FUNCTIONAL OLIGOSACCHARIDES IN FOOD AND NUTRITION: FROM SIMPLE STRUCTURES TO HIGH DIVERSITY

13 September 2018

Dr. Yong Miao

Outline

- **Functional oligosaccharides**
- **Resistant dextrin**
- **Fructooligosaccharides (FOS)**
- **Human milk oligosaccharides (HMOs)**

Functional oligosaccharides

- **What are functional oligosaccharides?**
  - Food ingredients which have health benefits
    - Have positive effects on human health, both in the prevention and in treatment of chronic diseases.

"*Let food be thy medicine and medicine be thy food*"

– Hippocrates

- **Characteristics**
  - Water soluble, so called soluble fiber
  - Can not be digested, so called resistant fiber
  - Can grow microbiomes or interact with microbiomes, so called prebiotics

Functional oligosaccharides

- Sources
  - Extraction or hydrolysis from biosourced polymers. Ex.: Resistant dextrin
  - Synthesis from simple mono- or oligo- saccharides. Ex. : Polydextrose, galactooligosaccharides
- Efficacy
  - In vitro: grow good bacterias, prevent pathogens growth
  - In vivo: health benefits by clinical trial

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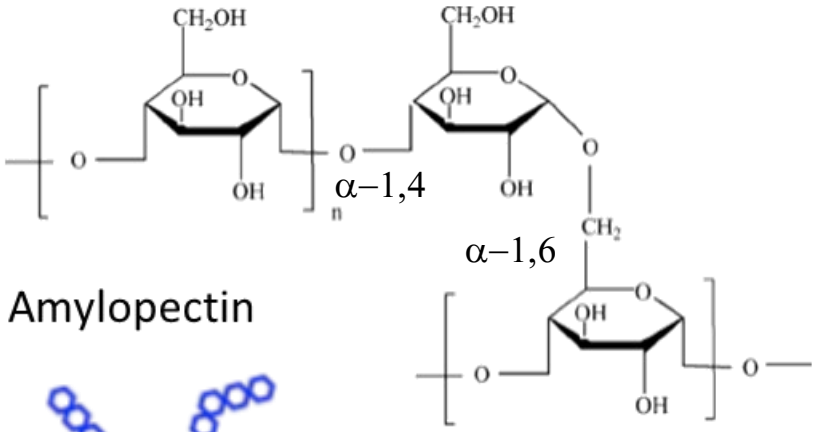
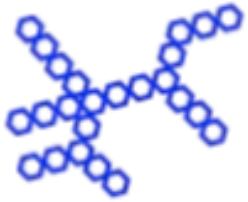
Resistant dextrin

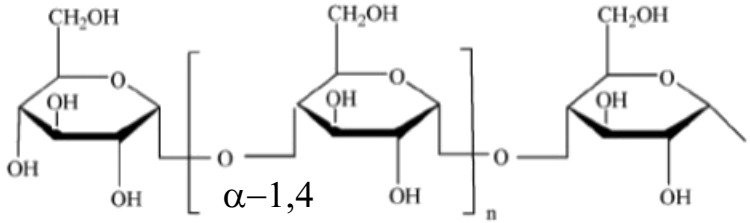
- Can be obtained from starch
- Two types of polymers in starch



Amylopectin



Branched chain, slippery texture



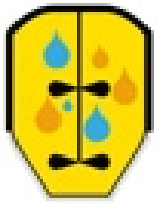
Amylose

Long linear chain and can form gel network

Starches	Banana	Wheat	Potato	Corn	Starches	High amylose maize	Pea
Amylopectin	83%	80%	77%	75%	Amylose	40%	61%

Resistant dextrin

› Production process

Starch (corn or wheat) + Acid →  60-80°C fluidification →  Drying

Drying → Dextrinization → Purification → resistant dextrin

Purification → Fiber enrichment → Industrial grade Yellow dextrin (glue)

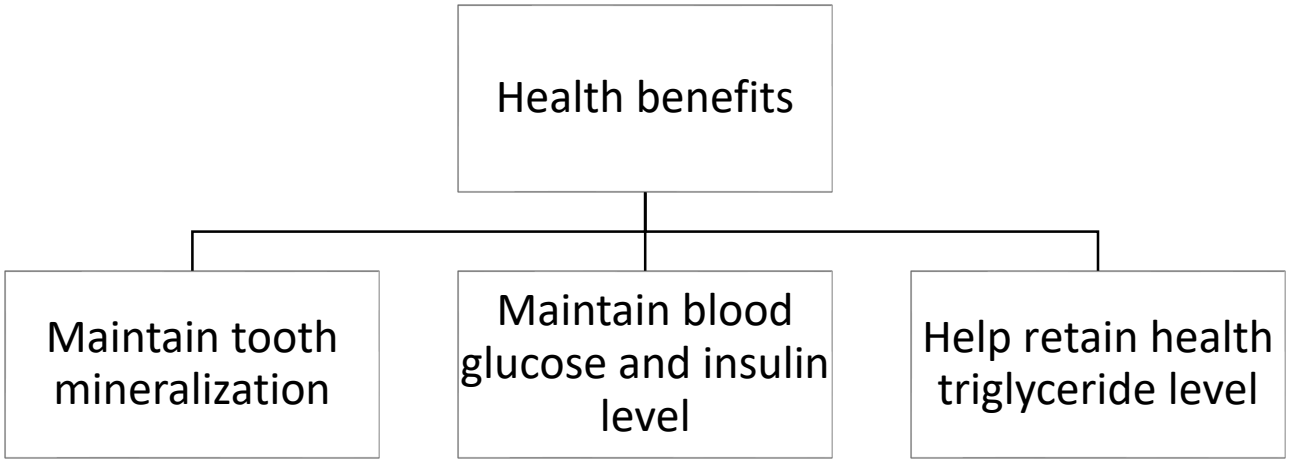
Starch (corn or wheat) → Pyrolysis → Enzymatic treatment → Resistant maltodextrin

Convert normal α-1,4 to random 1,2-,1,3-, 1,4-, α or β linkage

NUTRIOSE® soluble fibre by ROQUETTE Offering the best of nature™

Fibersol®-2 by Fibersol® fiber fit for all!

Resistant dextrin



Applications:

Functional drinks

Dietary meal

Confectionary

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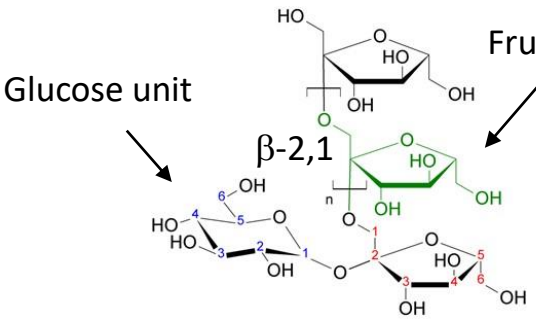
Fructooligosaccharides FOS

Sources:

Chicory

Rich in inulin

β-2,1 resistant to hydrolysis by salivary and intestinal digestive enzymes



Inulin

Chemical or enzymatic degredation

Fructooligosaccharides (FOS)

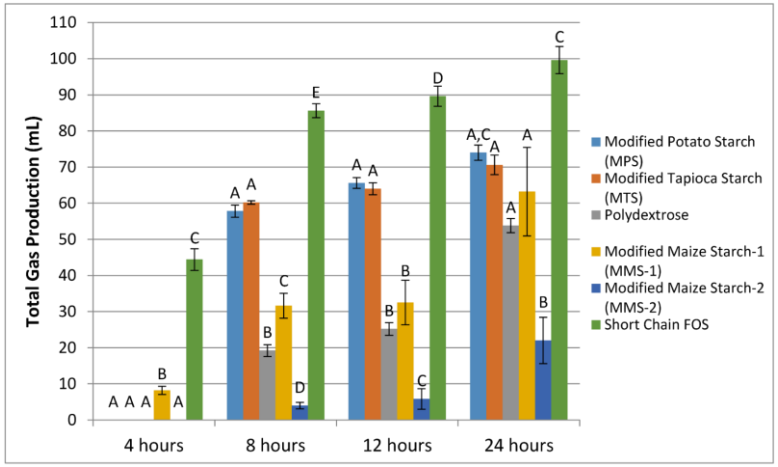
Health benefits:

- Microbiota modulation (prebiotics)
- Promote calcium absorption
- Nature sweetener.

Side-effect:

- Grow E. coli, Clostridium (pathogens)

J Appl Microbiol. **83** (3): 367–374



Jennifer M. Erickson et al., *Foods* **2018**, 7(2), 18

Comparison of potential prebiotic effects and fermentability of FOS and four other resistant starches using an in vitro fermentation system and measuring changes in total gas production, pH, and formation of SCFAs (short chain fatty acids)

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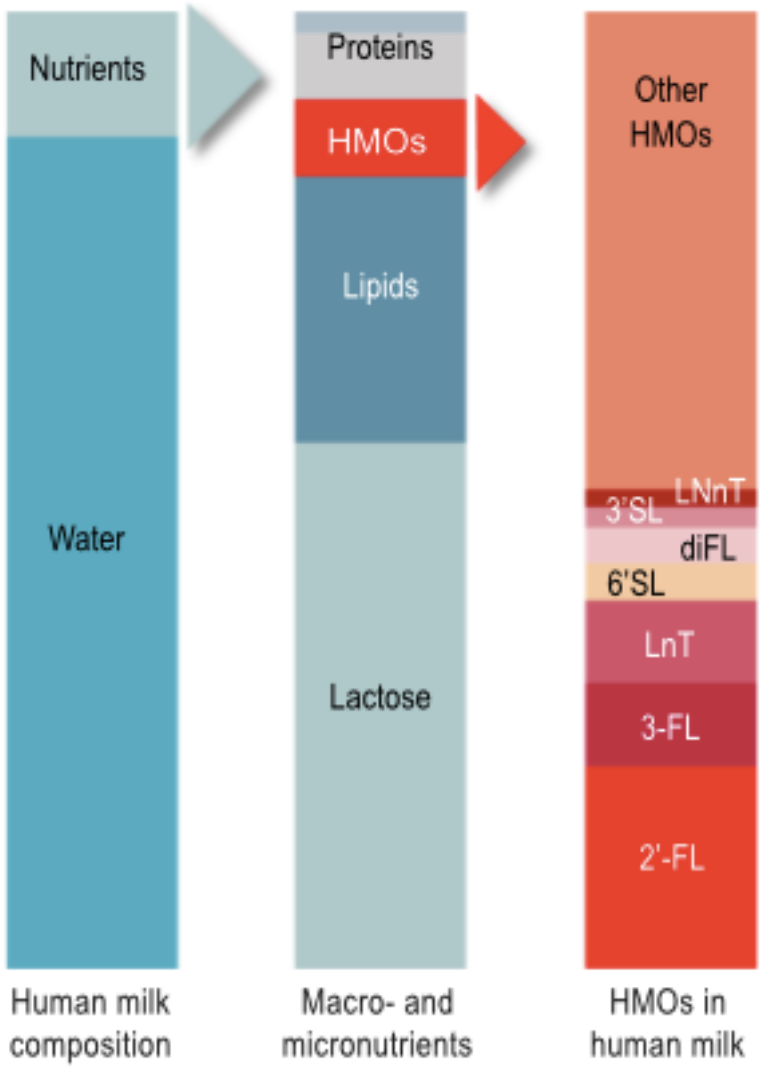
Human milk oligosaccharides (HMOs)

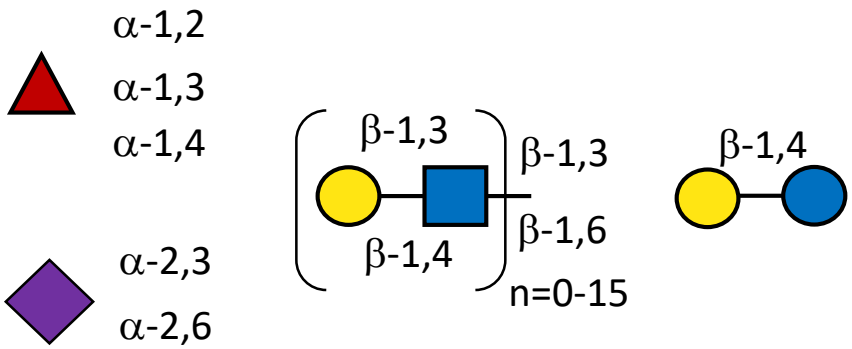
- HMOs are a group of unique oligosaccharides found in human milk
- HMOs are the 3rd LARGEST SOLUTE in human milk after lactose and fats
- Over 200 different oligosaccharides in human milk, with 2'-FUCOSYLLACTOSE (2'-FL) being the MOST ABUNDANT, 2.4 g/L
- The types and levels of HMOs VARY considerably among women, regions and the stages of lactation.
- A range of most significant abundant HMOs can be produced by fermentation and high diversity HMOs (>30 structures) can be produced by mucin extraction enabling SCALABLE PRODUCTION.
- Research indicates that commercially produced HMOs can mimic some of the HEALTH-PROMOTING EFFECTS of HMOs in human milk.



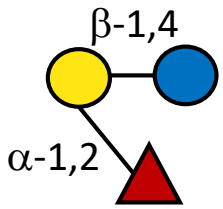
Human milk oligosaccharides (HMOs)

Structures of HMOs

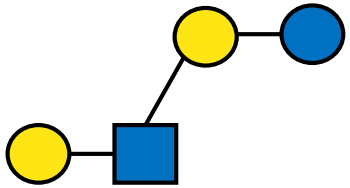
- HMOs contain Glucose, Galactose, Fucose and Sialic acid



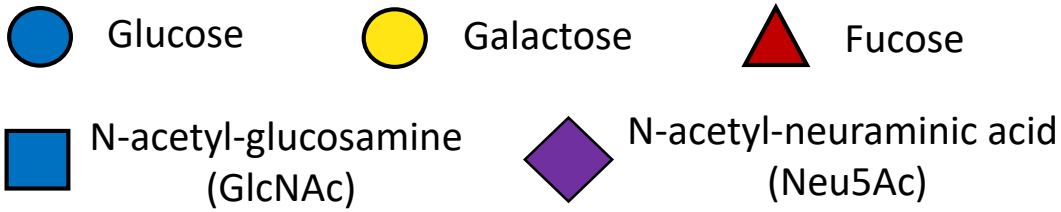
2-Fucosyllactose



Lacto-N-Neotetraose



Monosaccharide key:



Adapted from Bode, Adv. Nutr. 3: 383S–391S, 2012.

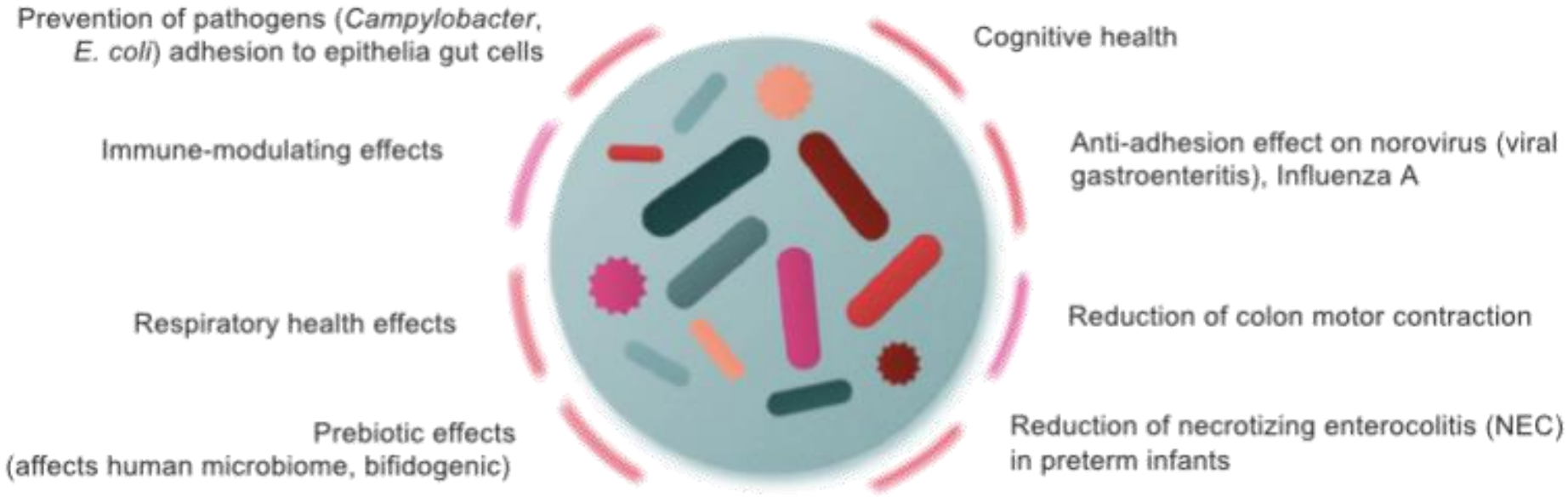
Human milk oligosaccharides (HMOs)

› HMOs health benefits

HMOs ARE IMPORTANT BIOACTIVES

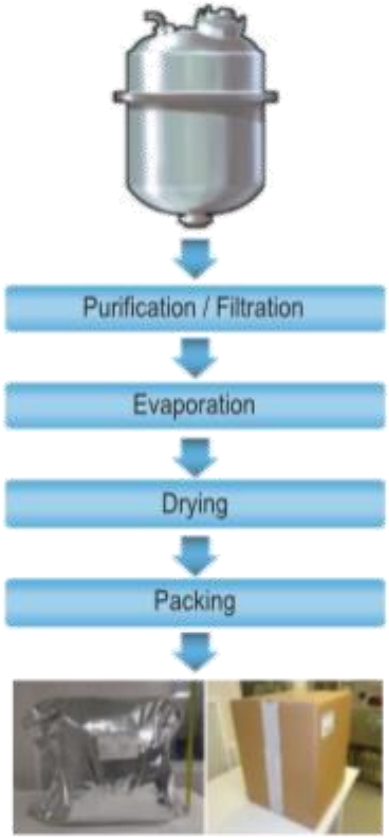
that promote and maintain health from birth to early life

- HMOs are highly bifidogenic and promote bifidomaterial-dominated microbiota
- HMOs strengthen gut barrier function and act as decoys for pathogens
- HMOs stimulate immune system



Human milk oligosaccharides (HMOs)

Manufacture of 2'-FL



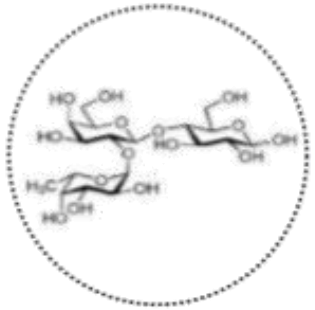
CARE4U™ 2'-FL

98-100% 2'-FL

Highly soluble, clear turbidity, excellent instant properties

MICROBIAL FERMENTATION

- Host organism is *E. coli K12* (commonly used for enzymes, insulin, vitamins, etc.).
- Glucose and lactose are fermented to form 2'-FL and other carbohydrates.
- Product is defined as non-GMO.
  (Neither the production strain nor any recombinant DNA are present in the final product. CARE4U™ does not consist of GMO and does not contain GMO according to the definitions of EU Regulation 1829/2003 and 1830/2003.)

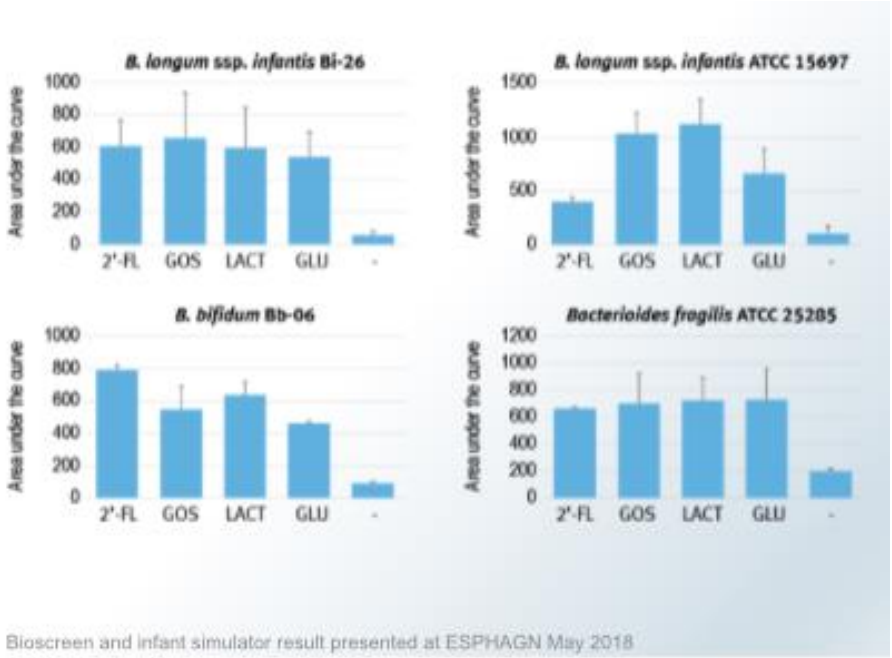


2'-fucosyllactose

Human milk oligosaccharides (HMOs)

HMOs are highly bifidogenic

- Growth of various potentially pathogenic or probiotic bateria using glucose, lactose, GOS and 2'-FL as a sole carbon source



Bioscreen and infant simulator result presented at ESPHAGN May 2018

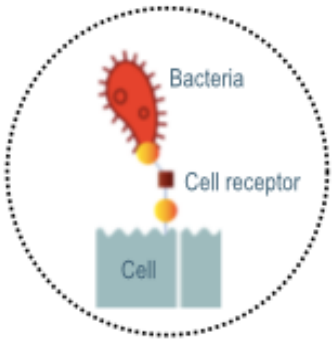
BIOSCREEN

Bacterium	Strain	Carbon source			
		GLU	LACT	GOS	2'-FL
Clostridium perfringens	ATCC 3626	+	+	+	-
Clostridium perfringens	ATCC 13124	+	+	+	-
Escherichia coli	ATCC 11775	+	+	+	-
Salmonella typhimurium	EELA	+	+	-	-
Escherichia coli (O111:K(58):H-)	CCUG 11412	+	+	+	-
Escherichia coli (O142:K86(B):H4)	CCUG 11442	+	+	+	-
Escherichia coli (O111:K58(B4):H2)	CCUG 42878	+	+	+	-
Lactobacillus acidophilus	**NCFM**	+	+	+	-
Lactobacillus paracasei	**Lpc-37**	+	+	+	-
Bifidobacterium animalis subsp. lactis	**Bi-07**	+	+	+	-
Bifidobacterium animalis subsp. lactis	**Bi-04**	+	+	+	-
Bifidobacterium longum subsp. longum	**Bi-05**	+	+	+	-
Lactobacillus rhamnosus	**HN001**	+	+	+	-
Bifidobacterium lactis	**HN019**	+	+	+	-
Bifidobacterium longum subsp. infantis	**Bi-26**	+	+	+	+
Bifidobacterium longum subsp. infantis	**ATCC 15697**	+	+	+	+
Bifidobacterium breve	**Bb-03**	+	+	+	-
Bifidobacterium bifidum	**Bb-06**	+	+	+	+

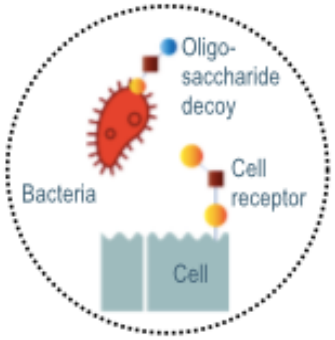
Human milk oligosaccharides (HMOs)

HMOs act as decoy for pathogens

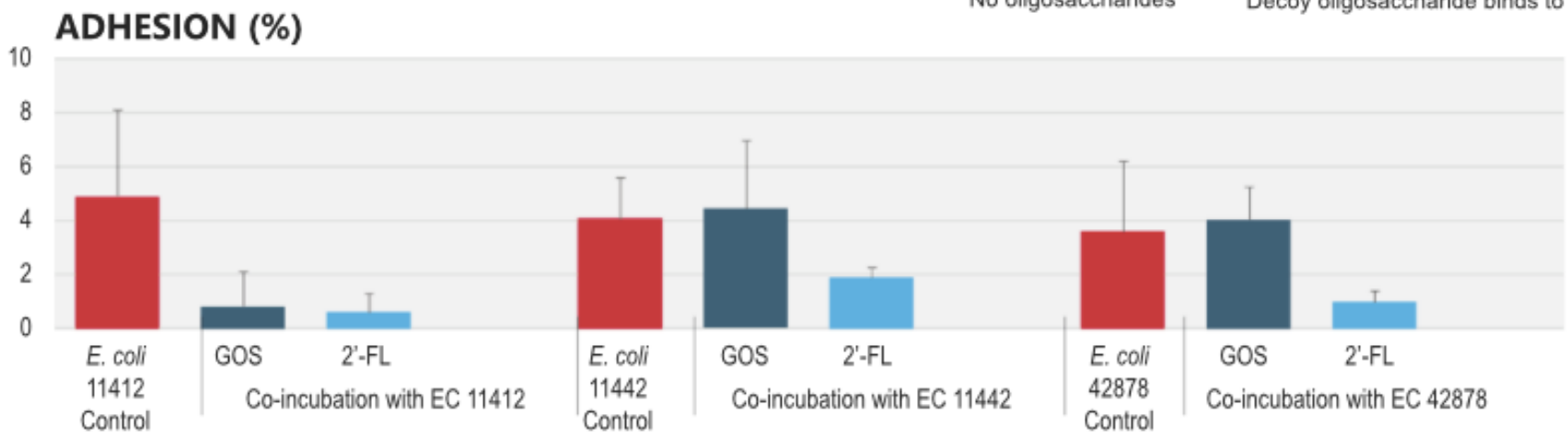
- HMOs are known to act as decoy receptors preventing the attachment of pathogens to epithelial cells, and may thus inhibit infectious diseases.
- Our study shows that 2'-FL decreases the adhesion of three *E. coli* strains of infant diarrhea origin on Caco-2 intestinal epithelial cells.



No oligosaccharides



Decoy oligosaccharide binds to pathogen



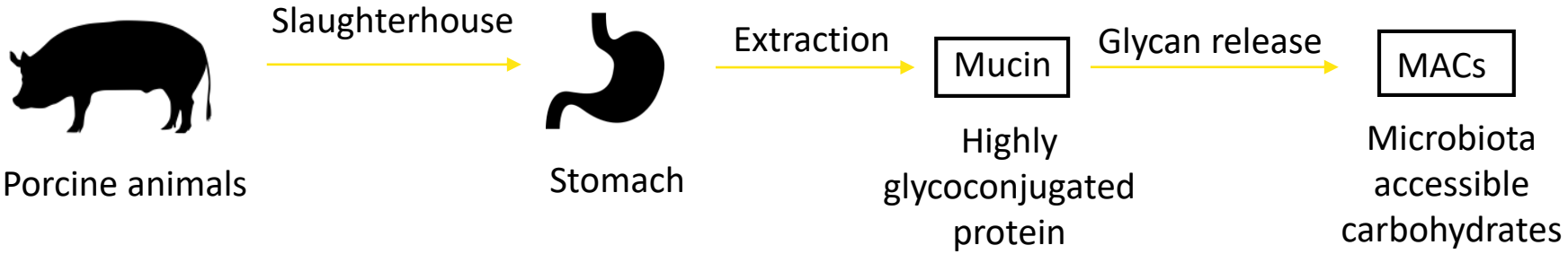
The effect of 2'-FL and GOS on adherence of *E. coli* 11412, -11442 and -42878 strains were studied in Caco-2 cells using Syto24 bacteria labelling and fluorometric detection

DuPont Nutrition & Health

Human milk oligosaccharides (HMOs)

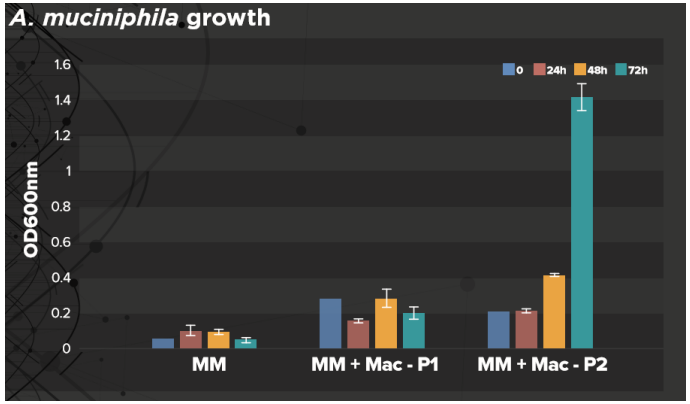
HMOs mimic extraction from mucin

- Mucin glycans and HMOs share structure similarities
- Mucin glycans and HMOs both contain fucose, lactose, glucose and sialic acid
- Mucin is glycoprotein and can be obtained from biomass (pork stomach)



High diverse, structural and functional HMO-mimics

EPITOPE	HMO (%)	GNU MAC (%)
Fucose blood group H (Fuca1-2Gal	33%	36%
3 linked sialic acid (NeuAca2-3Gal)	8%	10%
6 linked sialic acid (NeuAca2-3Gal/GalNAc)	13%	6%



. In vitro growth of A. muciniphila in the presence of two different formulations of microbiota accessible carbohydrates (MACs). 0, 24, 48 and 72 hours

Human milk oligosaccharides (HMOs)

Global HMO-containing launches

METAGENICS ULTRAGI REPLENISH™
(USA, Aug'16)

Medical food powder
"to support for patients with compromised gut function with digestive disorders including malabsorption"

ABBOTT SIMILAC PRO-ADVANCE™ & PRO-SENSITIVE™
(USA, Sept'16)

Standard and follow-on formula with 2'-FL
"helps strengthen baby's immune system to be more like the breastfed infant's"

NESTLÉ NAN CLINICAL CARE
(Spain, Nov'16)

Special-purpose ready-to-drink infant formula for hospitals, 2'-FL and LNnT

NESTLÉ NAN OPTIPRO® SUPREME / SUPREME HA
(Spain/Portugal, July'17)

Standard and follow-on formula *"with two oligosaccharides (2'-FL and LNnT) structurally identical to those found in breast milk"* and *"Important for development of immune system"*

WYETH NUTRITION ILLUMINA INFANT FORMULA
(Hong Kong, Nov'17)

Super premium formula with 2'-FL in 4 stage products (birth to >3 years) *"blocking intestinal infection", "supports defense system"* and *"helps prevention of allergies"*

NESTLÉ GOOD START® OPTIPRO SUPREME
(Mexico, Nov'17)

Premium infant formula with 2'-FL *"with HM-O to strengthen your immune system"*

Human milk oligosaccharides (HMOs)

Global HMO-containing launches

ABBOTT SIMILAC PRO-ADVANCE™
(Saudi, UAE, Oman, Kuwait, Bahrain)

Imported (U.S.) infant formula with 2'-FL
"helps support your baby's developing immune system by closing multiple gaps in immune function between formula-fed and breast-fed infants"

NESTLÉ NAN OPTIPRO
(Saudi, UAE, Oman, Kuwait, Bahrain, Feb'18)

ABBOTT SIMILAC
(Hong Kong, Jan'18)

Infant formula with 2'-FL
"HMO2 to fortify a child's immune system and digestive systems"

ABBOTT SIMILAC 3
(Mexico, Feb'18)

Toddler formula (1-3-year-old kids) with 2'-FL to
"…help your child strengthen their digestive health and immune system"

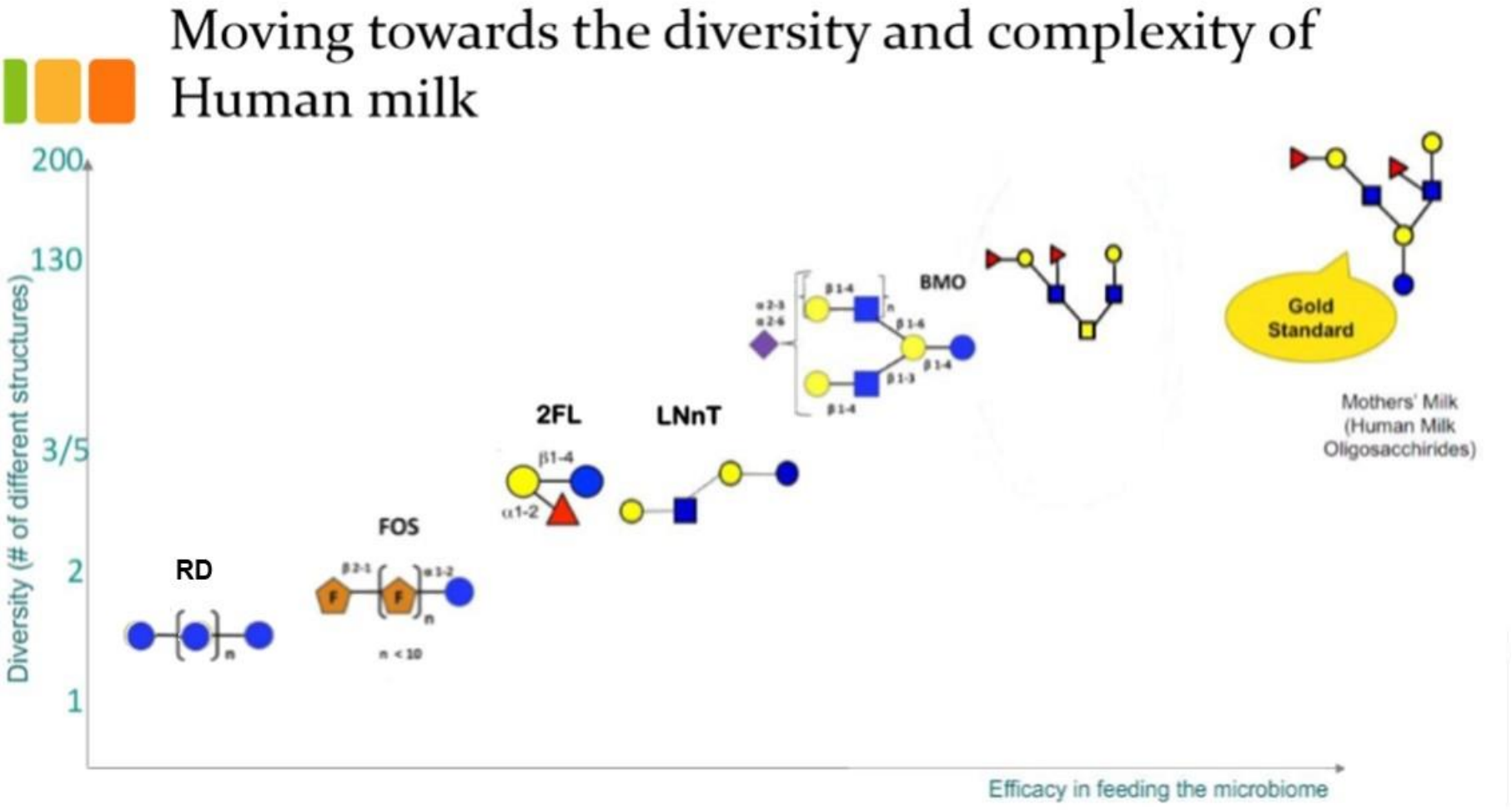
LAB. GUIGOZ OPTIPRO
(France, Apr'18)

Follow-on formula with 1g/L 2'-FL
"beneficially modulate the infant's microbiota, as well as the development of of his intestinal, immune, and potentially neurological system"

GERBER® GOOD START®
(USA, Jun'18)

Two infant formulas with 2'-FL + *B. lactis / L. reuteri*
"Support the developing immune system, balance the microbiota. Probiotics to reduce crying time and help reduce spit-up frequency"

Conclusion


Moving towards the diversity and complexity of Human milk
200
130
3/5
2
1
Diversity (# of different structures)
RD
FOS
n < 10
2FL
LNnT
BMO
Gold Standard
Mothers' Milk (Human Milk Oligosacchirides)
Efficacy in feeding the microbiome