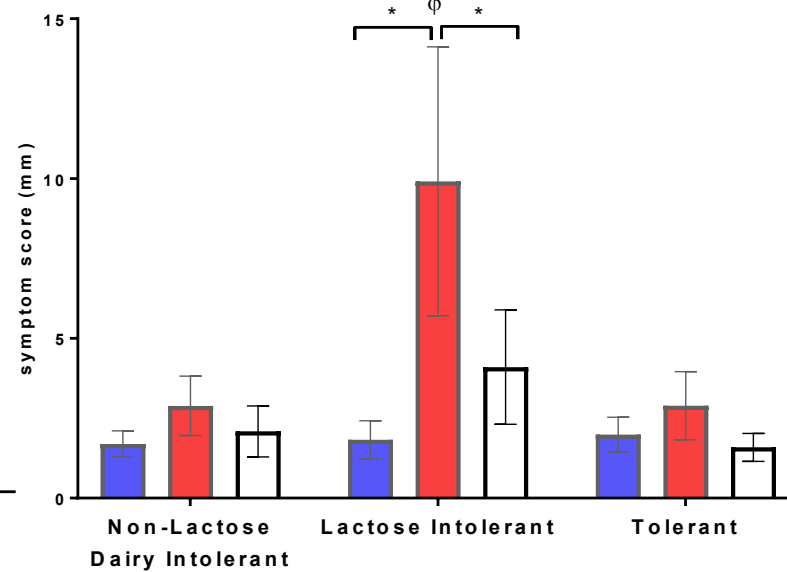
Ko Ngā Kai Whai Painga



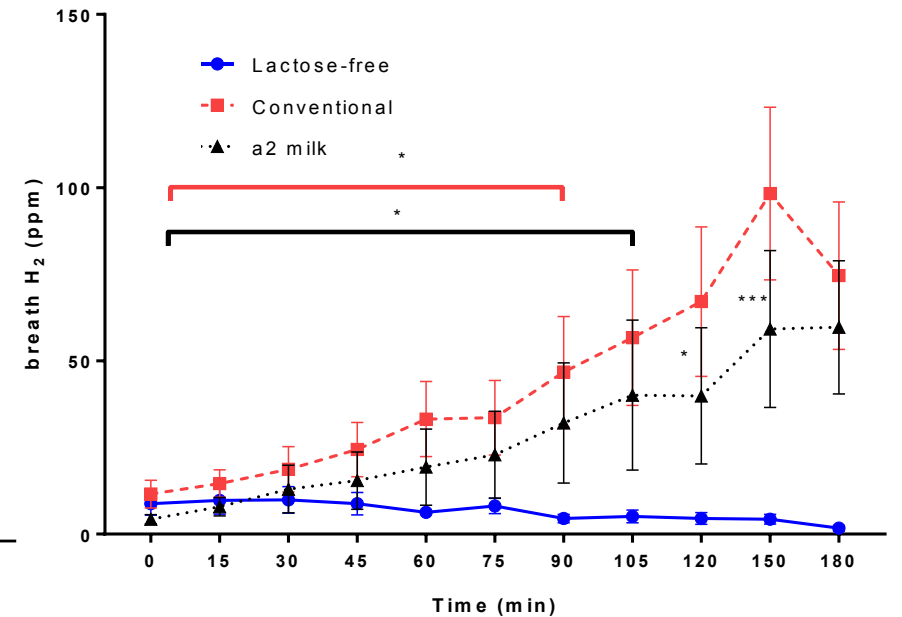
## Flatulence



## Faecal Urgency



## Breath H<sub>2</sub> Lactose Intolerant



**Lactose Intolerant:** reduced malabsorption, faecal urgency and nausea (not shown) with a2 Milk™

**Non-Lactose Dairy Intolerant:** more flatulence with a2 Milk™ → Different mechanism?

## Milk variability: digestive and nutrient responses

- Protein may play a mechanical or immune role
- Multiple aspects of milk impact nutrients and tolerance
  - Proteins, structure, interaction
- Dairy intolerance not limited to lactose
  - Mechanisms still unknown
- Malabsorption/intolerance not static

# Sheep Milk Digestion

Nutrients

Tolerance

# ShinDig Trial:

## Sheep milk nutrient bioavailability and digestive comfort



SPRING SHEEP  
- MILK CO. -  
New Zealand

Is protein digestion similar between sheep and cow milk?



Sheep milk



Cow milk

Dose: 650 ml

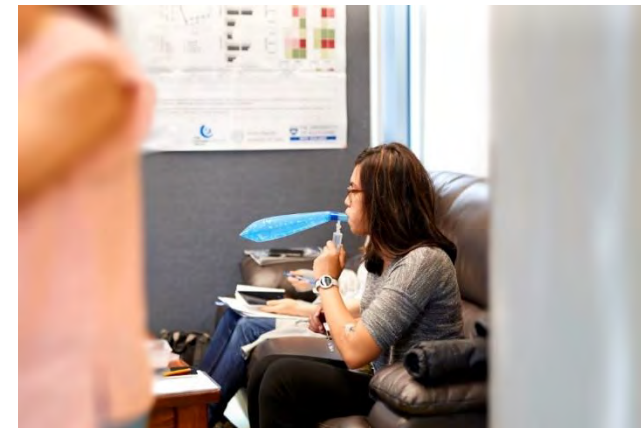
Nutrient	Sheep	Cow
Protein (g)	30	19
Fat (g)	33	21
Lactose (g)	25	33



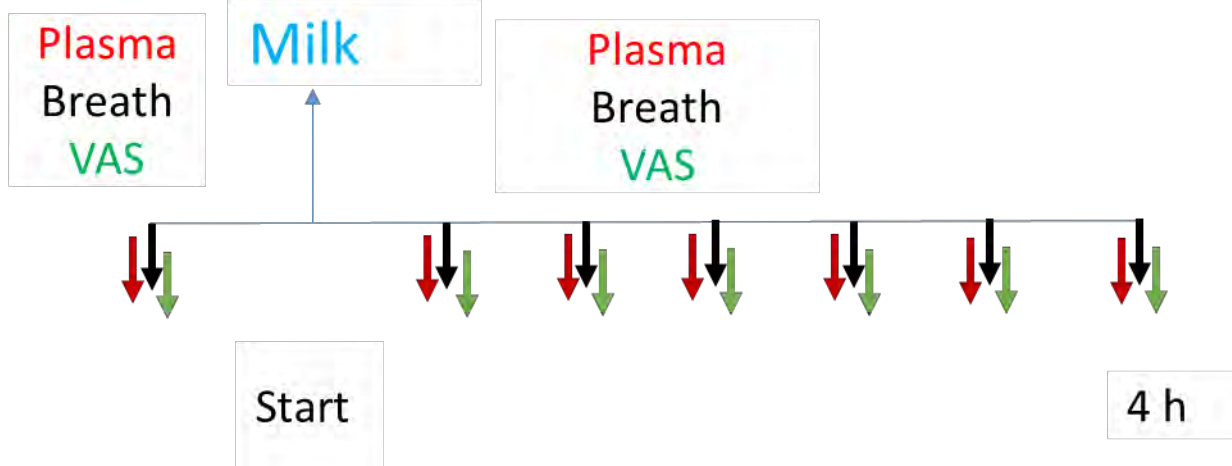
Lactose malabsorption



Digestive comfort (symptoms)



Nutrient response (proteins, fats, micronutrients)



# ShinDig Trial:

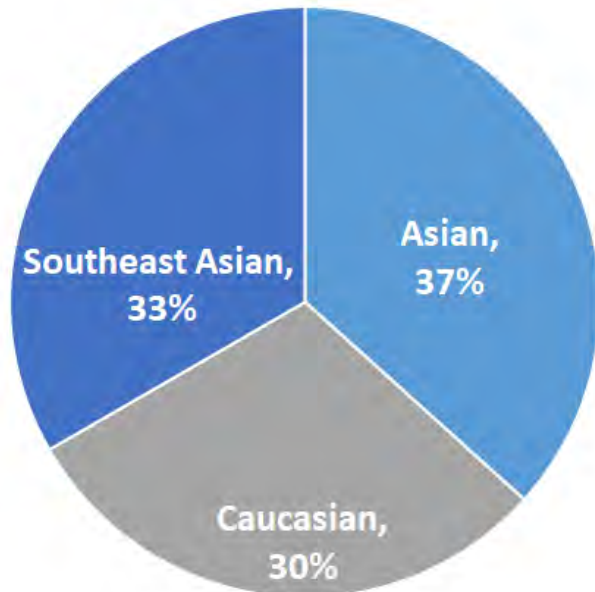
## Sheep milk nutrient bioavailability and digestive comfort



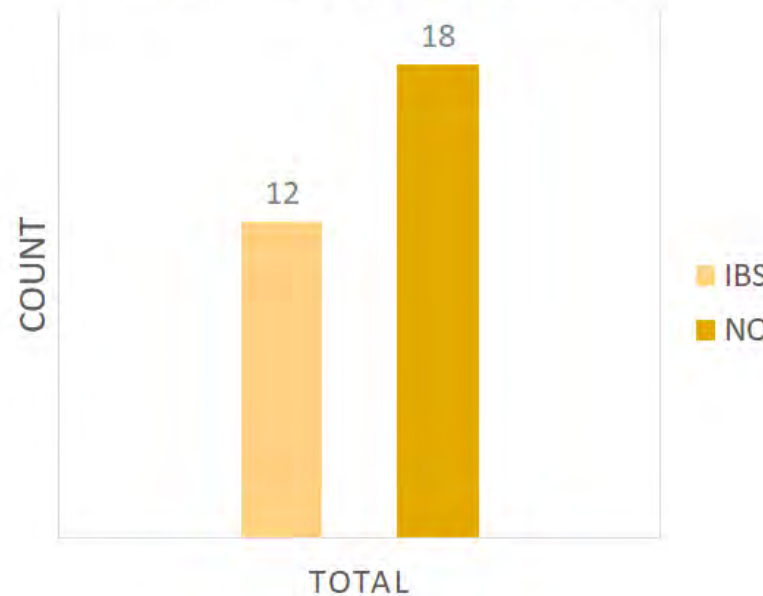
SPRING SHEEP  
- MILK CO. -  
New Zealand

Participants – “dairy avoiders”

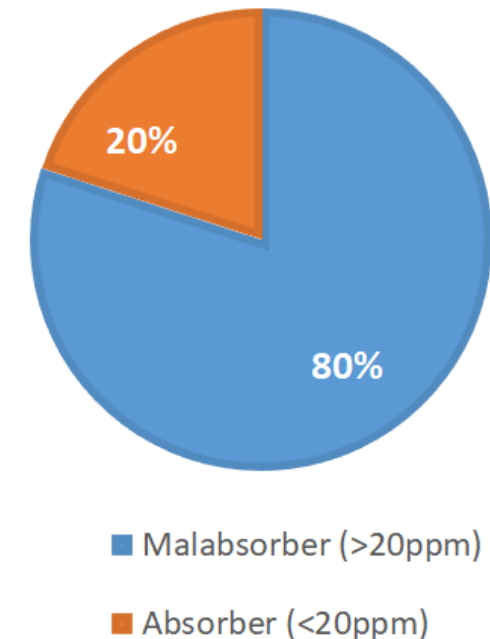
ETHNICITY



IRRITABLE BOWEL SYNDROME

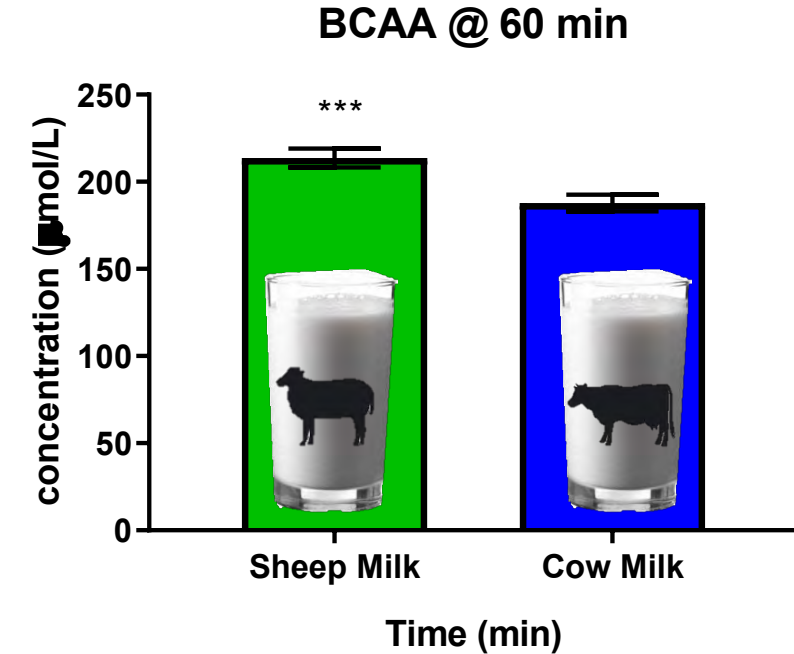
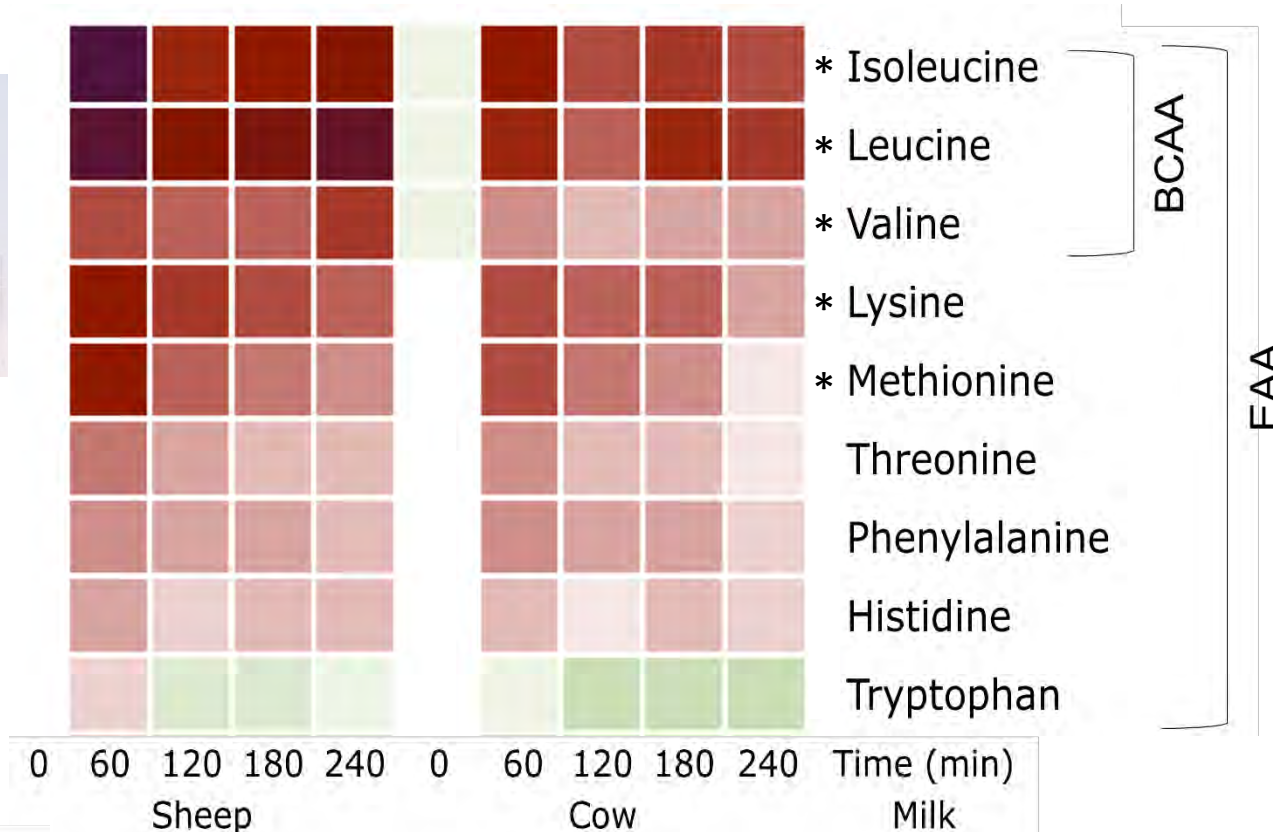


BREATH HYDROGEN

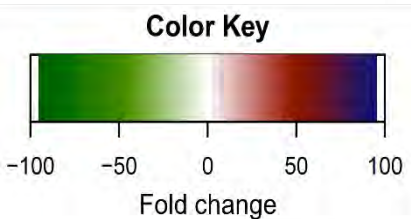


Underlying lactose/food intolerance

# ShinDig Trial: Protein more readily digested



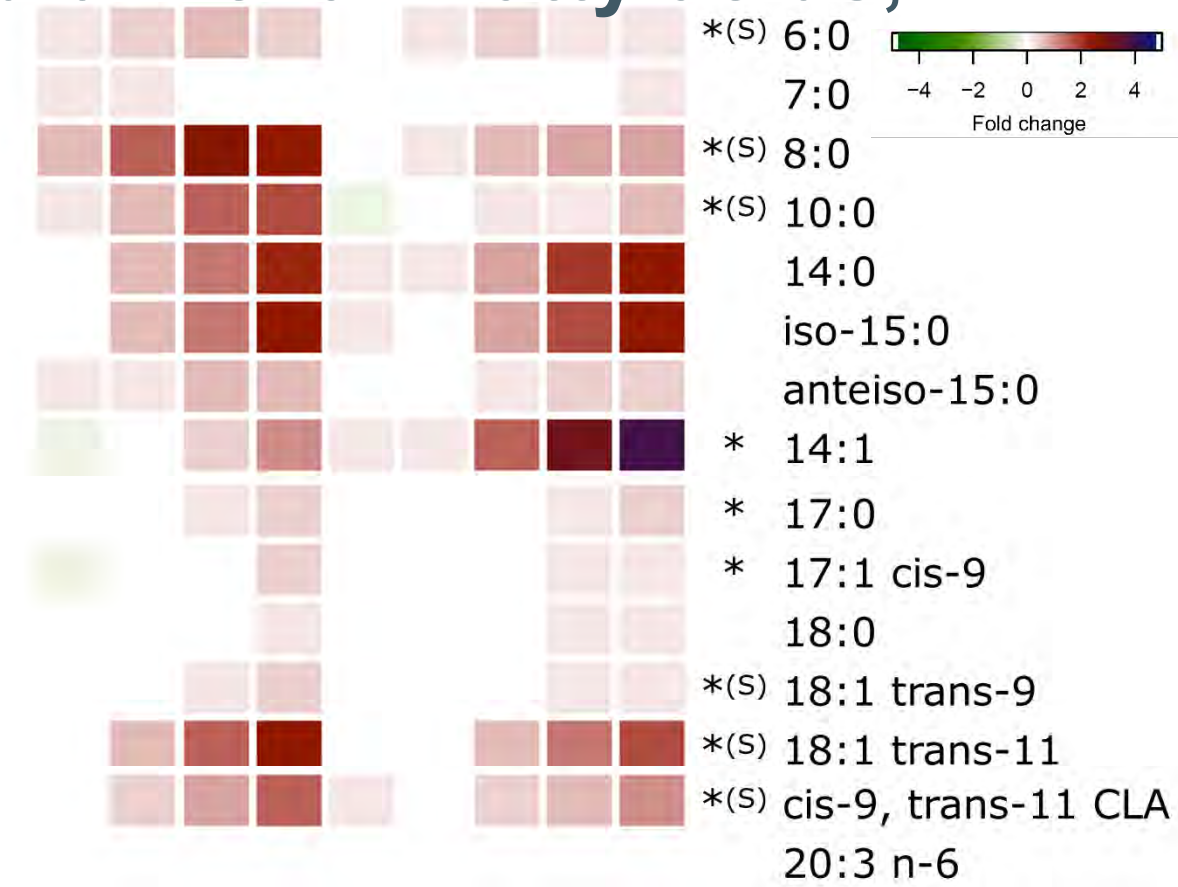
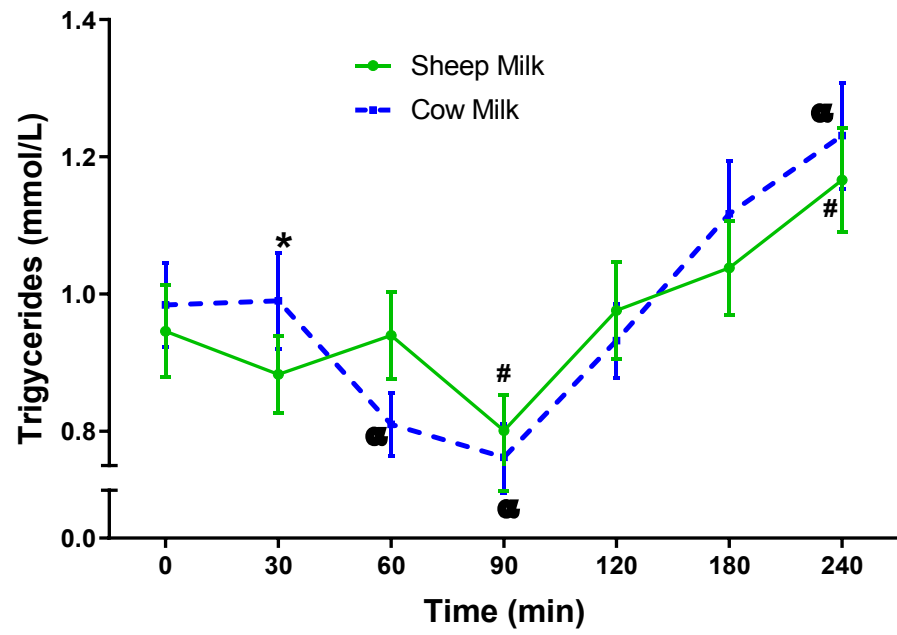
- Sheep milk elevated:
- BCAAs
  - Lysine & methionine



\*  $p < 0.05$  difference between sheep and cow



# ShinDig Trial: Same fat response, more medium chain fatty acids,



Sheep milk resulted in more:

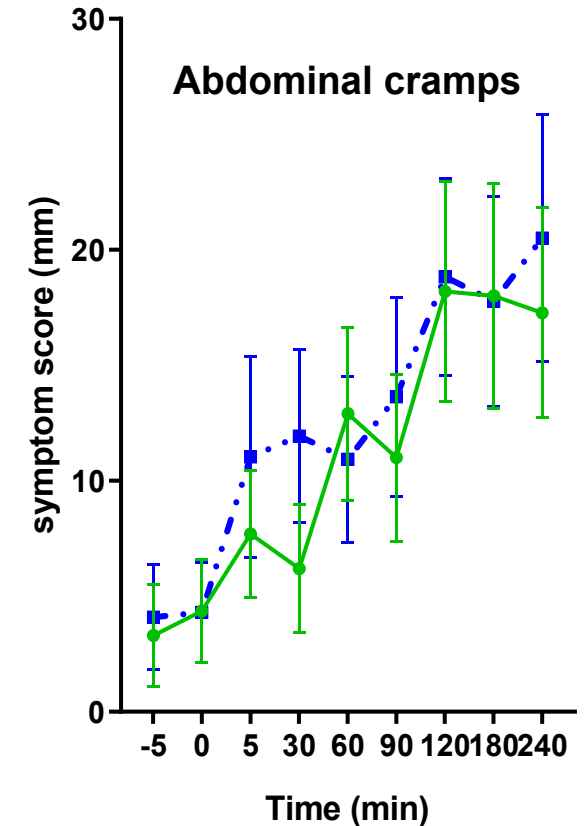
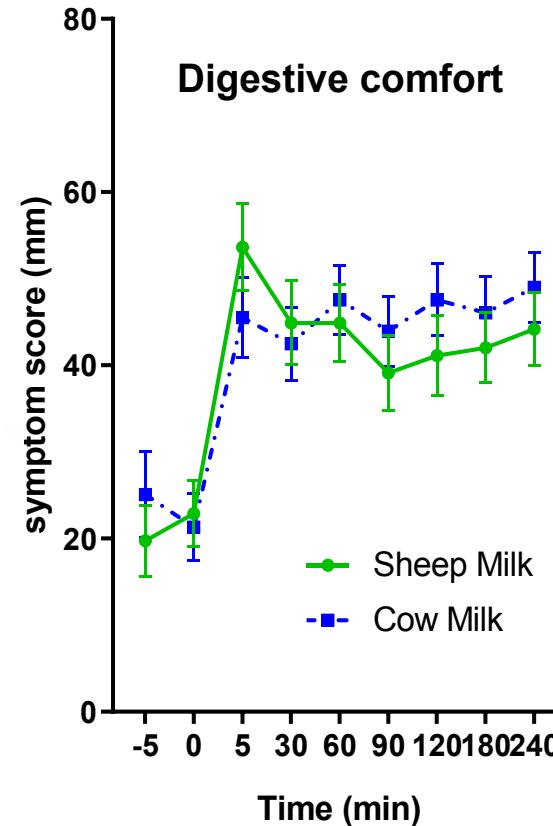
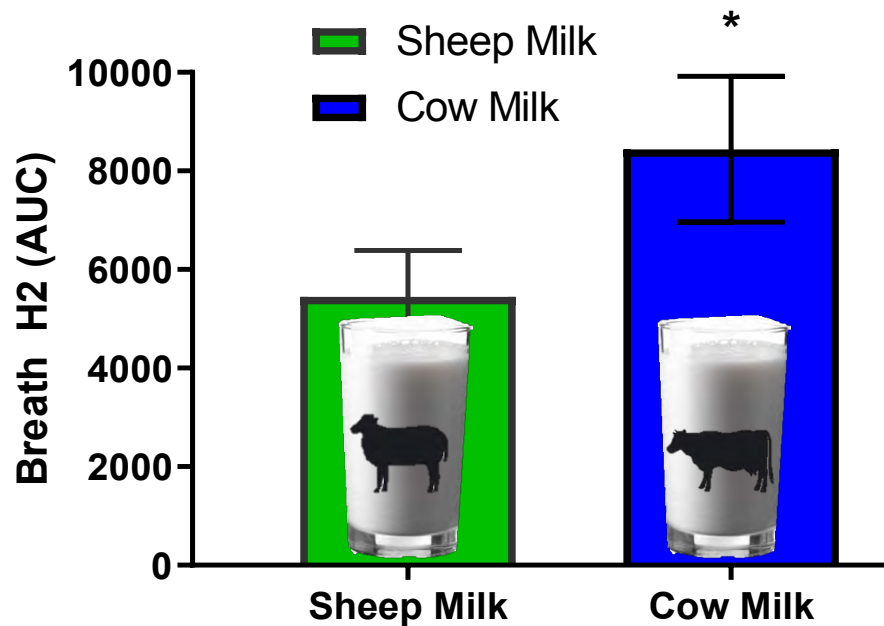
- Medium-chain fatty acids
- Ruminant trans fatty acids, including CLA

\*  $p < 0.05$  difference between sheep and cow

0 60 120 180 240 0 60 120 180 240 Time (min)  
Sheep Cow Milk



# ShinDig Trial: Less malabsorption – and less lactose



More malabsorption from cow milk  
1/3 higher lactose in cow milk  
→ Are differences only due to content?

No difference in pain  
→ Same for lactose tolerant?

## ShinDig Trial: Summary

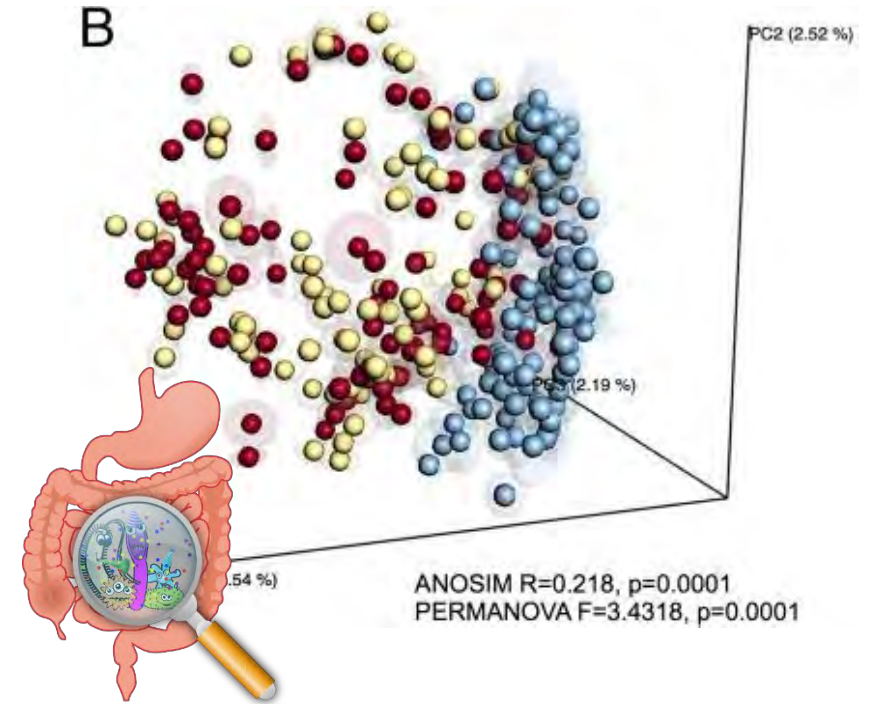
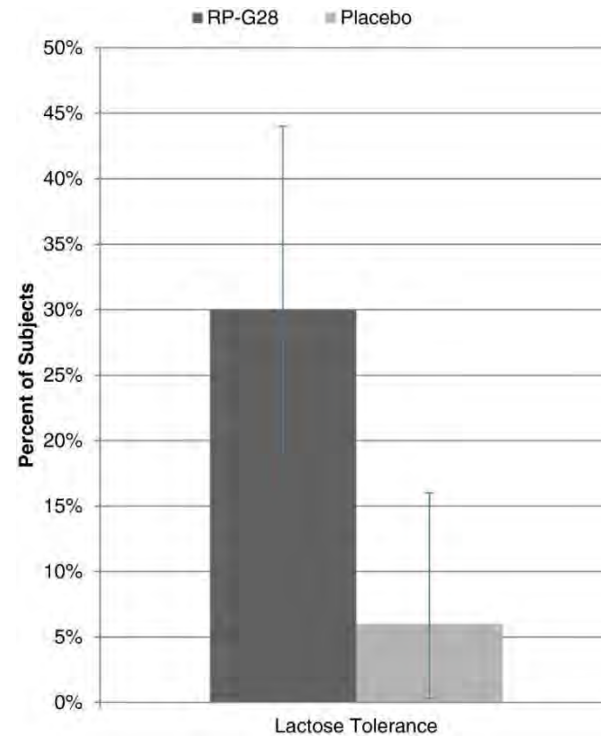
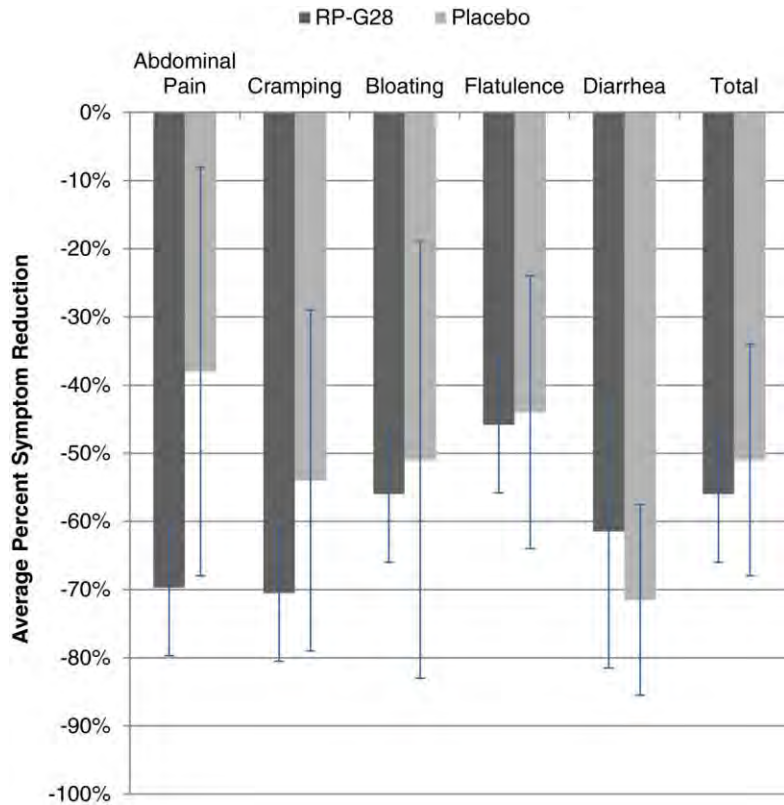
- Sheep milk proteins more readily digested
  - BCAAs (leucine, isoleucine, valine), methionine, and lysine
- Sheep milk fats have a different response
  - Same overall rise in blood despite higher content
  - More medium-chain fatty acids
- Sheep milk may reduce lactose malabsorption
  - Lower malabsorption, but also lower lactose content

# The future: Adaptation and nutrient delivery

Los aMiGoS: long-term a2 Milk™ for Gut Comfort

New Zealand Milks Mean More – NZ3M

# Can tolerance be improved? Adapted?



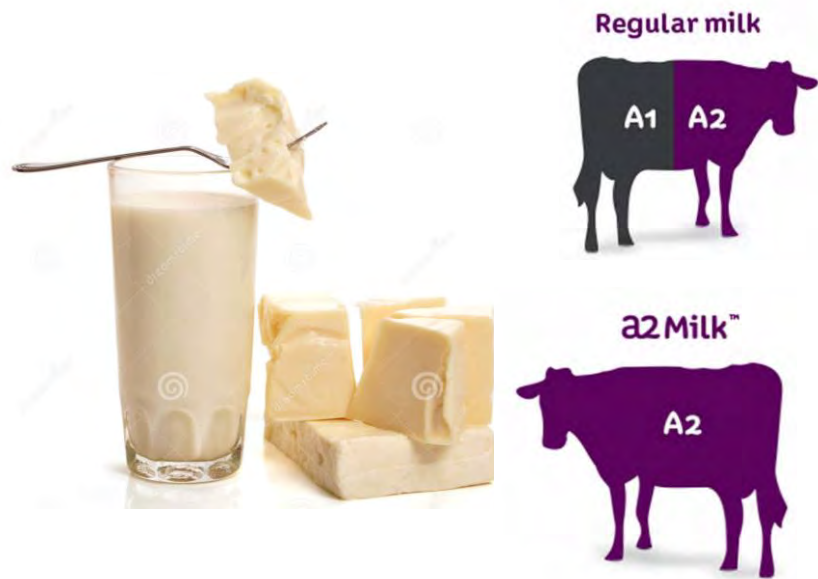
“The majority of people with lactose malabsorption do not have clinical lactose intolerance.”



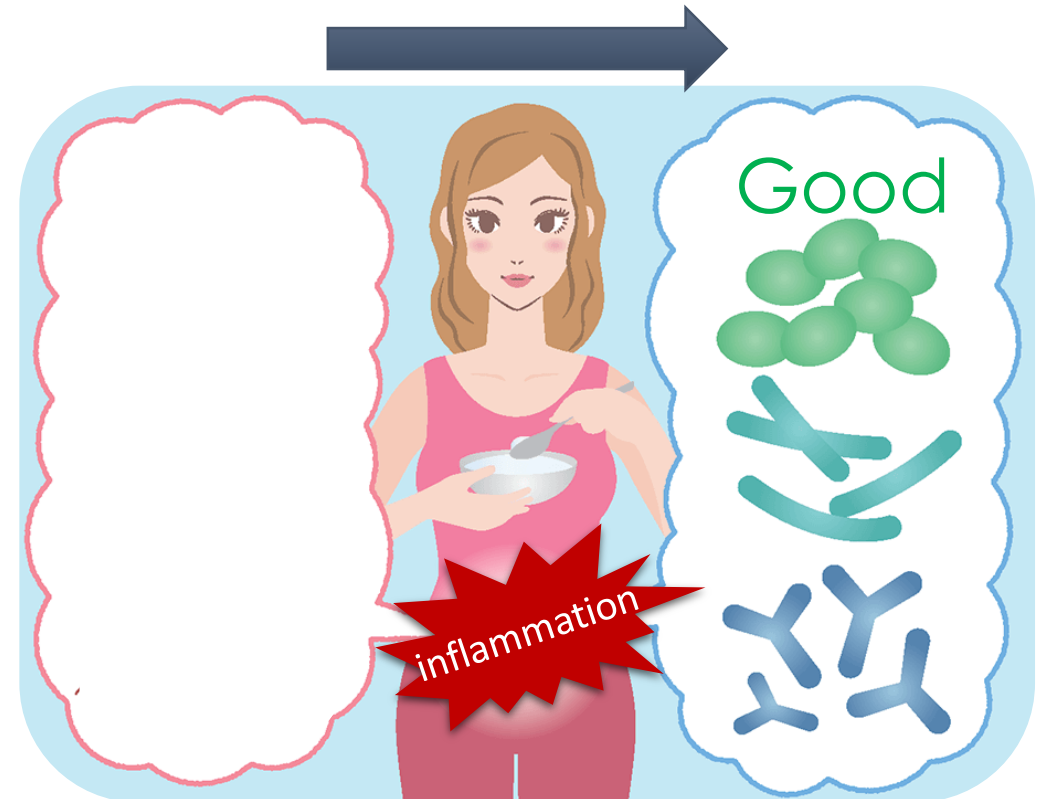
# Los aMiGoS:

## Is Lactose tolerance impacted by repeated exposure to a2 Milk™, with effects on Gut Comfort Symptoms

Does long term exposure to  $\beta$ -casein variants impact lactose malabsorption?  
Can lactose absorption be improved with elimination of intestinal inflammation?



**2 weeks**



# NZ3M: New Zealand Milks Mean More

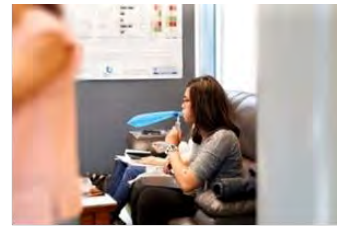


Validation of digestive and nutritional outcomes that support improved health and wellbeing



## Dairy products

- Different ruminant milks
- Varying processing technologies



Breath



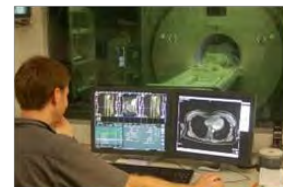
Blood / Plasma



Faecal composition



Muscle biopsies



Imaging



Subjective feelings



Programme Leader:  
**Prof Warren McNabb**



MINISTRY OF BUSINESS,  
INNOVATION & EMPLOYMENT  
HIKINA WHAKATUTUKI



THE UNIVERSITY OF  
**AUCKLAND**  
Te Whare Wananga o Tamaki Makaurau  
NEW ZEALAND

# NZ3M: Building evidence of dairy product impacts

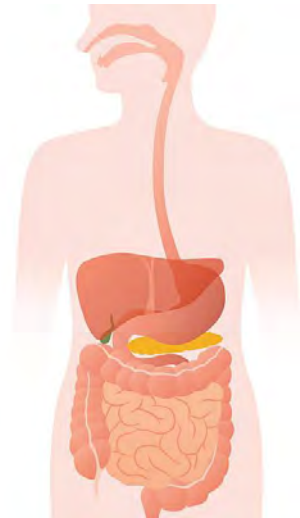
Food structure  
(intervention)



*Physical state, complexity  
of structures/matrices*

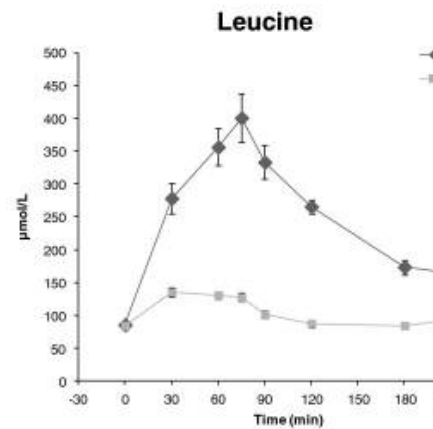
*e.g. native vs heated*

Digestion  
(mechanism)



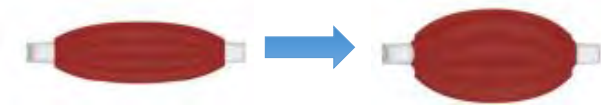
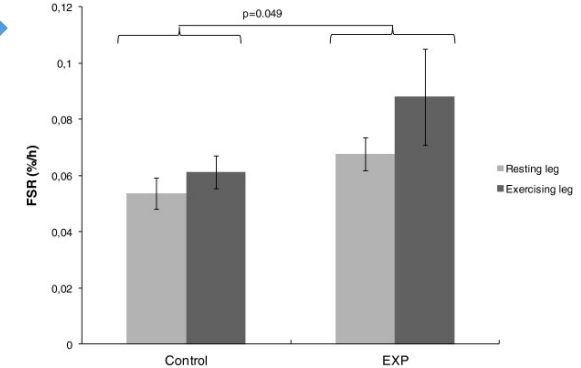
*e.g. fast vs slow*

Appearance of nutrients  
(outcome)



*e.g. blunted vs enhanced,  
Rapid vs delayed*

Functional outcomes  
(impact)



*e.g. muscle growth*

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**Prof Warren McNabb**

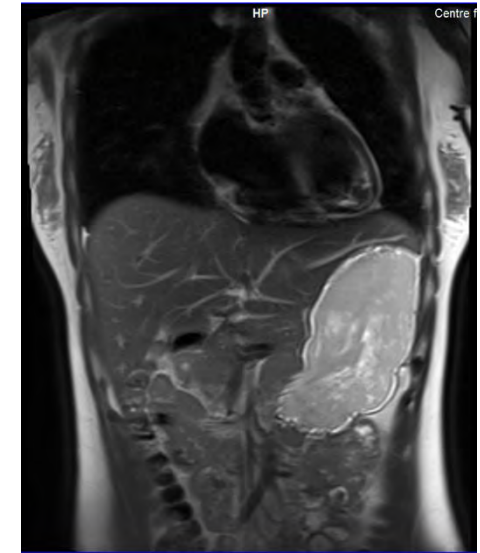
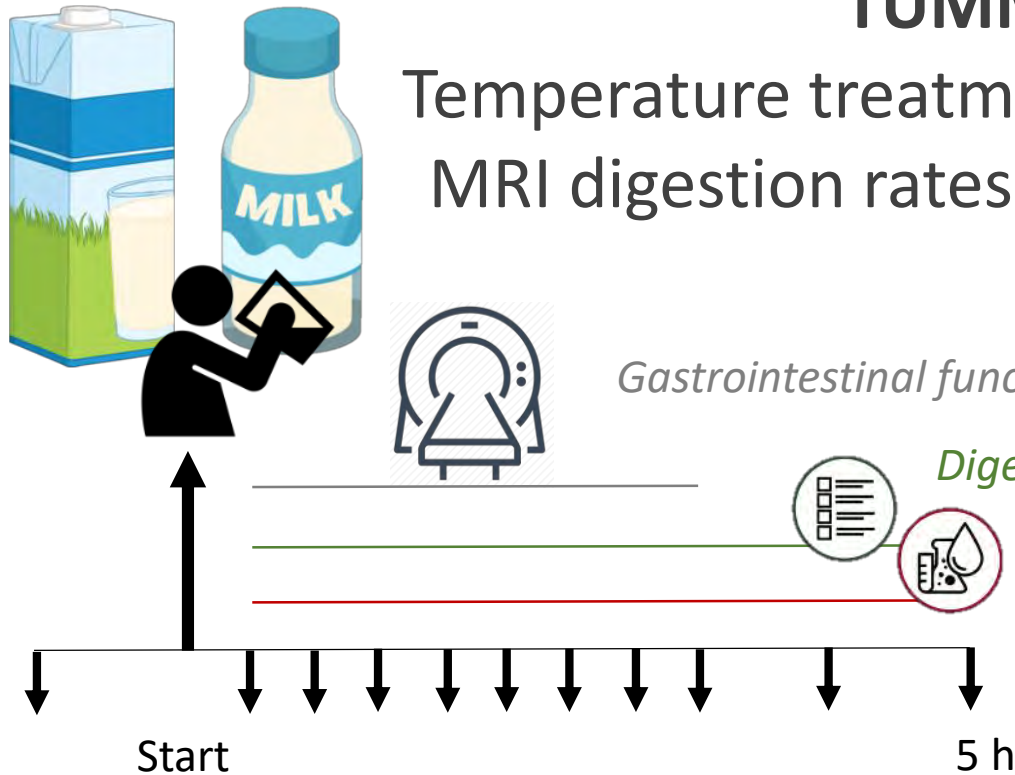


# NZ3M: New Zealand Milks Mean More



## TUMMI Trial:

Temperature treatment of Milk impacts on MRI digestion rates and nutrient delivery



Stomach full of milk (MRI)

- Impact of processing/ differences in properties
- Validate against in vitro and pre-clinical models
- Inform product development

National  
**SCIENCE**  
Challenges

HIGH-VALUE  
NUTRITION

Ko Ngā Kai  
Whai Painga

Programme Leader:  
**Prof Warren McNabb**



## Insights and questions

- Milk digestion
  - Processing affects digestion and metabolic responses
  - Species-specific differences understanding required

*How can we use this to improve health?*

- Dairy intolerances
  - Lactose malabsorption affects majority – others?
  - Mechanisms other than lactose intolerance?
  - Protein intolerances?
  - Adaptation?

*Can we understand how and provide solutions?*

# Acknowledgments

Thank you Participants!



## Research Team & Support

Prof David Cameron-Smith  
Prof Warren McNabb  
Prof Nicole Roy  
Prof Richard Mithen  
Dr Matthew Barnett  
Dr Linda Samuelsson  
Dr Li Day  
Dr Ali Hodgkinson

Aahana Shrestha, Pankaja Sharma, Utpal Prodhan, Sarah Mitchell, Clara Han, Jimmy Nilsson, Josefin Karlström, Jakob Martinsson, Jenny Mistretta, Matthew Bourke, Franny Markstedt, Julia Ängemalm, Sofia Egelrud, Ville Nyberg, Erik Linden, Vivian Kim, Isabella Kreber, Emil Talani, Petter Johansson, Nora Farnisa, Chris Keven, Janene Biggs, Hieke Schwendel, Michael Agnew, Hedley Stirrat, Arvind Subbaraj

National  
**SCIENCE**  
Challenges



MINISTRY OF BUSINESS,  
INNOVATION & EMPLOYMENT  
HIKINA WHAKATUTUKI

Funding



SPRING SHEEP  
— MILK CO. —  
New Zealand



Dairy Goat  
Co-operative

Institutional Affiliations



**MASSEY**  
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