Research Study

Probiotic *Bacillus subtilis* PXN® 21® protects against α-synuclein aggregation in *C. elegans*

This paper, published in *Cell Reports* in January 2020, explores how a spore forming bacteria can slow or even reverse the accumulation of one of the major proteins associated with Parkinson's disease, using a well-researched nematode model.[1]

The Background:

Parkinson's disease (PD) is the second most common neurodegenerative disorder globally, after Alzheimer's disease. Around 10 million people worldwide are diagnosed with PD. The main symptoms are tremor, rigidity and bradykinesia (an abnormal slowness of movement), and many people with PD will also experience cognitive impairment.

Introduction:

α-synuclein is a protein which is abundant in the human brain. In Parkinson's disease, the α-synuclein protein misfolds, forming a toxic clump or aggregate. We do not know exactly what causes the protein to misfold and clump together but these misfolded proteins are important in the development of PD.

Parkinson's disease currently cannot be cured, but certain medications can improve symptoms. α-synuclein has now become a major target for potential PD therapies. Recent studies focus on reducing α-synuclein gene expression or promoting its removal/recycling in the hope that this may stop - and potentially reverse - the damage these deposits have caused to the brain.

Recent evidence:

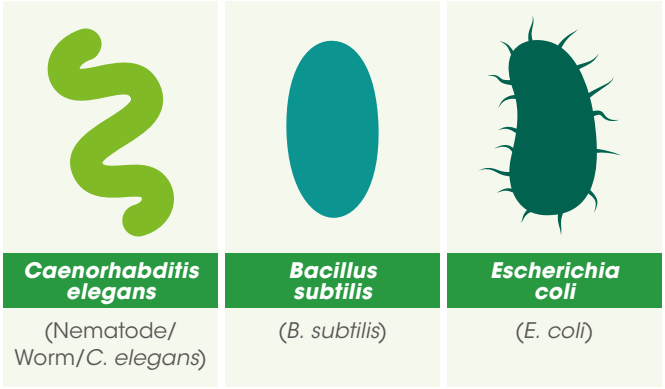
Recently, the human gut microbiome has emerged as a potentially important player in PD.[2] The GI microbiome of patients with PD was found to be notably different to healthy controls, with increases noted in *Akkermansia* and decreases in *Prevotellaceae* species.[3] Interestingly differences in GI microbiome analysis correlated with clinical features of PD.

It is now well-documented that gut bacteria can modulate disease outcomes in distant organs, including a variety of neuropsychiatric disorders, such as anxiety, depression, bipolar affective disorder and migraine.[4]

Faecal transplants from patients with PD have been shown to aggravate Parkinson's symptoms in mouse models of PD, indicating that differences in the microbiota are not just a result of the disease, but also impact on its progression.[5]

The Study:

The protagonists:



Caenorhabditis elegans	***Bacillus subtilis***	***Escherichia coli***
(Nematode/ Worm/*C. elegans*)	(*B. subtilis*)	(*E. coli*)

The human microbiota is composed of trillions of microorganisms, posing a challenge for understanding the effects of individual species and strains.[6] However, bacterial-feeding nematodes - like *Caenorhabditis elegans* - offer the ability to recreate many aspects of human physiology and generate key insights into human disease processes.

To assess the effect of gut bacteria on α-synuclein aggregation, the research team in Edinburgh and Dundee Universities used a well-established *C. elegans* model for Parkinson's disease (strain NL5901) that expresses human α-synuclein.

The worms were fed with different bacterial diets: *E. Coli* (normal lab diet for *C. elegans*), *B. subtilis* PXN® 21® (ADM Protexin Ltd.) or a combination of both bacteria and were assessed for α-synuclein aggregation at different stages.

The Results:

C. elegans fed with *E. coli* accumulated α-synuclein aggregates very early in development. In contrast, *C. elegans* fed with *B. subtilis* showed almost no α-synuclein aggregation from larval stage through to early adulthood (Figure 1).

Worms that were fed E. coli during larval stage (the early development phase of *C. elegans*) saw significant reductions of α-synuclein aggregates when they were switched to a *B. subtilis* diet.

B. Subtilis also improved locomotion defects associated with the toxic clumps.

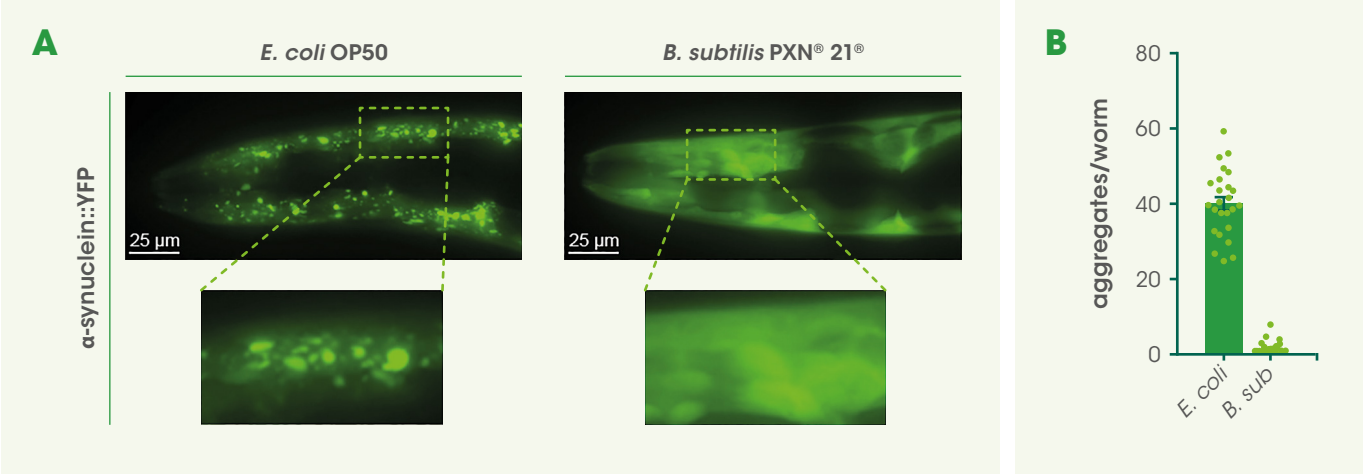


Figure 1: *B. subtilis* PXN® 21® inhibits and reverses α-synuclein aggregation in the *C. elegans* model NL5901

B. subtilis' mechanism of action:

B. subtilis is known to increase the lifespan and stress tolerance of *C. elegans*.[7-9] One of the mechanisms used by *B. subtilis* to exert these effects is to increase biofilm formation – this is a slimy matrix material that the bacteria produce and live within, like a community, enabling enhanced communication and nutrient sharing. Biofilm formation is associated with an increase in the secretion of nitric oxide (NO) and colony stimulating factor (CSF), two bacterial products essential to extend *C. elegans* longevity. Nitric oxide is also important in keeping α-synuclein aggregation levels low in *B. subtilis* fed nematodes.

Studies have shown that disturbances in the metabolism of certain fats (sphingolipids) have been linked to α-synuclein aggregation in PD. This study shows that *B. subtilis* up-regulates lipid metabolism pathways, reducing α-synuclein aggregation.

Conclusion:

B. subtilis PXN® 21®, a probiotic strain that is available for human consumption, inhibits aggregation and efficiently removes pre-formed aggregates in a *C. elegans* model expressing human α-synuclein.

The bacterium imparts its protective effect on α-synuclein through the alteration of multiple protective pathways in the host, including biofilm formation and sphingolipid metabolism.

These findings provide a strong basis for exploring the potential of *B. subtilis* PXN® 21® in human clinical trials.

B. subtilis inhibits and reverses α-synuclein aggregation in a _C. elegans_ model of synucleinopathy/ Parkinson's disease. _B. subtilis_ protection is effective throughout _C. elegans_ aging.

***Bacillus subtlis* PXN® 21® is a commercial bacteria strain and is used within the Bio-Kult live bacteria range. It can be found in Bio-Kult Advanced, Bio-Kult Migréa and Bio-Kult Mind.**

References:

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