Metaproteomics as a key approach to identify impacts of High Fat (HiF) diet on the gut microbiome

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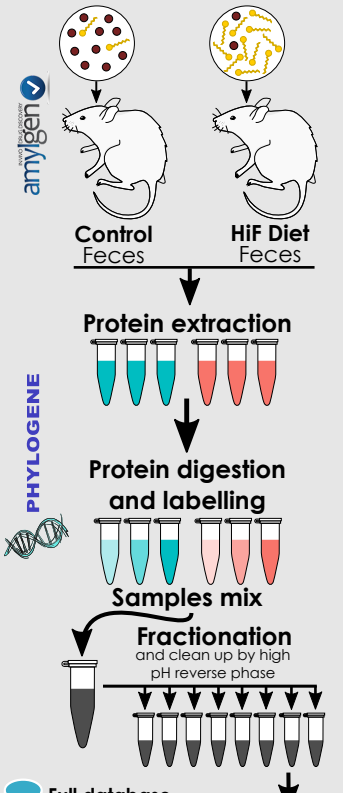
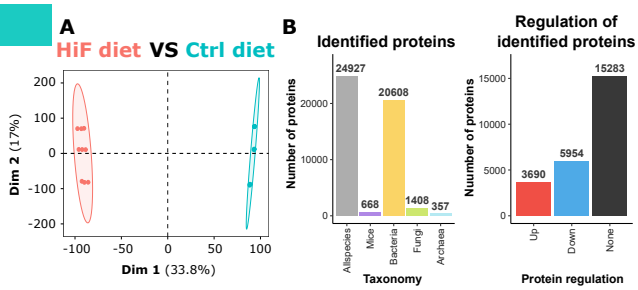
ABSTRACT

The gut microbiome is a vast and complex ecosystem playing a pivotal role primarily in digestive functions and in global health. Often referenced as the forgotten organ, the microbiome is involved in a plethora of essential biological mechanisms such as metabolism, defenses against pathogens and has recently been implicated in a broad range of disorders, from inflammatory bowel disease to autism. Our increasing knowledge in the gut microbiome and its importance is largely attributed to studies based on the 16S ribosomal RNA (16S) identification for bacteria profiling and metagenomic WGS analysis. However these approaches remain limited and incomplete to explain the full extent of microbiota-host interactions and the understanding of mechanisms of actions. Although modern mass spectrometry-based metaproteomics has been described in literature to be a powerful tool to assess and measure both of the host and microbiota proteins as well as posttranslational modifications, its capabilities are still underexploited. In this study, we addressed the effects of a HiF diet on the microbiome on mouse model by the analysis of feces. A major outcome of this study was an important decrease of the alpha diversity and an alteration of GABA balance.



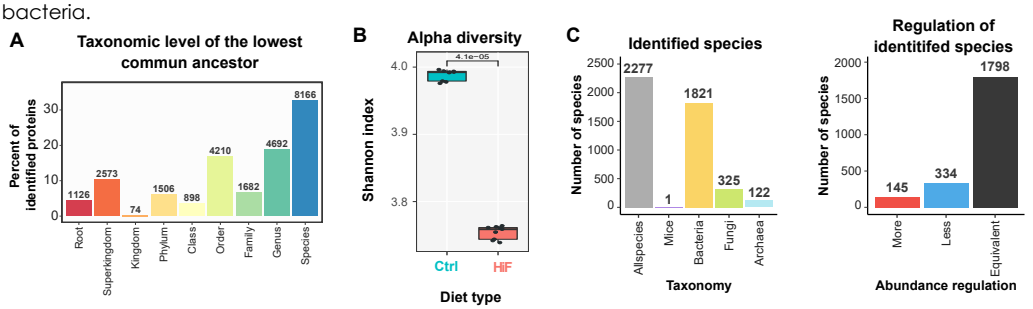
METAPROTEOMIC

Proteins were analyzed by mass spectrometry and identified by Proteome Discoverer 2.1. Proteins considered as significantly differentially expressed (limma, Ritchie et al., 2015) are proteins with an adjusted p-value < 0.05 and absolute value of Fold Change Log2 > 0.5.



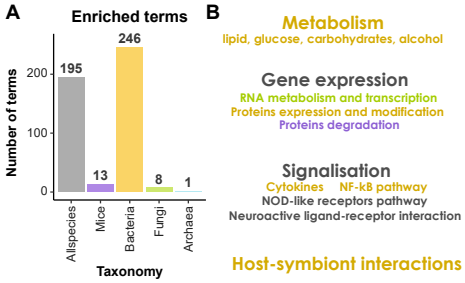
TAXONOMIC ANALYSIS

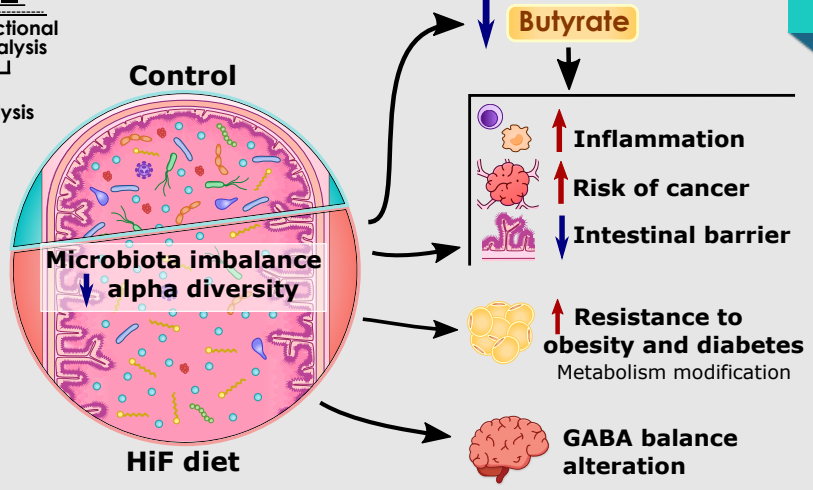
Peptides and proteins taxonomy was assigned by Unipept tool (Gurdeep Singh et al., 2019). Differentially abundant species are identified by the median of fold change and p-value for associated proteins. Key species are identified by this method, including more abundant related to resistance to obesity bacteria, less abundant butyrate-producing or inflammation-related species or imbalance of GABA-modulating bacteria.



FUNCTIONAL ANALYSIS

Proteins sequences were submitted to EggNOG mapper (Huerta-Cepas et al., 2019, 2017) to associate each protein to its closest annotated orthologue which will be used for functionnal analysis. Functional terms used for annotation are GO terms, COG category, COG and KOG terms and KEGG pathways, reactions and modules. Differentially expressed proteins were compared to the reference dataset composed by all annotated proteins by a modified Exact Fisher test (Huang et al., 2009a, 2009b).





Conclusion

Taken together, combination of differentially abundant species and the impacted biological processes lay out increases in inflammation processes, risk of cancer and intestinal barrier disruption through alteration of inflammation-modulating and butyrate-producing species. These results also suggest alterations on the "gut-brain axis" with, GABA-modulating bacteria imbalance and related function modifications. Finally, the results show profound metabolism modifications as well as mechanisms related to resistance to obesity and diabetes due to increase of key bacteria species in HFD mice.

PHYLOGENE
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