

HygiBiome™ – A Novel and Unique Platform to Enhance Microbiome Research for Development of Preventative and Personalized Medicine, Diagnoses, and Therapeutics

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Microbiome research is now soaring, promising solutions and cure to almost any disease, from metabolic disorders through cancer, autoimmune diseases, depression, and autism¹⁻⁷. The human gut microbiome is now considered the second genome of the human body, and the source of genetic diversity between people^{8,9}. In recent years, it has also been established that the gut microbiome is a key factor in immunity, mitigating metabolism, and modulating drug interactions⁷. Understanding the genetic and metabolic signatures of the gut is predicted to become a fundamental practice in medical evaluation and projected to influence the way we eat, sleep, and exercise¹⁰⁻¹⁵. The ability to understand the gut microbiology and biochemistry is bound to create a paradigm shift in our perception of human health, chronic disease management, detection of disease biomarkers, and drug development. This paper describes the significant advantages of using the FDA cleared HyGleaCare® platform and the novel HygiBiome approach to bring microbiome research to its next stage.

HygiBiome is the microbiome arm of HyGleaCare Inc.^{16,17} that commenced operations in 2015, is utilizing the FDA cleared HyGleaCare colon irrigation system¹⁸⁻²⁴. The HyGleaCare Prep replaces the traditional oral preparation for colonoscopy that is so burdensome and even impossible for many patients. At HyGleaCare, the patients undergo colon irrigation that releases them from the stool in their bowel in approximately one hour. To this date, over 10,000 patients were prepped with over 97% adequate colon cleanliness and zero severe

adverse events²⁵. Based on HyGleaCare's bowel cleaning results and patient satisfaction, the company is striving to become the new Standard of Care (SOC) for colonoscopy preparation in the US with nation-wide located centers. HyGleaCare also holds the unique patent which is currently the only non-invasive way to obtain fresh, *de novo*, stool, from throughout the colon²⁶.

Today, companies already offer personalized gut microbiome-based dietary guidelines, and some of them also provide personalized pro- and pre-biotics, as well as food supplements³²⁻³⁵. Albeit, the vast majority of these studies and recommendations result from analysis of home-collected fecal samples. The same applies to drug development and biomarkers studies performed based on non-invasive collection methods that are currently underway^{3,7,36-38}. These samples have many drawbacks when used as the ultimate samples for technological development. These drawbacks include the combination of a non-sterile collection environment, collection by untrained individuals, and the limitation of collecting only fecal samples (often originated from the sigmoid colon). Thus, it is clear that in order to move the field forward, there is a need for a professional and noninvasive approach to sampling the gut lumen^{29,39}. HyGleaCare's platform is perfectly positioned for this task.

Our vision includes leveraging on our patented process by creating and curating a unique, smart, and meaningful Artificial Intelligent (AI)-driven, database from noninvasively collected samples originated in the colon interior²⁷⁻²⁹. This database will include comprehensive information collected from the colonoscopy screening population and any other patients that will use HyGleaCare's services. The HyGleaCare platform will allow the collection of stool from a healthy, screening, population, allowing tracking the full range of prevalent diseases in the population over the ages of 50. This is the sweet spot that will drive studies for disease diagnosis, prevention, and therapy. Our database will be generated from samples collected from the colon lumen, using proprietary Standard Operating Procedures (SOPs), and analyzed ubiquitously. Such a database,

containing the microbial and biochemical signature of the colon, will support original and conclusive research for nutritional guidance and related drug development.

In recent years, there is numerous evidence that describes the different microbial environment of different biogeographic locations of the colon³⁹⁻⁵¹. Most of these studies were done using invasive methods. The combination of the HyGleaCare platform with HygiBiome's technology will enable an easy, affordable, and improved profiling of the microbiome communities and biochemical environment of the different regions of the gut. By partnering with research entities in industry, academy, and the health system, we will generate biogeographic-related and intelligent input for medical and health purposes. We are also working on establishing collaboration with diagnostic labs and companies for analysis of microorganisms and immunochemistry in stool samples collected at HyGleaCare centers. This will be an elective choice for patients undergoing the HyGleaCare prep and can help them make the most of current scientific advancements as part of their normal healthcare routine. Such analyses can promote understanding of various conditions such as pre-cancerous conditions, colon dysbiosis, leaky gut, specific disease, Histamine intolerance, and food allergies.

Constipation relief with HyGleaCare colon irrigation has been well-tolerated by chronically constipated patients, with no serious adverse events. It has also been reported that it effectively caused peristaltic activity in these patients, resulting in improved bowel movement in weeks subsequent to the HyGleaCare procedure^{25,30,31}. Using our access to this population, we expect to have much information in our database as per the colonic microbiome aspects of chronic constipation, that can become an excellent base for collaborative research. Moreover the HyGleaCare prep has proved to be effective, safe and a well tolerated alternative to traditional prep for many patients^{18,23,31}, including for patients that often present failed colonoscopy preps. The latter can include patients with Irritable Bowel Syndrome (IBS), Inflammatory Bowel Disease (IBD), Crohn's disease, chronic

constipation, Celiac, Ulcerative Colitis, carcinoma of the rectum, dementia, diabetes, and patients with motility issues (data derived from an internal study to be published, n>1,500). By providing a nation-wide infrastructure of centers in which such patients can undergo colonoscopy prep, our database will include the most valuable information from these patients. The accessibility of HyGleaCare to patients and the ease of the colon irrigation procedure, can enable not only the microbiome profiling of many diseases but also tracking diseases progression and performing longitude studies without the need for invasive, complicated and expensive procedures. We strongly believe that the combination of HyGleaCare's unique approach with HygiBiome's scientific infrastructure will be a real game changer as it comes to future drug and therapeutic developments.

Stool banking services are now becoming a common practice^{52,53}. Fecal Microbiota Transplantation (FMT) is a process in which a donor stool is directly infused into a recipients' gastrointestinal tract to remedy and reconstruct the colon's microbiome⁵⁴. While the FDA approved FMT as procedure for treating recurrent, life-threatening, *Clostridium difficile* infections^{7,55-59}, FMT holds a myriad of challenges and the prospective of its medical use are controversial⁶⁰. In contrast, autologous Fecal Microbiota Transplantation (auto-FMT, or aFMT) is gaining attention as a way to safely reconstruct dysbiotic colon⁶¹⁻⁶⁵. Auto-FMT is predicted to allow patients to regain their health without the risks involved with introducing donor stool. We envision that HyGleaCare's patients undergoing their routine colon irrigation procedure, could choose to have their fresh, *de novo*, stool collected during this process. In this way, HyGleaCare® centers will be the place where the stool will be collected, and forwarded for testing, archiving data, and storing of the samples by trained personnel using validated and standardized protocols. As disclosed in our USPTO granted patent²⁶, we envision that the US-wide HyGleaCare's centers network will become a platform for performing infusion of auto-FMT. Additional infusions covered by this patent include FMT^{66,67}, probiotics infusion,

infusion of future chemical drugs, and combinations of phages therapies targeting distinct receptors or pathogens^{3,68}.

HygiBiome is ready to become a powerful platform for further innovations and growth in the microbiome discipline. Using our noninvasively collected samples and database, we will provide unique access to data that can be used in collaborative research with our partners. With the increase in drug development costs, an analysis of an optimal sample provided by HygiBiome can represent the microbial and biochemical content of the colon lumen and is expected to reduce the cost of drug development by lowering required screening affords. Moreover, with our access to screening population, our database will store information related to many common diseases. We postulate that such a database can be a turning point in future medical and other health related cutting-edge studies. Currently, we are establishing several scientific collaborations and launching our patented infrastructure to promote development and implementation of novel solutions for wellness and nutrition, diagnosis, therapeutics, personalized medicine and drug development.

To hear more about the HygiBiome™ platform, please contact us at HygiBiome@hygieacare.com.

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