Blastocystis Subtyping

Over the last several years, Genova has made great effort to continually reinvent how to approach gastrointestinal and nutritional evaluation from the perspective of personalized medicine. Genova's corporate values include growth and learning which translate into a desire to contribute to the evolution of our scientific and clinical perspectives in healthcare. With this aim, we have added novel biomarkers, unique analysis, and advanced interpretation to our laboratory evaluations. One such addition to our suite of stool profiles was the analysis of *Blastocystis* subtyping performed by next-gen DNA sequencing.

At the point in which Genova launched our ***Blastocystis* subtyping**, this evaluation was only available for research purposes. Genova was the first commercial lab to offer reflexive subtyping at no additional cost to patients or clinicians. This was done to investigate the clinical relevance of subtypes 1-9 to our vast population of patients while enhancing clinicians' awareness of the clinical conversation around these subtypes.

Over the past 18 months since launching *Blastocystis* subtyping, Genova has periodically conducted analyses of the peer-reviewed literature as well as our own internal data related to *Blastocystis* subtypes. Details of this analysis are summarized below.

The **Genova Diagnostics Statistical Science Group** conducted analysis of more than 125,000 patients' **GI Effects Profile** results to determine the detection frequency of each of the nine *Blastocystis* subtypes and to discern any evidence for statistically significant relationships between 76 analytes measured on the panel and the incidence of positive results for each subtype test. A Bayesian model selection procedure was employed to determine optimal candidate models for predicting the presence of each *Blastocystis* subtype. The purpose of this analysis was to determine whether particular subtypes demonstrate any discernable clinical or functional pattern within the test results (such as an inflammatory pattern, a microbiome shift, or an immune response, etc).

Interestingly, we were able to corroborate the peer-reviewed literature around the frequencies of subtypes, including that subtype 3 is the most common subtype residing in human microbiomes. However, we were unable to confirm any broad relationships between specific subtypes and non-*Blastocystis* report data. Though a number of statistically significant regressors were identified, the overall degrees of goodness-of-fit our models exhibited were quite modest for all subtypes. This indicates that the clinical utility of segregating *Blastocystis* subtypes is still uncertain and not yet associated with any actionable GI pattern.

The peer-reviewed literature surrounding the utility of *Blastocystis* subtypes for treatment selection also remains inconclusive to date, and human intervention studies are very limited. Owing to these developments, ***Genova has decided to pause Blastocystis reflex subtyping until further evidence of its clinical value can be demonstrated.*** Genova will continue to investigate the relationship between subtypes and both clinical symptoms and biomarker data to improve our scientific understanding of the role these subtypes play in potential disease development.

Genova remains committed to providing reliable laboratory data that is clinically useful and scientifically sound. We are also committed to contributing to the growing body of clinical knowledge, even when the discoveries are unexpected or are inconclusive. One of the goals of any laboratory evaluation resides in the power to inform clinical decisions and improve outcomes. With this, Genova will be continuing to focus its exploration of other factors contributing to the root causes of disease while conducting ongoing analysis to evaluate whether *Blastocystis* subtyping has the capacity to direct patient care more effectively.