

# The gut microbiota, a hallmark of human aging, could implicate risk and effect of COVID19 in the elderly

Natalia Molinero<sup>1</sup>; Cristina Jiménez Arroyo<sup>1</sup>; Diego Taladrí<sup>1</sup>; Elena Campos Sánchez<sup>2</sup>; Andrea Canto Méndez<sup>2</sup>; Beatriz Tejedor<sup>2</sup>; Ignacio Ruiz Fernández<sup>2</sup>; Carlos Jiménez<sup>2</sup>; Manuel Ramos<sup>2</sup>; Luis Carlos Antón<sup>2</sup>; Margarita del Val<sup>2</sup>; Elena Povedano<sup>3</sup>; Sebastián Ruiz Santacruz<sup>3</sup>; Diego Ramiro<sup>3</sup>; Miriam Cobo<sup>4</sup>; Fernando Aguilar<sup>4</sup>; Lara Lloret<sup>4</sup>; Benjamin Sanchez Rigau<sup>5</sup>; Anabel Álvarez Ciara<sup>5</sup>; Santiago Álvarez Rodríguez<sup>5</sup>; Glòria Guirado Carbó<sup>6</sup>; Glòria Castells Carles<sup>6</sup>; Carles Cristòfol Adell<sup>6</sup>; **M.Victoria Moreno-Arribas<sup>1</sup>**

**Background:** Branyas’ project aims to enrich and refine the predictive risk profiles of Covid-19, focusing on genetic, comorbidity, lifestyle, immunological and microbiome variables for which innovative bioinformatic and big data tools as well as powerful next generation sequencing technologies have been used. CIAL-CSIC researchers in this project attempted to deepen the compositional and functional profiles of the gut microbial communities of elderly nursing homes and search for potential microbial biomarkers capable of individually predicting COVID19 risk and prognosis in this community, its relationship with other factors and expand them to the entire population. A further objective is to study the trajectory of the human microbiome and prolonged symptoms over time and their association with cognitive and motor impairment in this vulnerable population.

**Methods:** Demographic, clinical, dietary, comorbidities and medication data, and biological samples (blood and stool) from 216 participants from different nursing homes in Catalunya were recruited during 2021. Forty-one participants dropped out for different reasons, and finally the study enrolled 175 participants, 73 had followed-up engagement for 3 months to observe possible changes in their gut microbiomes. Fecal samples (n=280) were obtained and stored under anaerobic conditions at -80°C until use. Fecal total DNA was extracted using an optimized protocol and shotgun sequencing analysis approach was performed to deepen the structural, compositional and functional microbial profiles present. Fecal short-chain fatty acids (SCFA) profiles were also assessed using Gas Chromatography with Flame-ionization Detection (GC/FID) as an indicator of the functionality of the microbiome.

**Results:** First comparisons with fecal SCFAs have suggested differences depending on participants’ grouping. The results showed slightly higher levels of acetic and propionic acids and total SCFAs in participants who did not suffer COVID19, suggesting a possible impairment in the production of these beneficial metabolites in those after COVID19 infection. Furthermore, by focusing on the severity of the symptoms of infected participants higher levels of acetic acid and total SCFAs in participants with mild/moderate symptoms compared to participants with severe symptoms were observed. However, analysis of SCFAs by grouping participants that suffer from Alzheimer’s disease or not did not show appreciable changes in SCFAs levels, but more variability in non-diseased participants was observed.

The taxonomic and functional profiles of the microbiome derived from shotgun sequencing analysis allowed assessment of the preliminary trends observed with SCFAs and find responsible microbial communities and functions. Furthermore, the compositional and functional characteristics will provide a global snapshot of the microbiome and possible changes depending on the conditions of the individuals, possibly showing biomarkers of COVID19 risk as well as determining which populations and functions could be involved in these relationships.

**Conclusions:** Analysis of the gut microbiome in the Branyas project allows deeper investigation into potential microbial biomarkers of COVID19 risk and their relationship with a range of other immunological, lifestyle and genetic variables. In addition, the integrated study of microbiome functionality through metabolomics and lipidomics will identify requirements of the elderly vulnerable population giving more effective strategies in the prevention and treatment of pathologies associated with immune and cognitive function.

<sup>1</sup> Instituto de Investigación en Ciencias de la Alimentación (CIAL), CSIC-UAM

CSIC-UCJ

<sup>2</sup> Centro de Biología Molecular Severo Ochoa (CBMSO), CSIC-UAM

<sup>5</sup> Farmacia de Dalt

<sup>3</sup> Instituto de Economía, Geografía y Demografía (IEGD-CSIC)

<sup>6</sup> Universitat Autònoma de Barcelona

<sup>4</sup> Instituto de Física de Cantabria (IFCA,