SHOTGUN METAGENOMIC PROFILING OF GUT MICROBIOTA CHANGES IN A MOUSE MODEL OF ALZHEIMER'S DISEASE

Dason M.S. [a, *], Favero F. [b, *]; Gravina T. [b]; Gagliardi M. [c]; Mellai M. [c]; Re A. [a, #]; Corazzari M.[c, #]; Corà D. [b, #].

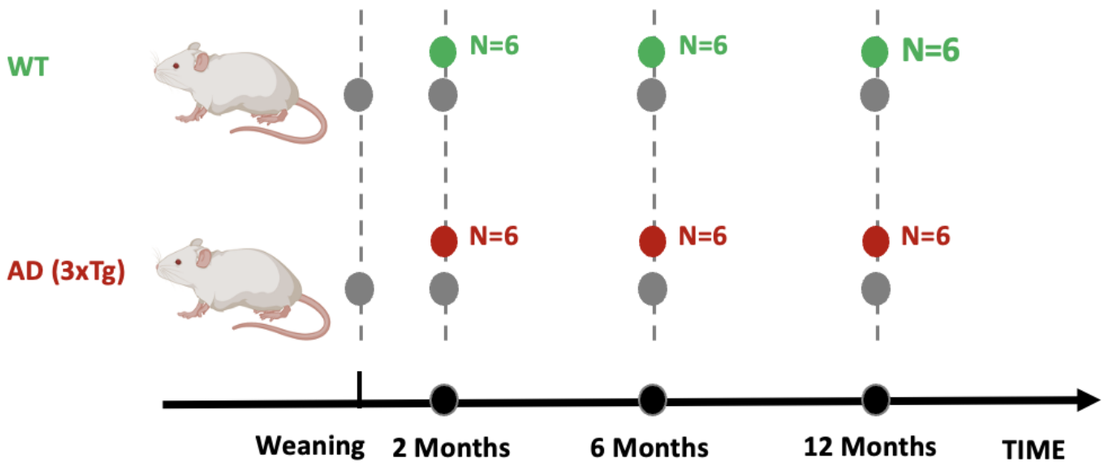
[a] *Politecnico di Torino, Department of Applied Science and Technology, C.so Duca degli Abruzzi, 24, 10129 Torino, Italy;*
[b] *Università del Piemonte Orientale, Department of Translational Medicine and Translational Research Centre for Autoimmune and Allergic Disease (CAAD), C.so Trieste, 15/A - 28100 Novara;*
[c] *Università del Piemonte Orientale, Department of Health Science, and Translational Research Centre for Autoimmune and Allergic Disease (CAAD)), C.so Trieste, 15/A - 28100 Novara.*
** = co-first authors*
 # = co-last authors

SUMMARY

Alzheimer's disease (AD) is a progressive neurodegenerative disease and the leading cause of dementia worldwide, with age constituting the strongest risk factor. Emerging evidence suggests an association between the gut microbiota and the progression of neurodegenerative diseases, including AD via the two-way biochemical-signaling pathway known as the gut-brain axis.

In this present study, we propose a computational shotgun metagenomics reconstruction data pipeline to investigate age-related changes in the gut microbiome of Wild Type (WT) and transgenic 3xTgAD Alzheimer's disease mouse models at 2 months (T = 1), 6 months (T = 2) and 12 months (T = 3) of age. The aim of our study is to deepen, via an ab-initio shotgun approach, the role of the modulation of the gut at different temporal stages of the disease and its potential impact on disease progression.

STUDY DESIGN



= samples for which we have 16S data and published results (Favero et al., 2022)

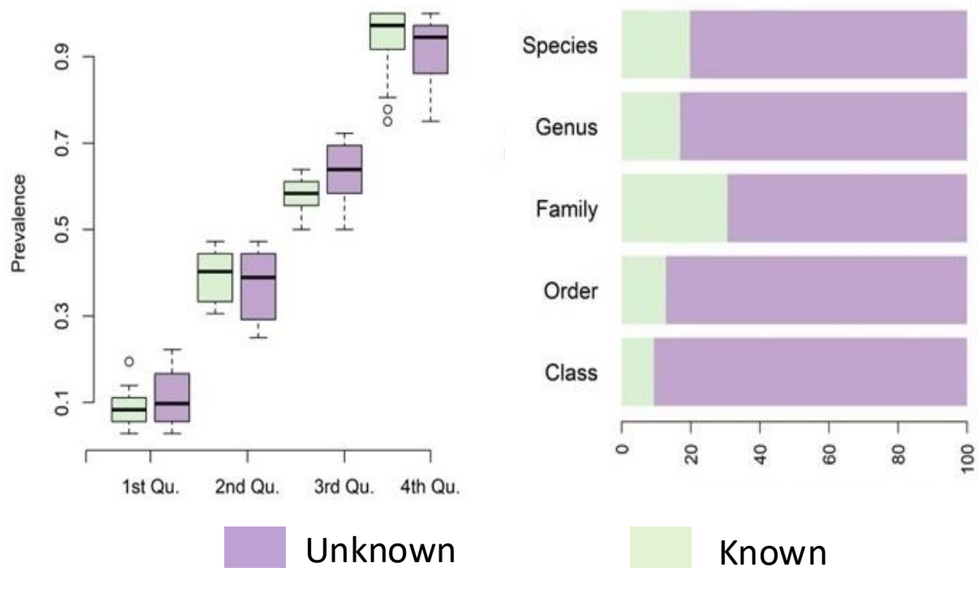
= samples for which we have unpublished shotgun sequencing data, WT mice

= samples for which we have unpublished shotgun sequencing data, AD mice

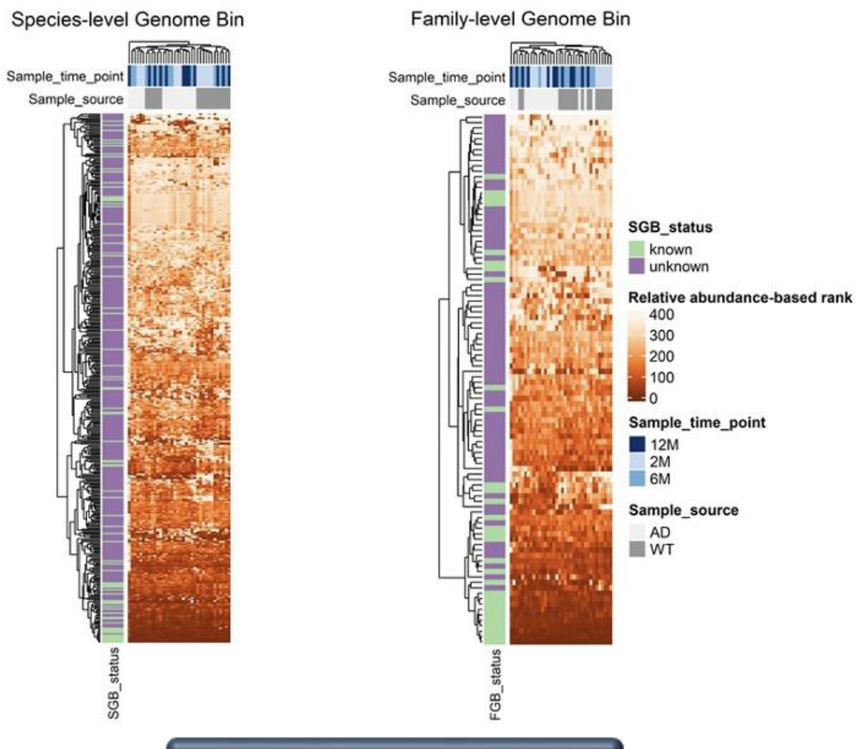
RESULTS

(A) Fraction of taxonomically known and unknown bacterial genomes detected in our dataset.

9 Phyla , 75 Classes, 78 Orders , 98 Families , 301 Genera, 385 Species



(B) Heatmap showing the relative abundance of Species and Families in all the samples in the dataset.



DISCUSSION

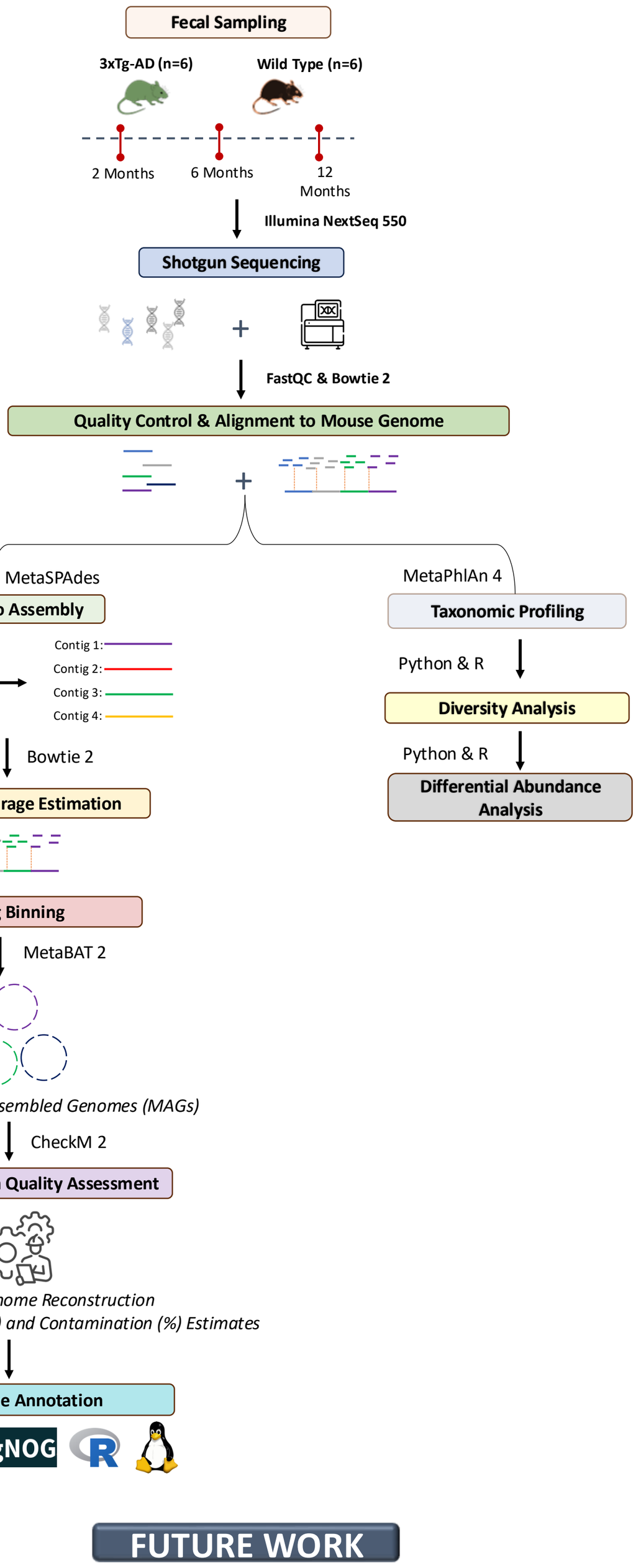
- In our analysis, we observed a distinct variability in microbial species composition between the Alzheimer's disease (AD) group and control groups. More generally, each time point was seemingly associated with distinct changes in microbiome composition. This observation supports our hypothesis of the difference in gut microbiota composition between AD and healthy states.

- A great majority of the bacterial species we identified in our analysis were unknown species, therefore warranting further investigation.

REFERENCES

(1) Pasolli, E. et al. Cell (2019). **(2)** Favero, F. et al. PLOS One (2022). **(3)** Lu, Y. et al. (2023). **(4)** Oddo, S. et al. (2003).

WORKFLOW



FUTURE WORK

- Proteomic Analysis of proteins for both known and unknown species to enable the functional characterization of their repertoire of proteins.

- Inclusion of multi-omics datasets and molecular approaches to comprehensively study gut microbiota dynamics and the corresponding effects on the host physiology as it pertains to Alzheimer's disease onset and progression.

ACKNOWLEDGEMENTS

Finanziato dall'Unione europea NextGenerationEU
Ministero dell'Università e della Ricerca
Politecnico di Torino
UPO Università del Piemonte Orientale

Supported by NextGeneration EU PRIN 2022 PNRR Prot. P2022AFS8P