

## Right in the Gut: “Reaching Ideal Gut Health Together”

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**Problem Addressed:** With the modern advent of antibiotics and exceptional medical care, the developed world has largely shed the encumbrances of many infectious diseases. The focus of human suffering has now transitioned to Chronic Inflammatory diseases and disorders including Cancer, Obesity, Diabetes, and Cardiovascular Disease. A full 70% of Global disease now results from chronic inflammation<sup>1</sup>. It has been shown that the gut microbiome, the community of commensal microorganisms within a host, plays a central role in altering host metabolism and immune function in Chronic Inflammatory diseases such as Obesity and Type 2 Diabetes Mellitus<sup>2,3</sup>. There is now evidence to support a theory that in the gut ecosystem the mycobiome, a collection of commensal fungi, with *Candida albicans* being the most prevalent species, may be the driving factor in the development of a state of chronic inflammation<sup>4-15</sup>. It is unknown if certain dietary components (high sugar, low fiber) alter the gut microbiota in a way that favors the growth of the invasive hyphal form of *C. albicans*, possibly in the inner mucus membrane of the gastrointestinal tract. The presence of fungal species in the inner colonic mucus membrane has yet to be determined. Dietary components that promote the invasive form of *C. albicans* and other fungi have yet to be determined.

Chronic Inflammatory-related diseases are a Global leading cause of death for high-income economies<sup>16</sup>. The economic and health burden of obesity has earned it the reputation as one of the greatest public health threats of this century<sup>17</sup>. The rise of global obesity rates have paralleled the rates of Type II Diabetes Mellitus, the leading cause of Cardiovascular Disease (CVD)<sup>18</sup>. It is estimated that 642 million people globally will suffer from Type II Diabetes by the year 2040<sup>18</sup>. In 2015, the United States recorded obesity rates of 36.5 % and 30.3 million people with Diabetes, while the State of Alabama reported obesity rates of >35% and Diabetes rates at 12% of the Adult population<sup>19,20</sup>. The State of Alabama, with a 19.1% lower mean income than that of the U.S. in the 2016 census, consistently ranks as one of the top 5 states for obesity and diabetes prevalence<sup>19,20,21</sup>.

It has been shown that ethnic minority populations as well as low-income communities are disproportionately affected by obesity and adverse health outcomes. Contributory factors include the persistence of limited access to healthful fibrous foods, a diet disproportionately high in processed foods containing large amounts of sugar and a lack of nutrition education<sup>22,23,24</sup>. A diet deficient in plant polysaccharide fiber reduces healthy gut microbial diversity, leads to the erosion of the colonic mucus barrier and increases inflammation<sup>25,26</sup>. It is possible that this erosion makes it possible for *C. albicans* to invade the inner mucus lining. Low microbial diversity patterns have been found in individuals with higher body mass index (BMI), insulin resistance, dyslipidemia, and increased inflammatory markers<sup>27</sup>. A diet rich in certain seafood products is able to reverse gut microbiome dysbiosis in diabetic mice<sup>28</sup>.

**AIM1: YEAST GUT?** Determine if *Candida albicans*, or other yeast species are able to exist in the invasive hyphal form within the inner mucus membrane of the gastrointestinal tract. Design a mouse model with and without *C. albicans* colonization. Use fungal FISH analysis and PCR techniques to analyze the colonic mucus layer<sup>29</sup>. This technique could subsequently be applied to human colonic biopsies as well as other chronic inflammatory disease animal models. **Anticipated Outcome:** *Candida albicans* (and, possibly other fungal species) are the fundamental microbes of a commensal biofilm that inhabits the inner mucous layer attached to the epithelial lining of the human gastrointestinal tract. When *C. albicans* accesses this mucus layer, fungal cytolytic proteins are able to disrupt the epithelial barrier and initiate a cascade of inflammatory events<sup>7</sup>.

**AIM 2: TO START YEAST, JUST ADD SUGAR** Determine the main dietary components that promote the invasive form of *C. albicans* and other fungi within the gastrointestinal tract. This would apply to the same mouse model(s) described above. **Anticipated Outcome:** Diets low in fiber and high in sugars and refined carbohydrates will be shown to alter the gut microbiome in a way that promotes the growth of invasive yeast species in the gut mucosa.

**AIM2: DON'T LET THEM EAT CAKE** In Jefferson County, AL, establish a coalition between UAB, the Central AL Food Bank, Alabama Farmers, the Alabama Seafood Industry and the State of Alabama to identify food insecure citizens, provide and distribute only *healthful* Alabama produce, Alabama Seafood products and related items to food insecure program participants. Food distribution would occur at set locations on a weekly basis throughout Jefferson County. Voluntary program participants will receive nutritious Alabama produce and seafood along with healthy recipes for those food items. In exchange, UAB will collect and analyze basic health markers at specific intervals over a period of time. Health care providers could also track any changes in healthcare costs for these individuals during the program. **Anticipated Outcome:** Program participants should see a reduction in food insecurity while at the same time experience a diet-induced reduction in overall chronic inflammation. This should result in improved health diagnoses and less severe chronic inflammatory disease symptoms in participants.

**AIM3: LET THE DOUGH RISE!** Promote UAB in our community by educating the public about the importance of the gut microbiome to health and show how it is directly linked to diet and lifestyle. Use UAB social media, blogs, podcasts, Birmingham-based multimedia outlets, Jefferson County k-12 school system along with community educational platforms in order to disseminate information. An educational medical and scientific advisory board will be formed in order to determine content in the areas of gut health, microbiome research and nutrition, with an emphasis on UAB research. This approved content will then be distributed. **Anticipated Outcome:** This effort may reduce chronic inflammatory disease in Jefferson County as well as the overall burden of healthcare costs for the State of Alabama. This may positively impact local consumer purchasing trends in the health food industry and gain the interest of Industry leaders.

**Potential Team Members:** Kenda Rigdon, Lindsay Pappas (lpappas@uab.edu).

(Unconfirmed Potential Team): UAB Depts. of Microbiology, Immunology, Pathology, Nutrition Science, Nursing, Education, Communications, University Relations, Central AL Food Bank, WBHM Radio, Local News/Radio Affiliates, Alabama Farmers Coop., Organized Seafood Assn. of AL, Jefferson Cty K-12 School System, Whole Foods.

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