BITS :: Call for Abstracts 2024 - Oral communication

Type	Oral communication
Session	Young BITS-RSG Symposium
Title	A comprehensive analysis of metagenomic data in subjects with Multiple Sclerosis
All Authors	Tortarolo D(1), Contaldo SG(1), Aucello R(1), Pantini F(1), Pernice S(1), Volpatto D(1,2), Sirovich R(2), Bosio L(1), Rolla S(3), Maglione A(3), Ferrocino I(4), Rosso R(3), Clerico M(3), Varese GC(5), Beccuti M(1) and Cordero F(1)

Affiliation

(1) Department of Computer Science, University of Turin, Turin
(2) Department of Mathematics "Giuseppe Peano", University of Turin, Turin
(3) Department of Clinical and Biological Sciences, University of Turin, Turin
(4) Department of Agricultural, Forestry and Food Sciences, University of Turin, Turin
(5) Department of Life Sciences and Systems Biology, University of Turin, Turin

Motivation

The human gastrointestinal tract is a habitat for a diverse array of commensal and mutualistic microbes, collectively called the gut microbiota. There is growing speculation regarding the involvement of the gut microbiota in developing neurological diseases[1]. It is hypothesized that dysbiosis in the gut microbiota could trigger pro-inflammatory responses in the gut and the periphery. Consequently, altered gut microbiota is a potential additional mechanism underlying multiple sclerosis (MS) and other related diseases. Previous studies have revealed the presence of gut microbial dysbiosis at the onset of MS, characterized by alterations in the number of microbial taxa and their functions. Specifically, a decreased abundance in taxa involved in producing short-chain fatty acids and the induction of Tregs was observed. These findings emphasize the significance of gut microbiota in its involvement in host immune system dysregulation.

Methods

In the context of SUS-MIRRI.IT project (www.sus-mirri.it), funded by the Italian government under the NextGeneration EU-funded Recovery and Resilience National Plan (PNRR), we developed a workflow to analyze metagenome data. The workflow is implemented in a Collaborative Working Environment (CWE) platform on High-Performance Computing (HPC) infrastructure. The platform is hosted on the open-access High-Performance Computing for Artificial Intelligence (HPC4AI) laboratory (https://hpc4ai.unito.it), providing cloud and HPC systems for AI applications. The metagenome workflow is divided into three steps: pre-processing, core, and post-processing. The pre-processing step is devoted to analyzing and visualizing the meta-data of the samples to obtain an overview of the sample distribution over the relevant features collected in the experimental context (i.e., age, sex, body mass index, etc). The core step is to check the quality of the input FASTQ files. Then, decontamination is performed to discard all reads unrelated to the microbiome. Lastly, we used state-of-the-art algorithms like Kraken2 [2] and Metaphlan4 [3] for taxonomic classification. Finally, a highly curated post-processing analysis that includes sample normalization, decontamination, prevalence filter, abundance estimation, and calculation of diversity measures; identification of biomarker species explaining the effect differentiating the phenotype of interest; classification of microbial species as human-associated or not and which body site of origin, based on an NLP-based, literature-mining module, and metadata exploratory analysis and regression model computation.

Results

The metagenome workflow is applied to study the gut microbiota composition in subjects with MS. The cohort comprises 18 healthy subjects and 79 MS patients, all clinically evaluated. The anamnestic characteristics, diet, and lifestyle habits were collected for all subjects involved in the study. The stool samples were collected before any treatment. DNA was extracted from stool samples, and shotgun metagenomic sequencing was performed.
No significant differences in sex, age, BMI, or smoking habit distribution were observed in the pre-processing step. The reads were aligned with the BWA algorithm against the human genome (hg38 and CHM13) for host contaminant removal in the core step. Taxonomic classification was performed with Kraken2 against bacterial NCBI databases. In the post-processing step, the contaminants species are removed based on a prevalence value of less than 5% No significant differences in alpha diversity nor distinct groups in beta diversity representation were evident over the features considered.
The Linear discriminant analysis of effect size (LEfSe) [4] method highlighted bacterial taxa that might perform as biomarkers for a defined clinical feature. Subjects with MS showed a bacterial ecosystem characterized by an increased relative abundance of Clostridia and Streptococcaceae. On the contrary, healthy subjects were enriched in Oscillospiraceae (Faecalibacterium prausnitzii) and Rikenellaceae. Our results confirm a dysbiosis of gut microbiota between healthy and MS subjects. Clinical, dietary, and lifestyle characteristics will be further analyzed to identify any clinical implications for microbiota alteration. Moreover, we will explore the metagenome data of the Eukaryota, Virus, and Archea kingdoms over the MS subjects to define a core microbiome.

Info

[1] Cryan JF, O’Riordan KJ, Sandhu K, Peterson V, Dinan TG. The gut microbiome in neurological disorders. Lancet Neurol. 2020;19:179–194. doi: 10.1016/S1474-4422(19)30356-4

[2] Wood, Derrick & Lu, Jennifer & Langmead, Ben. (2019). Improved metagenomic analysis with Kraken 2. Genome Biology. 20. 10.1186/s13059-019-1891-0.

[3] Blanco-Míguez, Aitor & Beghini, Francesco & Cumbo, Fabio & McIver, Lauren & Thompson, Kelsey & Zolfo, Moreno & Manghi, Paolo & Dubois, Leonard & Huang, Kun & Thomas, Andrew & Nickols, William & Piccinno, Gianmarco & Piperni, Elisa & Punčochář, Michal & Valles-Colomer, Mireia & Tett, Adrian & Giordano, Francesca & Wolf, Jonathan & Segata, Nicola. (2023). Extending and improving metagenomic taxonomic profiling with uncharacterized species using MetaPhlAn 4. Nature Biotechnology. 41. 1-12. 10.1038/s41587-023-01688-w.

[4] Segata, Nicola & Izard, Jacques & Waldron, Levi & Gevers, Dirk & Miropolsky, Larisa & Garrett, Wendy & Huttenhower, Curtis. (2011). Metagenomic Biomarker Discovery and Explanation.. Genome biology. 12. R60. 10.1186/gb-2011-12-6-r60.

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Availability	-

Dissemination Material

Social

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Summary

Take a peek into the gut bacteria of people with Multiple Sclerosis! We're diving deep into the world of microorganisms like bacteria, viruses, and more, using a simple system on high-power computers. Let's uncover the secrets together! #MSResearch #MicrobiomeDiscovery

Corresponding Author

Name, Surname	Riccardo, Aucello
Email	riccardo.aucello@unito.it

Submitted on	02.05.2024