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## MOTHER'S MILK AND THE MICROBIOME

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## The Gut Microbiome

Am J Gastroenterol Suppl (2012) 1:15-21

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## Gut Microbiota: Fun Facts

Getting to know your gut microbiota

A large quantity (trillions) of bacteria and other microorganisms inhabit your intestines, fulfilling key functions for your health and well-being.

- Gut microbiota's weight can reach up to **1 to 2** lbs.
- The GI tract surface is as big as **2 tennis courts**.
- In our body, bacteria outnumber human cells **10 to 50** times greater than human cells.
- In our body, bacteria outnumber human cells **10:1**.
- The total volume of gut bacteria in the gastrointestinal tract is **400 ml**.
- Last year, we've identified 2,500+ bacterial species.
- 95% of gut bacteria live in the gastrointestinal tract.

www.colostate.edu/foodsci/hntr/012171-eng

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## Protection

- I. Direct inhibition
- II. Nutrient/receptor competition
- III. Stimulation of immune defenses

Legend:
 

- cell surface receptors
- defensins
- antimicrobial peptides
- pathogen
- PAMP receptor
- bacteriostatin
- IgA
- mucus

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## Digestion

- Indigestible carbohydrates
  - Bacteria encode enzymes we lack
  - SCFA
- Fat
  - Can modify bile acids
  - Certain bacteria are thought to aid in fat digestion
- Protein
  - Proteolytic processes degrade proteins into amino acids
- Synthesis of essential amino acids
  - Microbially synthesized can contribute 19-22% of daily requirements.
- Synthesis of vitamins
  - vitamin K and B
  - B12: site of synthesis vs absorption
- Absorption of ions (Calcium, Magnesium, iron)

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## Obesity

- Germ-free mice required 30% more calories to maintain same weight as normal littermates
- Germ-free mice transplanted with normal microflora gained weight.
- Increased energy harvest associated with higher levels of the phylum Firmicutes

\* Turnbaugh and Backed studies from Gordon lab (2008)

### Obesity

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The diagram shows two human figures, one lean and one obese, with their respective gut microbiomes. The bar chart compares 'Number of OTUs' (Operational Taxonomic Units) for 'Lean' and 'Obese' groups. The obese group shows a significantly higher number of OTUs, indicating greater microbial diversity. A scatter plot below the chart shows a positive correlation between 'Number of OTUs' and 'Body Mass Index (BMI)'.

Ley et al. 2006. Nature

### Obesity

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#### Gut dysbiosis = loss of community balance

The diagram illustrates the gut wall with 'Eubiosis' (balanced community) and 'Dysbiosis' (loss of balance). Dysbiosis leads to an 'Inflammatory Immune Response' involving 'Immune cells'.

Sheflin et al. (2014) Curr. Oncol. Reports 16: 406.

### Obesity

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The diagram shows 'Obese mice' with 'Microbiota transfer' to 'Recipient mice', which then develop 'Increased adiposity'. Conversely, 'Lean mice' transfer their microbiota to 'Recipient mice', which remain 'Lean'.

When co-housed the "lean" mice transferred their microbes and their phenotype to the "obese" animals!

Ridaura, V. K. et al. Science 341, 1241214 (2013).

### Developing Tolerance

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The diagram shows the gut wall with various immune cells and cytokines involved in tolerance development: IL-4, IL-6, IL-13, IL-10, TGF-β, IL-35, IL-30, TGF-β, IL-22, IL-27, and IL-28. It also shows 'gut barrier' and 'gut permeability'.

[https://www.youtube.com/watch?v=gnZEge78\\_78](https://www.youtube.com/watch?v=gnZEge78_78)

### Microbiota and Health

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The diagram shows a human silhouette with four key areas of impact:
 

- 1. Dietary intake**: Affects the gut microbiome.
- 2. Altered gut bacteria**: Leads to dysbiosis.
- 3. Biologic effects**: Affects host metabolism and immune system.
- 4. Host disease**: Includes obesity, diabetes, and inflammatory diseases.

Singh et al. 2017. J. Transl. Med.

### Microbiota and Health

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The tree diagram shows 'Gut Microbiota' at the base, branching into various health outcomes:
 


- Metabolic syndrome**: Includes elevated lipids, NAFLD/NASH, hypertension, and insulin resistance.
- Immune/inflammation**: Includes asthma, Crohn's disease, and ulcerative colitis.
- Diabetes/ metabolic syndrome**: Includes obesity, insulin resistance, and type 2 diabetes.
- Cardiovascular disease**: Includes atherosclerosis and stroke.
- Other**: Includes obesity, cancer, and Alzheimer's disease.

Nagpal et al. 2014 Front Med. dx.doi.org/10.3389/fmed.2014.00015

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## HOW DO WE GET THESE MICROBES?

Birth influences and early feeding patterns are CRITICAL for a healthy adult microbiome.



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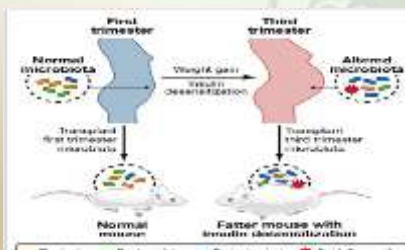
## Colonization Influences



Putignani et al (2014) Ped Res 76, 2-10.

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## Gestational Diabetes

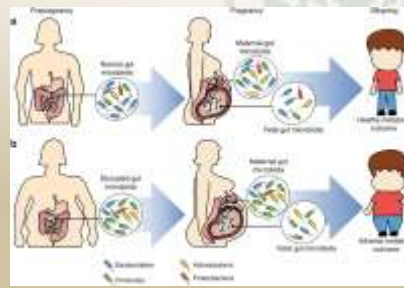


Koren et al (2012) Cell 150:470

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## Fetal Programming

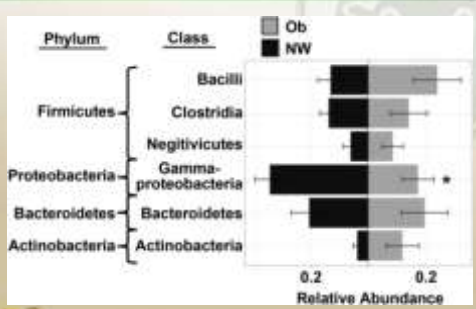
Maternal obesity is a strong predictive factor of childhood obesity and may be due to microbiota effects.



Gohir et al (2015) Ped Res 77:196.

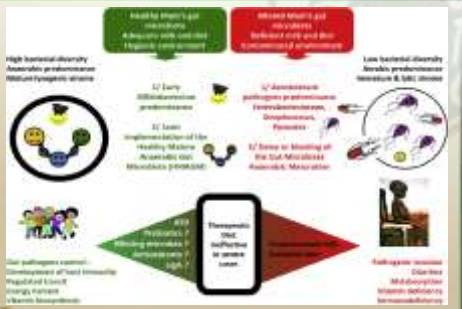
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## Maternal Weight and Microbiota



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## Malnutrition and Microbiota



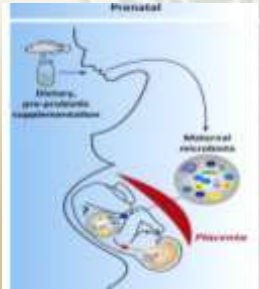
## Placental Microbiome Colorado State University

Small populations of microbes have been detected in the placenta.

Composition most closely mimics the mother's oral microbiota.

May lead to pre-natal exposures to microbes that start priming the immune system.

Link peridontal health and pre-term infancy?




**Placental**

Maternal oral microbiota

Placental microbiome

Image: M.J. Schwan

## Mode of Delivery Colorado State University

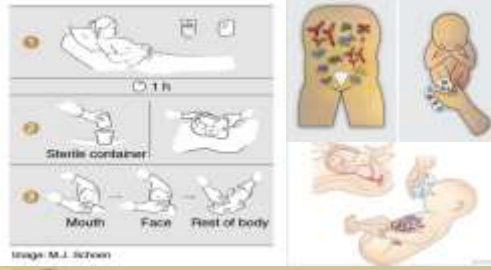


<b>Allergic Rhinitis</b>	
All Cesareans	1.37 (1.14-1.63)
Repeat Cesareans Only	1.78 (1.36-2.31)
<b>Asthma</b>	
All Cesareans	1.24 (1.05-1.53)
Private	1.53 (1.10-2.10)
Forces & Hybrid Cesareans <sup>3</sup>	1.83 (1.12-2.97)
<b>Celiac Disease</b>	1.89 (1.12-3.06)
<b>Diabetes Mellitus (Type 2)</b>	2.18 (1.04-4.56)
<b>Gastroenteritis<sup>4</sup></b>	1.48 (1.24-1.76)
<b>Gastroenteritis AND Asthma</b>	2.14 (1.38-3.23)

1. Hakkarinen et al. 2011, PLoS One; 2. Besser et al. 2012, JAMA Pediatrics; 3. Besser et al. 2012, JAMA Pediatrics; 4. Besser et al. 2012, JAMA Pediatrics

Nature Rev Microbiol (2010) 9:27-38      Clin Perinatol. 2011; 38:321-331

## Restoring Microbiota Colorado State University



1. Birth

2. Sterile container

3. Mouth    Face    Rest of body

Image: M.J. Schwan

Dominguez-Bello et al. (2016) Nature Med 22:250

## Microbial Dynamics Colorado State University

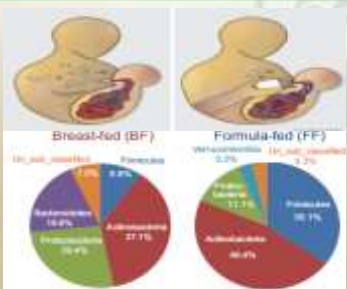
<https://www.youtube.com/watch?v=Pb272zsixSQ>



Birth    1 month    6 months    12 months    2 - 3 years

Arrieta et al. Front. Immunol. | http://dx.doi.org/10.3389/fimmu.2014.00427

## Breast vs. Formula Colorado State University



**Breast-fed (BF)**

- Streptococcus: 14.8%
- Staphylococcus: 16.4%
- Enterobacteriaceae: 16.4%
- Actinobacteria: 27.1%
- Firmicutes: 8.2%
- Other: 17.1%

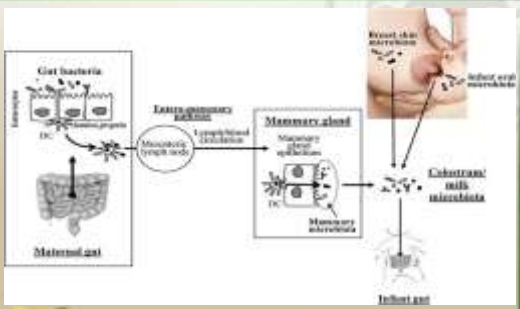
**Formula-fed (FF)**

- Streptococcus: 0.2%
- Staphylococcus: 1.2%
- Enterobacteriaceae: 11.3%
- Actinobacteria: 60.4%
- Firmicutes: 20.7%
- Other: 5.2%

BF had more than Proteobacteria and Bacteroidetes  
FF had more Firmicutes and no Bacteroidetes

Donovan et al. (2012) Advances in Nutrition 3(3):450S-455S

## Milk Microbiome Colorado State University



Maternal gut

Extracellular vesicles

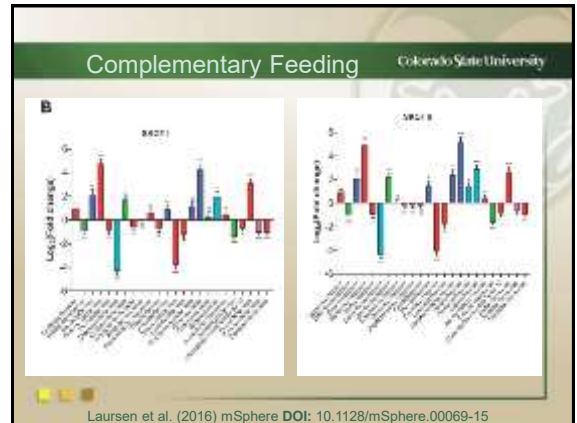
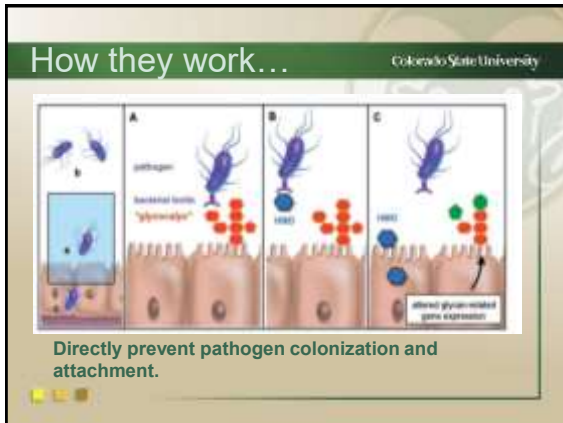
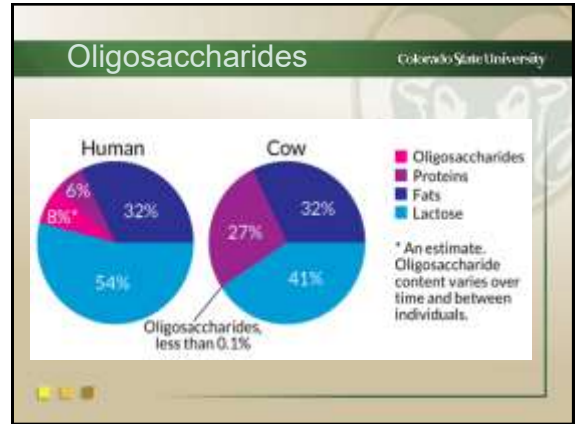
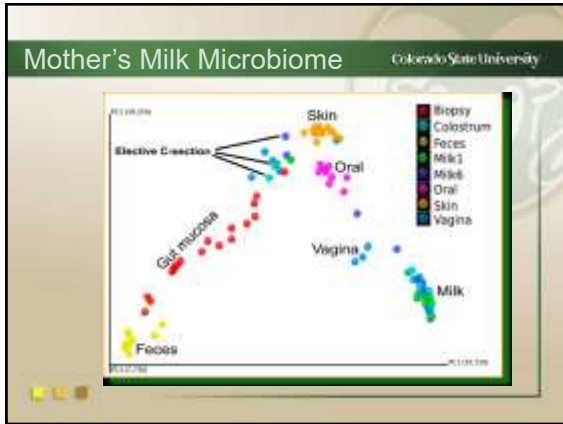
Milk

Infant gut

Image: Breast skin microbiome

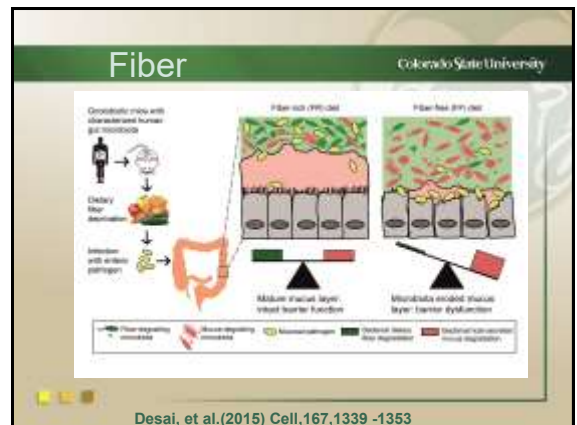
Image: Infant oral microbiome

Image: Infant gut microbiome



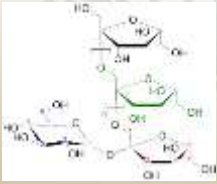
### What should I eat?

Feeding the Microbiome of Mom and Baby.



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**Prebiotics** are non-living indigestible polysaccharides (food components) that stimulate the growth of beneficial bacteria (*Bifidobacterium*).



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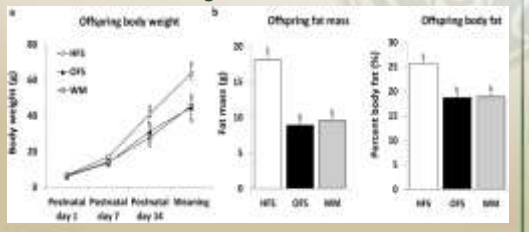
### Prebiotic Sources

- Diet
  - Major dietary sources are consumed in limited amounts in a typical American diet
- Supplements
- Fortification in foods
  - Yogurt
  - Infant formula
  - Artificial sweeteners

Food with Prebiotics	Prebiotic fiber by weight	Amount needed for 1g serving
Oatmeal	64.5%	8.3 g
Immature Artichoke	35.5%	19 g
Cardulose greens	24.3%	24.7 g
Raw garlic	17.3%	34.3 g
Raw leek	15.7%	31.3 g
Raw onion	9.6%	69.8 g
Cooked asparagus	5%	120 g
Raw asparagus	3%	170 g
Raw wheat bran	3%	130 g
Whole wheat flour, unbleached	4.2%	115 g
Raw banana	1%	400 g

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### Maternal Prebiotics Reduce Offspring Weight Gain in Rats



Paul et al. 2016. *Scientific Reports*. doi:10.1038/srep20683

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### Omega 6:3 in BM

Increased ratios of Omega 6:3 in breast milk associated with higher INFLAMMATION, INSULIN RESISTANCE, OBESITY, and reduced NEUROPROTECTIVE EFFECTS.

<p><b>Animal Sources:</b></p> <ul style="list-style-type: none"> <li>Sardines</li> <li>Wild Salmon</li> <li>Sablefish/Black Cod</li> <li>Flaxseed/Flaxseed oil</li> <li>Grass-fed Meats</li> <li>Grass-fed Dairy</li> <li>Pasture-raised Eggs</li> </ul>	<p><b>Plant Sources:</b></p> <ul style="list-style-type: none"> <li>Walnuts</li> <li>Chia Seeds</li> <li>Hemp Seeds</li> <li>Tofu+ Tempeh</li> <li>Cauliflower</li> <li>Broccoli</li> <li>Dark leafy greens</li> </ul>
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**Probiotics** are live bacteria or yeast that when eaten in sufficient amounts can be beneficial for intestinal health.



Slide from Katie McGirr, CSU Extension

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### Probiotic sources

- Food sources:
  - Fermented dairy foods like yogurt, kefir products, and aged cheeses
  - Some fermented non-dairy foods including kimchi, sauerkraut, and kombucha
  - Supplemented non-fermented foods: Good Belly



Slide from Katie McGirr, CSU Extension

## Summary:Pre/Probiotics

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- Prebiotic supplementation (2 months prenatal and during lactation) prevented excess adiposity and improved insulin sensitivity in offspring.
- Probiotics 2 weeks pre-natally activates immune responses and alters meconium microbiota.
- Probiotics given during the 3<sup>rd</sup> trimester and during lactation to mothers with skin allergies reduced eczema incidence in infants.

## Summary (cont)

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- Probiotics administered to C-section babies in the first 6 months of life reduced allergies in children at 5 years.
- Systematic review of probiotic use in pre-term infants suggest little risk and possible benefits of probiotic supplementation on NEC.

## Cautions

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- Antibiotics should not be overused, but have a lifesaving, important place in modern medicine.
- In the wrong place, even good bacteria go bad.
- We still have a long way to go
  - Many studies in animals rather than humans
  - Human studies on limited population size, ethnic/geographic/socioeconomic backgrounds

## Key Points

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- Disturbances in the maternal microbiota are heritable and can influence child health outcomes.
- Breastfeeding provides the infant with pre- and probiotics necessary for early immune development.
- Dietary management of the microbiota is critical for mother and child in the pre and early postnatal period.

## Useful info

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- Microbial changes during pregnancy, birth, and infancy. Nuriel-Ohayon et al (2016) Frontiers in Microbiology. Doi:10.3389/fmicb.2016.01031
- Consumerlabs: <https://www.consumerlab.com/>
- Natural Standards: <https://naturalmedicines.therapeuticresearch.com/>
- International Scientific Asscn of Probiotics and Prebiotics: <https://isappscience.org/>



Mothers' Milk Bank

Colorado Based. Nationwide Reach.

a program of Rocky Mountain Children's Health Foundation

<https://rmchildren.org/?gclid=CNJhtyc4MCFdO3wAodK78GJg>

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