

Understanding psychobiome and its pathogenic properties associated to Parkinson's disease

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Background

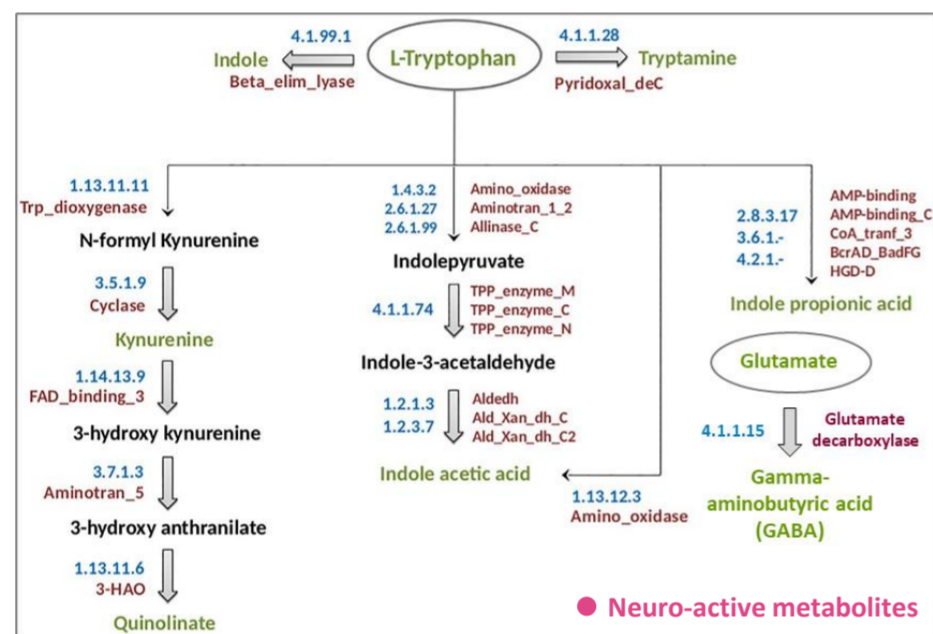
- Prevalence of Parkinson's disease (PD) has doubled in past 25 years with global estimates of over 8.5 million individuals having PD in 2019 (WHO's technical brief, 2022) [1]
- Role of 'gut microbiome' in regulating neurophysiology through 'Gut-brain-axis (GBA)' is being increasingly acknowledged [2,3]
- Understanding the possible association between gut microbiome's 'neuro-active functional potential' and PD etiology would be intriguing

Objective

- Studying functional potential for 'neuro-active metabolite production' of Parkinson's disease microbiome
- Analyzing the correlation of microbial 'neuro-active metabolite production' capabilities with Parkinson's disease etiology

Methods

Collation of microbial metabolic functions from literature implicated to influence gut-brain axis



Exhaustive analysis of completely sequenced gut bacterial genomes



Construction of a knowledgebase of gut bacteria predicted to have metabolic potential for production of 'neuro-active' metabolites



Utilizing the knowledgebase to identify altered 'neuro-active metabolic function' in PD patients (using publicly available gut microbiome data)

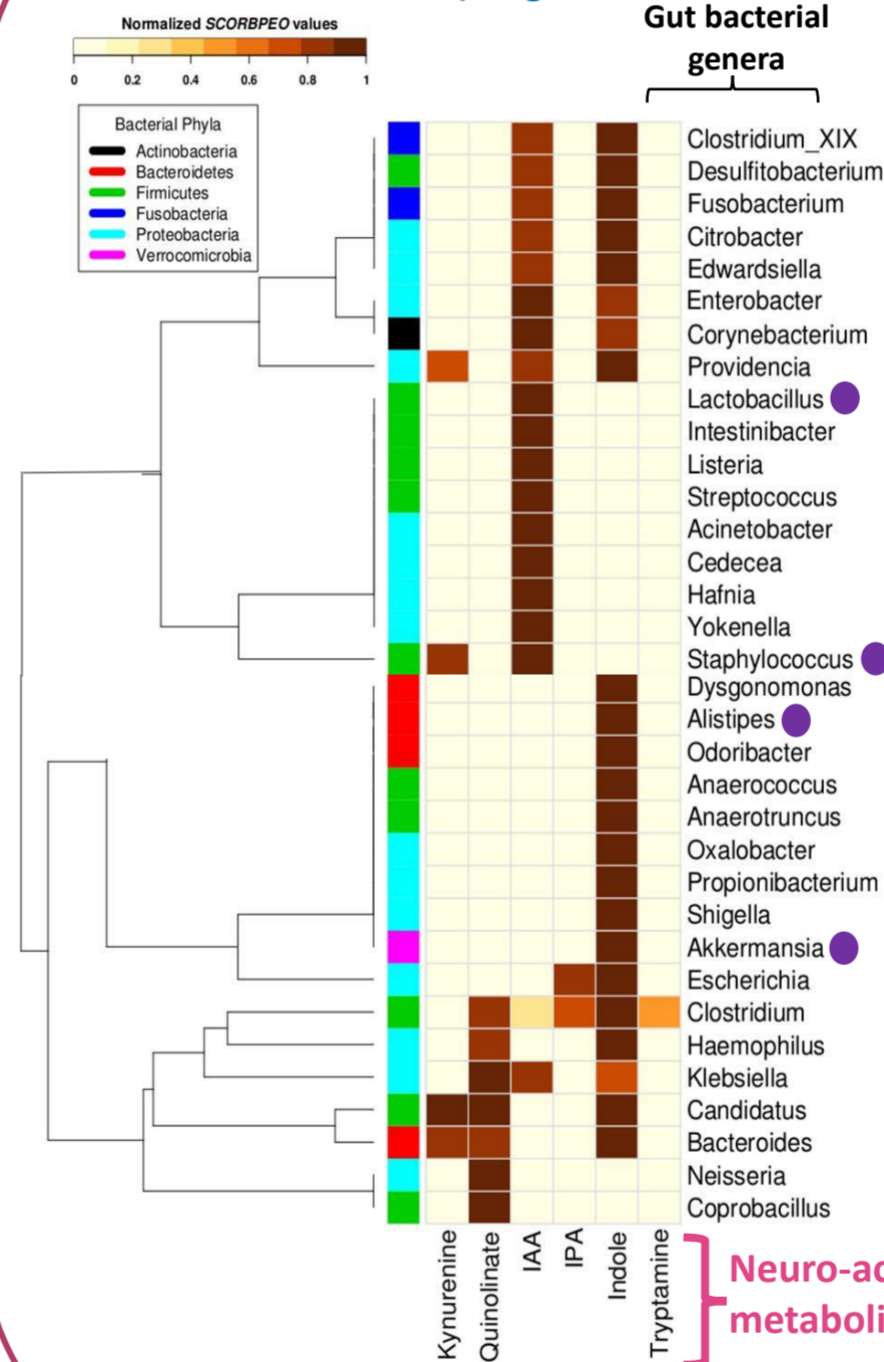
Building model based on 'neuro-active metabolic functional parameters' for assessing disease risk (Parkinson's disease)

References

- <https://www.who.int/news/item/14-06-2022-launch-of-who-s-parkinson-disease-technical-brief> (accessed on 04-03-2023)
- Liu L et al. *eBioMedicine* (2022)
- Carabotti M et al. *Ann Gastroenterol* (2015)

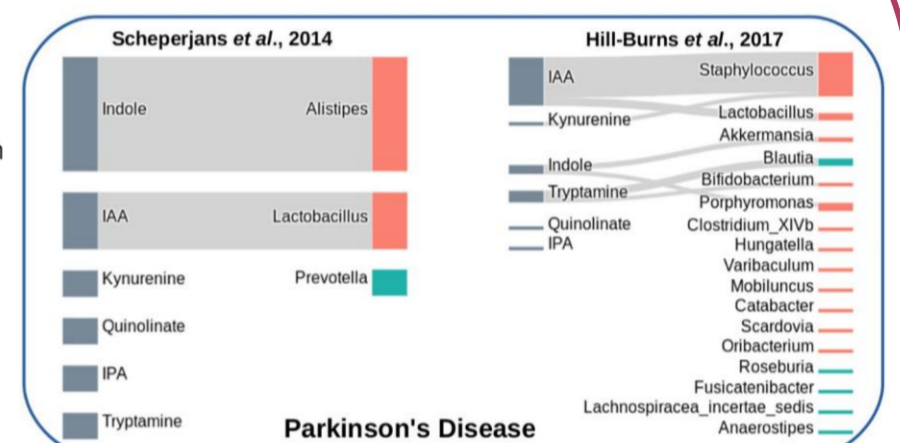
Results

Prediction of 'neuro-active metabolite production pathways' (via tryptophan metabolism) in gut bacteria



Relatively Abundant genera in Parkinson's disease

'Neuro-active metabolite production pathways' in PD microbiome



The model could assess the disease state (PD) with significant accuracy

Data used for model building and validation

Study	Sample type	Data type	Cohort size
Scheperjans et al. 2015	Stool sample	16S rRNA sequence read	PD patients: 74 healthy individuals: 74

Model performance

Primary predictive features	Train accuracy	Train AUC	Test accuracy	Test AUC
GABA, Indole	70.58	75.37	70.02	74.007

Key insights

- Possible involvement of bacterial taxa *Akkermansia*, *Alistipes*, *Lactobacillus*, *Staphylococcus* etc. in the etiology of Parkinson's disease through affecting tryptophan and glutamate metabolism
- The model built on metabolic insights (including indole & GABA production capabilities as primary predictive parameters), could assess the diseased state (PD) with significant accuracy.

Significance

- The insights suggest critical role of '*Lactobacillus*' in regulation of neurophysiology through GABAergic system, in addition to much known probiotic properties like immune/metabolism regulation in gut
- The psychobiome regulating indole and GABA producing pathways can potentially be leveraged towards improving 'care, risk-assessment and therapeutic' regimes of Parkinson's disease