OUR NEWEST ORGAN
MICHAEL G. SCHMIDT
MUSC SCIENCE CAFÉ
23 MAY 2017
Disclosures

• *No financial disclosures*

• We will be speaking of things one should not speak of, while eating...

• Paraphrasing the noteworthy naturalist of SC... Rudy Manke of USC... *the bulk of what we are about to discuss concerns recycling*...
The Emerging Science of the Human Microbiome

By BOBBI CONNER • MAY 16, 2017

This week Bobbi Conner talks with Dr. Michael Schmidt about research exploring the role that the human microbiome plays in good health and in disease. Dr. Schmidt is a Professor and the Vice Chair of Microbiology and Immunology at MUSC.
**Human Microbiome**

- **What do we know?**

  - You are 1 part human & 1 part microbe – formerly it was thought it was 10 parts microbe:1 part human
**Human Microbiome**

- **What do we know?**
  
  - You have are 1 part human 1 part bacteria, formerly thought it was 10 parts bacteria/1 part human
Tonight

Our journey will take us into the world of the human microbiome and explore why I believe it’s our next moon shot.

We’ll do this in three parts, with some fun facts along the way to help you retain what we’re going to experience.

With the end goal being that you will come to appreciate that this MUST be our next moonshot for if not now, when?
Did you know?

• At this moment 2 to 6 pounds of microbes are living in and on you?
  – Where are they?
  – Who are they?
  – What do they do?
  – Are they good or bad?
  – Can they be dragooned for good?

THE HUMAN MICROBIOME

Bacteria, fungi and viruses outnumber human cells in the body by a factor of 10 to one. The microbes synthesize key nutrients, fend off pathogens and impact everything from weight gain to permeability of the skin development. The Human Microbiome Project is taking a census of the microbes and sequencing the genomes of many. The total body count is not in but it is believed over 1,000 different species live in and on the body.

600+ SPECIES in the mouth, pharynx and respiratory system include:
- Streptococcus sanguis
- Neisseria sica
- Candida albicans
- Streptococcus salivarius

1,000 SPECIES in the skin include:
- Propionibacterium acnes
- Staphylococcus epidermidis
- Corynebacterium jeikeium
- Trichosporon
- Staphylococcus haemolyticus

25 SPECIES in the stomach include:
- Helicobacter pylori
- Streptococcus thermophilus

500–1,000 SPECIES in the intestine include:
- Lactobacillus casei
- Lactobacillus reuteri
- Lactobacillus gasseri
- Eubacterium coli
- Bacteroides fragilis
- Bacteroides thetaiotaomicron
- Lactobacillus rhamnosus
- Clostridium difficile

60 SPECIES in the urogenital tract include:
- Ureaplasma parvum
- Corynebacterium urealyticum

SOURCES: NATIONAL INSTITUTES OF HEALTH, SCIENTIFIC AMERICAN, HUMAN MICROBIOME PROJECT

Dean Tweed - PCSTV/IANWS / IMAGE: Fotolia
Where do our bacteria come from?
Human Microbiome

– Fun Facts for future figuring or trivial pursuit championships...

Your belly button can harbor over 2,300 species of bacteria
Where do our bacteria come from?
Mostly, from Mom
With Some, from Family and friends
With some from the environment and diet
Even the dog, Molly

INFLUENCE OF DOGS ON THE HUMAN MICROBIOME

1. Bacteria from a dog’s fur and paws is easily transferred to the skin of humans living in the same space. A 2013 study at the University of Colorado showed that adults share more microbes with their own dogs than they do with dogs owned by other people.

   Perhaps more unexpectedly, the same study showed that simply owning a dog has an impact on the sharing of microbes between one person and another living in the same place.

   Cohabiting couples who owned dogs had more bacteria in common with each other than couples who didn’t have dogs.

SOURCE:

2. UCSF scientists who conducted a study in 2013 suggested that living with a dog in infancy may lower a child’s risk of developing asthma and allergies, largely as a result of exposure to what they call “dog-associated house dust.”

   The researchers’ hypothesis was that babies and small children need to be exposed to harmless bacteria in order to “train” their developing immune systems.

3. Just as fascinating, and perhaps already a candidate for one of the year’s most heart-warming ideas, is a current University of Arizona study that’s exploring whether dogs can directly improve the health of older people.

   They’ve adopted unwanted dogs from the Humane Society, then given them to people over 50 who’ve either never owned a dog, or who haven’t had one for a while.

   Their theory is that good bacteria from the dogs may be transferred to their new owners, along with other health-boosting benefits.
Vaginal-birth baby and vaginal microbiota

C-section baby and mothers skin
Your first microbial encounter..

- Partial restoration of the microbiota of cesarean-born infants via vaginal microbial transfer

Partial restoration of the microbiota of cesarean-born infants via vaginal microbial transfer

María G Domínguez-Bello1,2, Cassandra M De Jesus-Laboy2, Nan Shen3, Laura M Cox2, Amnon Amir4, Antonio Gonzalez3, Nicholas A Bokulich5, Se Jin Song5, Marina Hoaśli1,6, Juanita Rivera-Vivas3, Kelmar Mendez7, Rob Knight8,9 & Jose C Clemente3,9

Exposure of newborns to the maternal vaginal microbiota is interrupted with cesarean birthing. Babies delivered by cesarean section (C-section) acquire a microbiota that differs from that of vaginally delivered infants, and C-section delivery has been associated with increased risk for immune and metabolic disorders. Here we conducted a pilot study in which infants delivered by C-section were exposed to maternal vaginal fluids at birth. Similarly to vaginally delivered babies, the gut, oral and skin bacterial communities of these newborns during the first 30 d of life were enriched in vaginal bacteria—which were underrepresented in unexposed C-section–delivered infants—and the microbiome similarity to those of vaginally delivered infants was greater in oral and skin samples than in anal samples. Although the long-term health consequences of restoring the microbiota of C-section–delivered infants remain unclear, our results demonstrate that vaginal microbes can be partially restored at birth in C-section–delivered babies.

estimated 15% of births require C-section delivery to protect the health of the mother or baby11,22.

Here we exposed C-section–delivered infants to their maternal vaginal fluids at birth and longitudinally determined the composition of their microbiota to assess whether it developed more similarly to vaginally born babies than to unexposed C-section–delivered infants. We collected samples from 18 infants and their mothers, including 7 born vaginally and 11 delivered by scheduled C-section, of which four were exposed to the maternal vaginal fluids at birth (Supplementary Table 1). Briefly, the microbial restoration procedure, or vaginal microbial transfer, consists of incubating sterile gauze in the vagina of mothers who were negative for group B Streptococcus (GBS), had no signs of vaginosis and had a vaginal pH < 4.5 during the hour preceding the C-section. Within the first 2 min of birth, babies were exposed to their maternal vaginal contents by being swaddled with the gauze, starting with the mouth, then the face and finally the rest of the body (Fig. 1a).

A total of 1,519 samples were obtained from anal, oral and skin samples of infants and mothers at six time points during the first month of life (1, 3, 7, 14, 21 and 30 d after birth; Supplementary Table 2). Microbiome composition was characterized by sequencing the V4 region of 16S rRNA ger as previously described3,22, and 1,016 samples were used for analysis after quality filtering (see Online Methods). No adverse events were reported for any of the infants in this study. Bacterial source tracking23 of the infant microbiome revealed that the microbiomes of the four C-section–delivered infants exposed to vaginal fluids resembled those of vaginally delivered infants, particularly so during the first week of life (Fig. 1b). The bacterial community distance between microbiome samples from exposed and unexposed infants are...
Your first microbial encounter..
Or, your first microbial encounter...

Be violent, bold, and firm. Laugh at the power of other men, because nobody born from a woman will ever harm Macbeth. Unfortunately for Macbeth, the Scottish nobleman Macduff was "from his mother's womb/ Untimely ripped," and thus not naturally "born of woman" (V.vii). Macduff was the only agent capable of destroying Macbeth. He killed Macbeth in battle.  *William Shakespeare, Macbeth Act 5, Scene 7*
Will this prevent Asthma, Allergies, Type 1 diabetes, Celiac Disease, Obesity?

based on 4 C-Sections, first month of life and over 1,500 microbial samples
How long till we get an answer as to body comp, rate of asthma or allergies?

N=1200 with 3-5 years microbial follow-up

Vaginal-birth baby and vaginal microbiota

Maria Domínguez-Bello
Associate Professor, Department of Medicine

C-section baby and mothers skin
• **The human microbiome before birth**
  – Blaser, MJ and Dominguez-Bello, MG
  – Bottom line...

  – The conservation of the microbiota within humans and other hominids suggests an ancient assembly that has been selected to optimize host fitness.

  – Pregnancy induces changes in the maternal microbiome just before the intergenerational hand-off of the microbiota. Interventions, including peri-partum antibiotics and Cesarean sections, may have unintended effects on babies.
• *Antibiotics, birth mode, and diet shape microbiome maturation during early life*

Two studies of more than 80 infants followed for the first 2 to 3 years of life now reveal the effects of birth mode, diet and antibiotic treatment on gut microbiome development (Yassour et al., Bokulich et al.) The investigators show that antibiotics, cesarean delivery and formula feeding can alter development of the infant microbiome, *reduce bacterial diversity* and transiently increase the presence of antibiotic resistance genes.
Facts about Autism

- Autism now affects 1 in 68 children and 1 in 42 boys
- Autism prevalence figures are growing
- Autism is one of the fastest-growing developmental disorders in the U.S.
- Autism costs a family $60,000 a year on average
- Boys are nearly five times more likely than girls to have autism
- There is no medical detection or cure for autism
- $169M goes directly to investigate this condition from the NIH (0.54% of NIH budget)
The inspiration –

- human epidemiological studies
- maternal obesity during pregnancy could increase children's risk of developing neurodevelopmental disorders, including ASDs

http://dx.doi.org/10.1016/j.cell.2016.06.001
Single species of gut bacteria can reverse autism-related social behavior in mice!

- Maternal high-fat diet (MHFD) induces behavioral alterations in offspring
  - Equivalent of fast food, several times per day, N=60.

- MHFD causes alterations in gut microbial ecology in offspring
  - Could predict from simply from pattern that the offspring would be impaired! WOW!

- MHFD offspring show deficient synaptic plasticity in the ventral tegmental area (VTA) and oxytocin production
  - Attended to Mechanism

- L. reuteri treatment restores oxytocin levels, VTA plasticity and social behaviors
  - One microbe, restores activity WOW!
Single species of gut bacteria can reverse autism-related social behavior in mice!
Asthma and the Microbiome
Asthma and the Microbiome

• Chronic Inflammatory immune disorder of the airways affecting 1:10 children in westernized countries (235 Million people worldwide), 40M in the US (13.3 % of adults & 13.8% of children), with a tragic 9 deaths per day!

• Does it run in families?
  – Yes, variations in two genes, ORMD13 and GSDML
Microbe-rich environments may trigger immune system, prevent asthma

By Virginia Darrow

Amish children growing up on farms that use animals have an immune response that may prevent asthma, according to a new study supported in part by NIEHS. The research was published Aug. 3 in the New England Journal of Medicine (NEJM).

The study compared children from two U.S. farming communities: one Amish and the other Mennonite. The two communities have many similarities, including shared genetic heritage, but the Amish use livestock for milk and meat production, while the Mennonites practice vegetarian farming with chickens. Previous studies had shown that asthma is rare among Amish children, whereas it is present at typical levels in Mennonite children.

The researchers saw a key difference in how the children's immune systems function. Based on the types of cells and the chemical signals activated, the Amish children actually used their innate immune systems (see sidebar). This response was also seen in the Mennonite children.

"The study augments prior work showing the significant role our environmental exposures play in asthma," said Peter Thorne, Ph.D., in a University of Washington release. "There is also evidence that the Amish and other Mennonite children may have a reduced risk of asthma due to their close contact with animals on farms. This study builds on this idea by showing that the immune system, in two populations with similar genetics, responded to microbial exposure by activating the innate immune system in a way that may lead to asthma protection in these communities."

Microbial richness in Amish homes

"The research team used air samples that did not measure electricity in the Amish and Mennonite homes to measure airborne particles and bacterial richness. The researchers found that the types of bacteria in the two groups of homes were different, and that the levels of electrostatic activity were nearly seven times higher in Amish homes."

"The higher electrostatic fields in electrostatic dust support the notion that the Amish microbial environment is much richer in microbial exposures than the Mennonite environment," the authors wrote.

Further, they noted that in electrostatically exposed homes, the number of bacteria increased. This increase in bacteria is thought to increase the immune response to a higher level of inflammation that prevents the emergence of asthma, according to a NIEHS editorial that accompanied the study. This observation is yet to be confirmed. Continuous exposure to the dust is thought to be required for this protective effect.

Innate vs. adaptive immunity

This study's findings are consistent with a model that has been established, called the "innate vs. adaptive immunity." The human immune system includes two main systems, innate and adaptive, which work together to protect people from disease. The innate immune system quickly attacks foreign microbes. This response activates the adaptive immune response.

The more specialized adaptive immune system can recognize and remember specific bacteria or viruses, providing long-lasting immunity, but it is slower to respond to new diseases. For example, these cells are the ones that respond to vaccines.
Innate Immunity in Asthma

Talal A. Chatila, M.D., M.Sc.

It is appreciated that the marked increase in the prevalence of asthma over the past few decades reflects changes in environmental exposures and living conditions associated with modern lifestyles. Of particular interest is the documentation of a protective effect of exposures associated with traditional farming, the influence of which has waned with increased urbanization and the advent of mechanized agriculture. On small family-based farms where children are reared in close proximity to farm animals and their sheds, increased exposure to the microbial products found in these environments, including lipopolysaccharides, has been associated with protection against asthma. It remains unclear how exposure to a traditional farming environment confers protection against asthma and whether such protection also applies in the context of large-scale industrialized farming. Stein et al. now advance our knowledge on both accounts in this issue of the Journal.

In their study, Stein et al. took advantage of a lifestyle attribute that differentiates two otherwise closely related U.S. populations in which the incidence of asthma is dissimilar. The Amish and the Hutterites are reproductively isolated farming communities that are linked by ancestry, having originated in German-speaking alpine regions of Europe. They also share a similar lifestyle that includes environmental exposures that often affect the risk of asthma, with one notable exception — whereas the Amish have maintained a traditional farming practice that revolves around single-family dairy farms and eschews mechanization, the Hutterites practice large-scale, highly mechanized communal farming. The prevalence of asthma and allergic sensitization among the Amish is low, but among the Hutterites the prevalence of both conditions is strikingly high, similar to that in the U.S. population at large. As such, these two communities are ideally suited for analysis of the influence of environmental exposures on susceptibility to asthma.

By studying children from these two communities, Stein et al. confirmed the discrepancy that exists in the communities’ incidences of allergy and asthma. The researchers also established the presence of a distinct microbial composition and an increased burden of lipopolysaccharides in dust samples collected from the houses of the Amish as compared with those of the Hutterites. After exposing samples of peripheral-blood lymphocytes from both populations to lipopolysaccharides, the samples from the Amish expressed more innate immunity-related cytokines than those from the Hutterites. The peripheral-blood lymphocytes of Amish children also exhibited a genetic signature...
**Brief report**

*Helicobacter pylori* infection prevents allergic asthma in mouse models through the induction of regulatory T cells

Isabelle C. Arnold,¹ Nina Dehzad,² Sebastian Reuter,² Helen Martin,² Burkhard Becher,³ Christian Taube,² and Anne Müller¹

¹Institute of Molecular Cancer Research, University of Zürich, Zürich, Switzerland. ²III. Medical Clinic, Johannes Gutenberg University, Mainz, Germany. ³Institute of Experimental Immunology, University of Zürich, Zürich, Switzerland.

Atopic asthma is a chronic disease of the airways that has taken on epidemic proportions in the industrialized world. The increase in asthma rates has been linked epidemiologically to the rapid disappearance of *Helicobacter pylori*, a bacterial pathogen that persistently colonizes the human stomach, from Western societies. In this study, we have utilized mouse models of allergic airway disease induced by ovalbumin or house dust mite allergen to experimentally examine a possible inverse correlation between *H. pylori* and asthma. *H. pylori* infection efficiently protected mice from airway hyperresponsiveness, tissue inflammation, and goblet cell metaplasia, which are hallmarks of asthma, and prevented allergen-induced pulmonary and bronchoalveolar infiltration with eosinophils, Th2 cells, and Th17 cells. Protection against asthma was most robust in mice infected neonatally and was abrogated by antibiotic eradication of *H. pylori*. Asthma protection was further associated with impaired maturation of lung-infiltrating dendritic cells and the accumulation of highly suppressive Tregs in the lungs. Systemic Treg depletion abolished asthma protection; conversely, the adoptive transfer of purified Treg populations was sufficient to transfer protection from infected donor mice to uninfected recipients. Our results thus provide experimental evidence for a beneficial effect of *H. pylori* colonization on the development of allergen-induced asthma.
Asthma and the Microbiome

- Gut microbial dysbiosis in human atopic diseases is characterized **NOT by GLOBAL changes to** the composition of the intestinal microbial population but by **taxa-specific shifts**
- Impacts- human immune system... which is most plastic during this window
Asthma and the Microbiome

- **Hygiene hypothesis** (Strachan)
  - Are we too clean during those first 100 days?
  - Now includes... mode of birth, abx exp, pets, farm life, etc)

- **Microflora hypothesis**
  - “it is clear that there is a microbial-immune cell interface, in which cross-talk between microbes and immune cells aids in the development of immune tolerance

- **Gut-Lung Axis**
  - How does the gut talk to the lung?
    - PAMPs (pathogen associated molecular patterns)
      - LPS, Peptidoglycan, CpG

- **Microbial-derived metabolites... Short chained fatty acids (SCFAs)**
  - Three major ones – Acetate, Propionate and butyrate (60:20:20) molar ratio
    - Modify gene expression in humans through inhibition of histone deacetylases (HDACs) and cytokine and chemokine production, and cell differentiation, proliferation and apoptosis!
Asthma and the microbiome: *defining the critical window in early life*

Leah T. Stiensma\(^1,2\) and Stuart E. Turvey\(^2,3\)\(^*\)

**Abstract**

Asthma is a chronic inflammatory immune disorder of the airways affecting one in ten children in westernized countries. The geographical disparity combined with a generational rise in prevalence, emphasizes that changing environmental exposures play a significant role in the etiology of this disease. The microflora hypothesis suggests that early life exposures are disrupting the composition of the microbiota and consequently, promoting immune dysregulation in the form of hypersensitivity disorders. Animal model research supports a role of the microbiota in asthma and atopic disease development. Further, these model systems have identified an early life critical window, during which gut microbial dysbiosis is most influential in promoting hypersensitivity disorders. Until recently this critical window had not been characterized in humans, but now studies suggest that the ideal time to use microbes as preventative treatments or diagnostics for asthma in humans is within the first 100 days of life. This review outlines the major mouse-model and human studies leading to characterization of the early life critical window, emphasizing studies analyzing the intestinal and airway microfloras in asthma and atopic disease. This research has promising future implications regarding childhood immune health, as ultimately it may be possible to therapeutically administer specific microbes in early life to prevent the development of asthma in children.

**Keywords:** Microbiota, Asthma, Early life, Critical window, Hygiene hypothesis, Microflora hypothesis
For Asthma and Age is critical

Thorburn et al. show that maternal intake of acetate reduces allergic airways disease in adult offspring. 

Gollwitzer et al. identify shifts in airway microbiota that are associated with decreased responsiveness to aeroallergens.

Cahenzli et al. associate increased microbial diversity with decreased IgE production and decreased disease severity in a mouse model of antigen-induced oral anaphylaxis.

Arnold et al. determine that neonatal (6 days post birth) Cag A-positive Helicobacter pylori infection protects against OVA and HDIM-induced airway hyperresponsiveness.

Lyons et al. show that perinatal exposure to B. longum induces T-reg and protects against allergic airway inflammation in adult mice.

Russell et al. show that perinatal exposure to antibiotics differentially exacerbates lung disease in adult mice.

Olszak et al. show that exposure of GF neonatal mice at birth (and continuing until 9-weeks post-birth) protects adult mice from allergic asthma symptoms.
Age is critical

Abrahamsson *et al.* associate decreased gut microbiota diversity at 1-week and 1-month of age with asthma development at 7-years of age.  

Teo *et al.* associate increased asymptomatic colonization with *Streptococcus* in the NP microbiome with chronic wheezing at ages 5 and 10 years.  

Fujimura *et al.* identify shifts in neonatal bacterial and fungal taxa that are associated with varying degrees of asthma risk by 4-years of age.  

Arrieta*, Stiensma* *et al.* associate decreased abundance of FLVR taxa and decreased acetate production at 3-months with atopy and wheezing at 1-year of age.  

Stiensma *et al.* identify the L/C ratio as a potential biomarker for identifying children at high risk of being diagnosed with preschool-age asthma.
Asthma and the Microbiome

• Chronic Inflammatory immune disorder of the airways affecting 1:10 children in westernized countries (235 Million people worldwide) with a tragic 9 deaths per day in US!

• Studies suggest that the ideal time to use microbes as preventative treatments or diagnostics for asthma in humans is within the first 100 days of life! Allergy Asthma Clin Immunol. 2017; 13: 3.
Body fat link to bacteria in feces

Researchers have found that certain gut bacteria are linked with being overweight or obese
Body fat link to bacteria in feces
Body fat link to bacteria in feces

• Study in Genomic Biology
  @Kings College Twin Research and Genetic Epidemiology

• Simple study
  – Collected stool samples, tasked who’s there and then assessed against 6 measures of obesity
  – Learned that participants with more diverse community of bacteria had generally lower levels of visceral fat that is store in the abdominal cavity near important internal organs

RESEARCH

Heritable components of the human fecal microbiome are associated with visceral fat

Michelle Beaumont, Julia K. Goodrich, Matthew A. Jackson, Icili Yet, Emily R. Davenport, Sara Vieira-Silva, Justine Debelius, Tess Pallister, Massimo Margino, Jeroen Raes, Rob Knight, Andrew G. Clark, Ruth E. Ley, Tim D. Spector and Jordana T. Bell

Abstract

Background: Variation in the human fecal microbiota has previously been associated with body mass index (BMI). Although obesity is a global health burden, the accumulation of abdominal visceral fat is the specific cardio-metabolic disease risk factor. Here, we explore links between the fecal microbiota and abdominal adiposity using body composition as measured by dual-energy X-ray absorptiometry in a large sample of twins from the TwinsUK cohort, comparing fecal 16S rRNA diversity profiles with six adiposity measures.

Results: We profile six adiposity measures in 3666 twins and estimate their heritability, finding novel evidence for strong genetic effects underlying visceral fat and android/gynoid ratio. We confirm the association of lower diversity of the fecal microbiota with obesity and adiposity measures and then compare the association between fecal microbial composition and the adiposity phenotypes in a discovery subsample of twins. We identify associations between the relative abundances of fecal microbial operational taxonomic units (OTUs) and abdominal adiposity measures. Most of these results involve visceral fat associations with the strongest associations between visceral fat and Oscillospora members. Using BMI as a surrogate phenotype, we pursue replication in independent samples from three population-based cohorts including American Gut, Flemish Gut Flora Project and the extended TwinsUK cohort. Meta-analyses across the replication samples indicate that 8 OTUs replicate at a stringent threshold across all cohorts, while 49 OTUs achieve nominal significance in at least one replication sample. Heritability analysis of the adiposity-associated microbial OTUs prompted us to assess host-gut-microbe interactions at obesity-associated human candidate loci. We observe significant associations of adiposity-OTU abundances with host genetic variants in the FAT1, TDRG1 and ELAV4 genes, suggesting a potential role for host genes to mediate the link between the fecal microbiome and obesity.

Conclusions: Our results provide novel insights into the role of the fecal microbiota in cardio-metabolic disease with clear potential for prevention and novel therapies.

Keywords: Fecal microbiome, Obesity, Visceral fat, Heritability, Genetic association, Twins
Body fat link to bacteria in feces

• Study in Genome Biology... by Michelle Beaumont @Kings College Twin Research and Genetic Epidemiology

• Simple study 1,313 twins- Observational study...
  – Collected stool samples, asked who’s there and then assessed against 6 measures of obesity
  – Learned... participants with more diverse community of bacteria had generally lower levels of visceral fat stored near the abdominal cavity near important internal organs, not previously linked...
All people have a unique microbiome, because each of us live a unique life; even identical twins!
Genetically Distinct

Humans are genetically distinct, because each of us live a unique life; even identical twins!
What's Next?

**Obesity**
- Hyperphagia
- FTO, MC4R, GHRL, SIM1
- Energy expenditure
- UCP2, UCP3
- Obesogenic environment

**Blood**
- Triglyceride clearance
- APOA5, GPIHPB1, LPC, LPL
- Hypo-cholesterol
- ABCA1, HMGCR, PCSK9, Statins

**Adipose tissue**
- Adipokine signaling
- ADIPOQ, IL6, LEP, RETN
- Fat storage
- PPARG, PPARGC1A

**Pancreatic dysfunction**
- Beta cell development
  - HNF1A, HNF4A, PAX4, PDX1, TCF7L2, FOXA2, NEUROD1
- Apoptosis/senescent
  - CDKN2A, GLIS3, WFS1
- Glucose sensing and insulin secretion
  - ABC2B, GCK, KCNJ11, MTNR1B
- Glucagon signaling
  - GGR
- Amylin toxicity
  - PCSK1
- Aging

**Skeletal muscle**
- Insulin sensitivity
  - AKT2, APPL1, HMGA1, IRS1, TBC1D4
- Glycogen capacity
  - PPP1R3A, PRKAG3

**Liver**
- De novo triglyceride production
  - GCKR, SREBF1, USF1
- Fat utilization
  - PPARA, FADS1, RBP4

**Sedentary lifestyle**
### Type 2 Diabetes Primary Panel

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THE NEXT MOON SHOT?

12 September 1962

- We set sail on this new sea because there is new knowledge to be gained, and new rights to be won, and they must be won and used for the progress of all people. For space science, like nuclear science and all technology, has no conscience of its own. Whether it will become a force for good or ill depends on man, and only if the United States occupies a position of pre-eminence can we help decide whether this new ocean will be a sea of peace or a new terrifying theater of war. I do not say that we should or will go unprotected against the hostile misuse of space any more than we go unprotected against the hostile use of land or sea, but I do say that space can be explored and mastered without feeding the fires of war, without repeating the mistakes that man has made in extending his writ around this globe of ours.

- There is no strife, no prejudice, no national conflict in outer space as yet. Its hazards are hostile to us all. Its conquest deserves the best of all mankind, and its opportunity for peaceful cooperation may never come again. But why, some say, the Moon? Why choose this as our goal? And they may well ask, why climb the highest mountain? Why, 35 years ago, fly the Atlantic? Why does Rice play Texas?[5]

- We choose to go to the Moon! ...[6] We choose to go to the Moon in this decade and do the other things,[7] not because they are easy, but because they are hard; because that goal will serve to organize and measure the best of our energies and skills, because that challenge is one that we are willing to accept, one we are unwilling to postpone, and one we intend to win ...
**Our Moon Shot?**

2018 US Budget $3.5 Trillion
Microbiome $122 Billion?
2018 Total NIH Budget $31.2B
2018 NASA – $18.5B
Microbially Unique

All people have a unique microbiome, because each of us live!
Finally

• Some will prove wrong but for the most part, our microbes are likely are oldest organ system
One more thing...

Without our bacteria we would be so much colder, 93.2°F/33°C rather than the 98.6°F/37°C
Thank you!

Questions?
OUR NEWEST ORGAN
MICHAEL G. SCHMIDT
MUSC SCIENCE CAFÉ
23 MAY 2017