Are probiotics just magic foo-foo dust?

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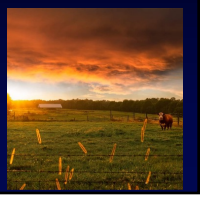
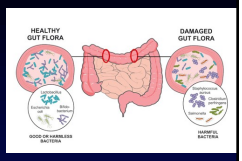


1

What is all this about Microbiome and animals

- The microbiome is everywhere and can do everything
  - According to the advertisers at least….
- The gut microbiome is more important than we realized
  - Impact efficiency, health, food safety, and carcass quality
  - Microbial "organ", endocrinology
  - Related to Health Outcomes
  - Wasteful Energy/N use
  - Fiber fermentation in hindgut



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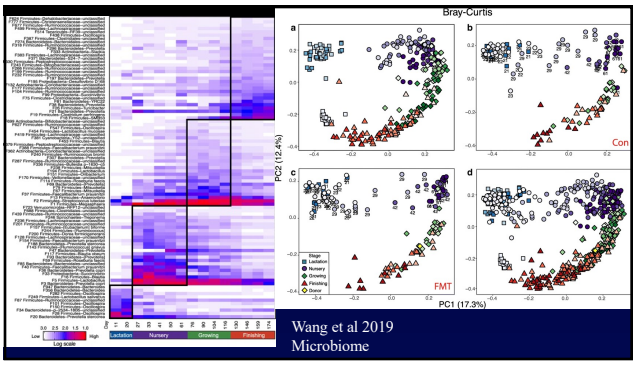

Wang et al 2019
Microbiome

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The gut microbiome's role in health

Immune function

Inflammation
Autoimmunity
immunomodulation

Brain function

The gut-brain axis
Mental health

Nutrient absorption and metabolism

Short chain fatty acids
Insulin resistance and deficiency
Energy capture

Diseases, syndromes, and functional aberrations

Type-1 and type-2 diabetes
irritable bowel syndrome
Atopic eczema
Cardiovascular illnesses
Leaky Gut

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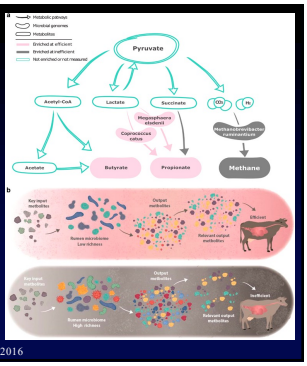
Visualizing eubiotic impacts

- Feeds and digesta are fermented to produce volatile fatty acids (VFA)
  - Gut health/integrity
  - Immune function
- Ultimately must link specific microbiota with outcomes or at least metabolites of importance
  - Conversion of lactate to propionate linked with improved RFI (efficiency)
  - DFM increased lactate utilizers (Pitta, 2010)



Shabat et al, 2016

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Evaluating cattle production holistically

Live animal

In vitro

Production metrics
Efficiency,
Sustainability
Carcass Quality
Foodborne Pathogens
Inflammation

VFA
pH
Ammonia
Methane
Digestibility

Diet

Diet components linked with microbiome, production and pathogens

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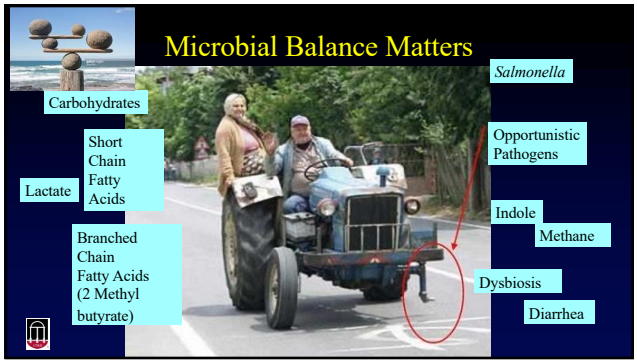

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Dysbiosis: disturbance in the force

- Dysbiosis is an imbalance or perturbation in the microbial population (rumen and hindgut)
  - Linked to performance and health issues
  - Change (good/bad)
  - Opportunity (vulnerability; transition)
- Acidosis and Laminitis
  - Cyclic feeding, FI and FE, SARA, MFD
  - Culling decisions driver
- Leaky Gut Syndrome
  - Loss of productivity, inflammatory response
  - Pathogen entry to the animal
  - LPS from microbes, hindgut acidosis?
  - Does the microbiome mean anything?

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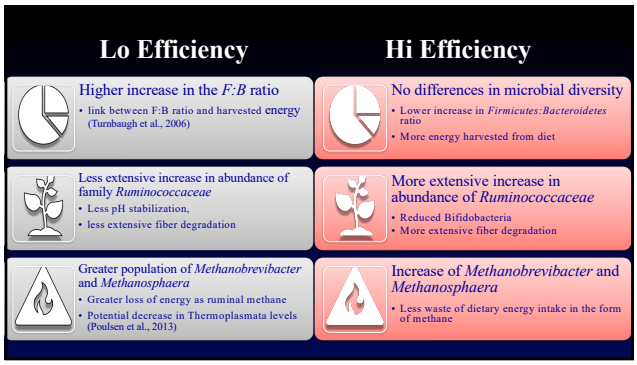

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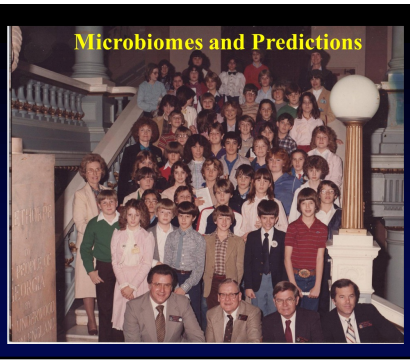
Microbiomes and Predictions

RICO
Smuggling
Triple Homicide
Pawn Shop
Engineer



Professor
Teacher
Legislator
Died at 25
Heart Surgeon
Missing

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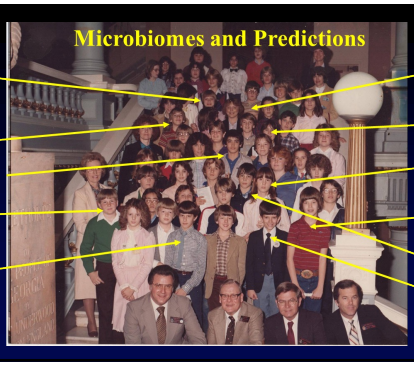
Microbiomes and Predictions



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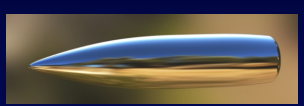
Tools of the microbial trade

- How can we prevent dysbiosis and improve the efficiency of the microbial fermentation to the animal?
  - Probiotics, prebiotics (OS), postbiotics, eubiotics
  - organic acids, natural botanicals (Grilli et al.; various)
  - feed additives, ionophores, bacteriocins/phage
  - diet changes (feeds with natural phytochemicals, citrus peel/pulp, copra) that act similarly to prebiotics on the microbial population
- How can we make the animal more efficient?
  - Using the microbial enzyme pool
  - Using the microbes for health
  - No silver bullet



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Category	Definition/Description	Product types
Eubiotics	**Feed additives that play an essential role in supporting animal performance** and animal welfare by supporting gut health.	Organic Acids, Essential Oils, Probiotics, Prebiotics, Postbiotics, Phytochemicals
Probiotics	"living microorganisms which, when administered in adequate quantities, are beneficial to the health of the host"	**Live** bacterial, yeast or fungal cultures. Includes: Lactic acid bacteria, *Bacillus*, *Aspergillus*, lactate-utilizing bacteria
Prebiotics	Fermentable substrate not used by host animal	Oligosaccharides, Fructooligosaccharides, Maltooligoasschariides, inulin, smaller disaccharides, organic acids (e.g., gluconate) , Β-glucans
Postbiotics	Yeast or fungal products or products of their fermentation	**Non-living** Yeast or Fungal fermentation endproducts; includes cell wall products or fermentation end products
Synbiotics	Feed additives that work synergistically through multiple modes of action	Probiotic coupled with a prebiotic, or a yeast product that contains prebiotics
Phytochemicals	Plant based compounds with activity (e.g., antimicrobial or anti-inflammatory) in the gut or in the host, also termed "natural botanicals" or "nutraceuticals"	Garlic oils, wintergreen, asparagus, dandelion greens, chicory

Table 1. Definitions used in this presentation, Adapted from (El Jeni et al., 2023)

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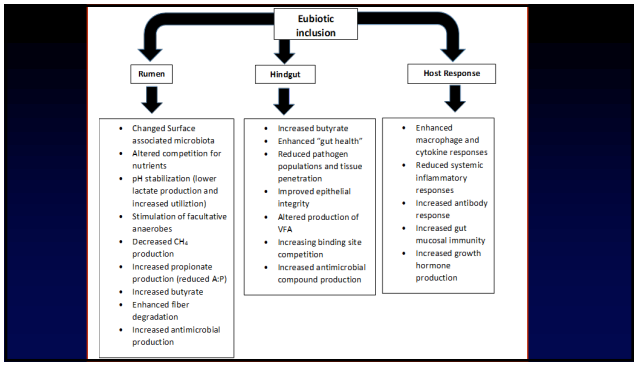

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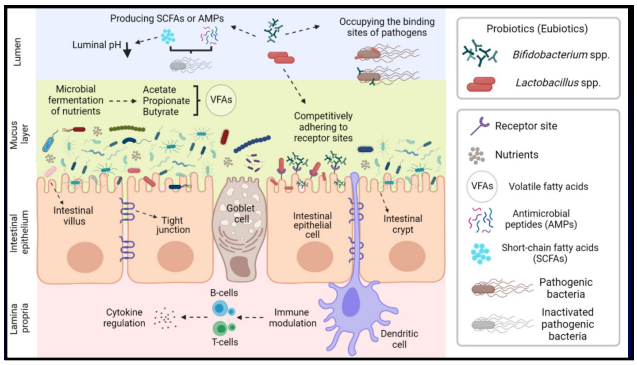

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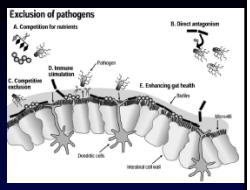
Microbial Impactors

- Production of acids
  - VFA and low pH
- Production of inhibitory compounds
  - Bacteriocins/colicins (proteins), antibiotics
- Competition for nutrients
  - Limiting nutrients, affinity for nutrients
  - "competitive exclusion"
- Competition for binding spaces physically
  - Mucosa surface, crypts, tight junctions (gut integrity)
- Stimulation of host immune system
  - Regulation of inflammation
- Combination of any of these



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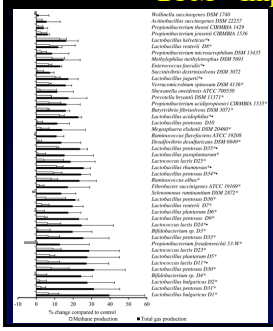
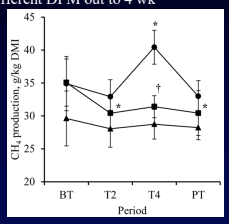
DFM – Impacts on methane vary



- Impact by several DFM on gas and CH_4 production in vitro
- Methane emission from sheep fed hay and 3 different DFM out to 4 wk



Jeyanthan et al., 2016

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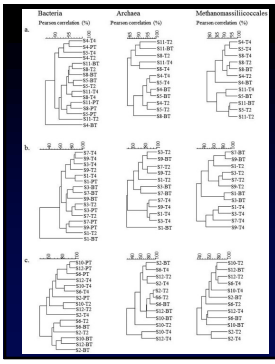
DFM - Changing the microbial population



- Propionibacterium DFM increased pH but did not change VFA
- Impacted methane production on low starch diet only
- Changed DGGE profile in sheep fed DFM
- Variance in effectiveness even within *Propionibacterium* effects common (Philippeau et al., 2017; Francisco et al. 2002)

A *L. bulgaricus*
B *L. pentosus*
C *P. freudenreichii*

Jeyanthan et al., 2016

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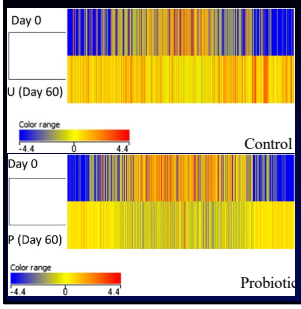
DFM – Host Gene Expression



- Lactating Holstein fed probiotics
- Decreased neutrophil count
- >11,000 genes differentially expressed
- 87 bovine pathways impacted
  - Growth hormone signaling increased
  - Inflammatory response downregulated
  - Systemic inflammation reduced

Adjei-Fremah et al., 2017

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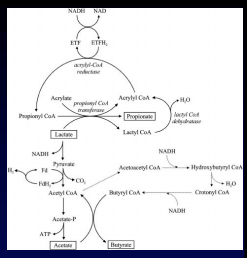
One theory of action

- Enhancement of indigenous *Selenomonas* and/or *Megasphaera* populations
  - Purified malate reduced methane, lactate concentrations, A:P ratio and increased pH in cattle and in vitro (Martin, 1990; 1992)
  - Alternative reducing equivalent sink (CH_4 drop)
- Feeding malate to cattle improved FE and ADG (Streeter and Martin, 1993)
  - Some eubiotics contain malate or fumarate
  - Stimulation of uptake of lactate increases pH and reduces SARA
  - Effects of dicarboxylic acid were similar to monensin and complementary



Prabhu, Altman, Eiteman, 2012

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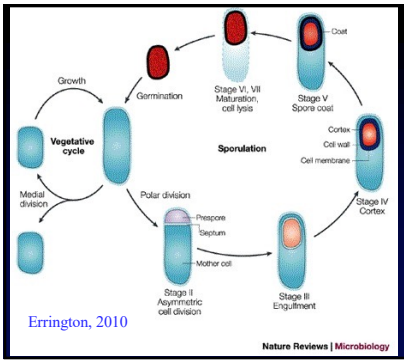
Bacillus products



- *Bacillus* are unusual bacteria
- Form endospores
  - Escape capsule
  - DNA and ribosomes
  - Resistant to heat, light, desiccation, UV, starvation
  - Pressure/heat resistant -Pellets
- Cycle between Spore and vegetative states through a relatively poorly understood germination process
- *Bacillus* contains some pathogenic members
  - Anthracis
  - Cereus
- Others are good probiotic candidates
  - Amyloliquifaciens
  - Subtilis (produces bacteriocin)

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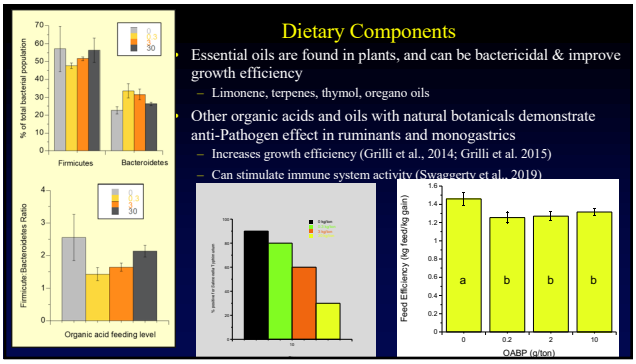
Dietary Components
Essential oils are found in plants, and can be bactericidal & improve growth efficiency
– Limonene, terpenes, thymol, oregano oils
Other organic acids and oils with natural botanicals demonstrate anti-Pathogen effect in ruminants and monogastrics
– Increases growth efficiency (Grilli et al., 2014; Grilli et al. 2015)
– Can stimulate immune system activity (Swaggerty et al., 2019)
% of total bacterial population
Firmicutes
Bacteroidetes
Firmicutes:Bacteroidetes Ratio
Organic acid feeding level
Feed Efficiency (kg feed/kg gain)
a
b
b
b
QABP (g/ton)

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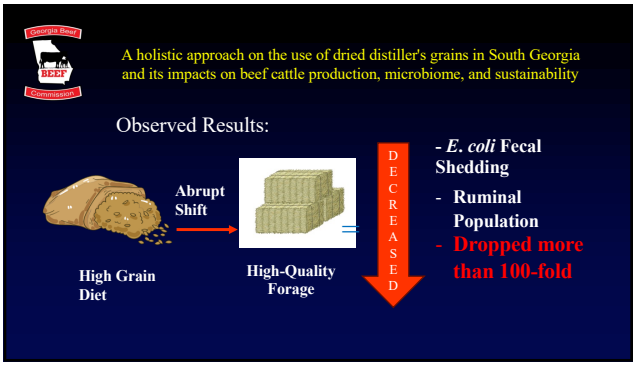
A holistic approach on the use of dried distiller's grains in South Georgia and its impacts on beef cattle production, microbiome, and sustainability
Observed Results:
Abrupt Shift
High Grain Diet
High-Quality Forage
DECREASED
- E. coli Fecal Shedding
- Ruminal Population
- Dropped more than 100-fold

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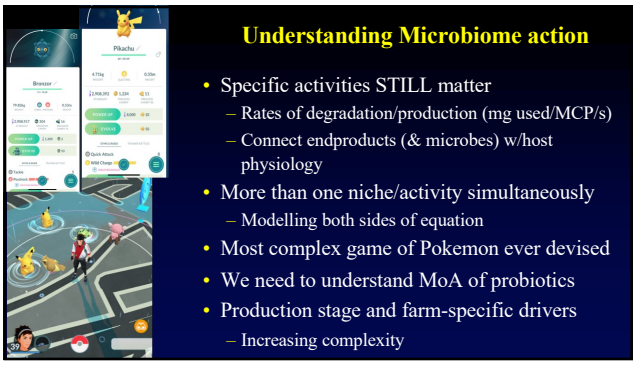
Understanding Microbiome action
• Specific activities STILL matter
– Rates of degradation/production (mg used/MCP/s)
– Connect endproducts (& microbes) w/host physiology
• More than one niche/activity simultaneously
– Modelling both sides of equation
• Most complex game of Pokemon ever devised
• We need to understand MoA of probiotics
• Production stage and farm-specific drivers
– Increasing complexity

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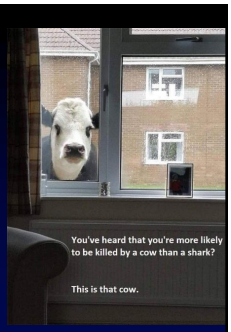
Conclusions

- Eubiotic approaches have a bright future and many routes of action
  - Impacts production efficiency, carcass quality, milk quality, milk quantity, food safety, & animal health
- Very diverse activity spectrum and choices
  - Decision fatigue; contradictory information
  - Indigenous versus endogenous benefits
- We must understand the activities, populations and niches (and pops) of microbes to determine "good/bad" microbiome to select best eubiotic
  - Sustainability and Efficiency = win/win
  - Quality and quantity….goals matter
  - Microbial interactions matter



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Food and Agriculture Organization of the United Nations

World Health Organization

Francis Fluharty
Dean Pringle
Lawton Stewart
Lance Baumgard
Robert Dove

Mike Azain
Ken Griswold
Todd Applegate
Pierre Frumholtz

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